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14. ABSTRACT

Age-related changes in memory function are not uniform even in the absence of dementia and contributing factors are unclear. Characterization of non-disease associated cognitive changes is crucial to gain a more complete understanding of brain aging.
Episodic memory was investigated in 13,979 ethnically diverse elderly (ages 72 to 85 years) with two to 15 years of follow-up, and with known dementia status, age, education and APOE genotypes at baseline. Adjusted trajectories of episodic memory performance over time were estimated using Latent Class Mixed Models. We also calculated the age-specific annual incidence rates of dementia in the non-demented elderly (n=10,659).
Two major episodic memory trajectories were estimated within each of the study groups: 1) Stables - consisting of individuals exhibiting a constant or improved memory function over time and 2) Decliners - consisting of individuals with a decline in memory performance over time. Compared with the individuals in the Stable trajectory, Decliners were more likely women, older, less educated, from non-White ancestry population and APOE-ε4 carriers. The highest annual incident rates of dementia were observed in the oldest age group (85 years old), among those of Caribbean-Hispanics ancestry and among Decliners who exhibited rates of incident dementia five times higher than those with Stable trajectories (rates= 15 per 100 person per year versus 3 per 100 person-per year).
Episodic memory can be preserved over time among elderly regardless of ethnic group. Age, gender, education and APOE genotype influence the maintenance of episodic memory over time. Declining memory over time is one of the strongest predictors of incident dementia.

15. SUBJECT TERMS
NONE LISTED

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1. INTRODUCTION

There is a significant deficit in the literature investigating the possible association between traumatic brain injury (TBI) and increased susceptibility to develop late onset Alzheimer's Disease (LOAD) later in life. We hypothesize that traumatic brain injury interferes with aging process by accelerating individual's memory decline and possibly accelerating LOAD like neuro-degeneration. In addition, genetic risk factors including non-coding and highly penetrant coding variants may interact with exposure to TBI to modify risk of LOAD. We will first characterize trajectories of episodic memory change in subjects stratified by LOAD and TBI status using the longitudinal data from multiple cohorts including: The National Institute of Aging Late-Onset Alzheimer's Disease (NIA-LOAD) Family Study,, The National Alzheimer's Coordinating Center and Alzheimer's Disease Genetics Consortium (NACC-ADGC), The Religious Orders Study and Rush Memory and Aging Project Alzheimer's Disease Center cohorts (ROSMAP). , The Washington Heights-Inwood Columbia Aging Project (WHICAP) and The Chicago Health and Aging Project (CHAP). . The Latent Class Mixed Model (LCMM) was used to estimate adjusted trajectories of episodic memory performance over time. Longitudinal studies of cognitive function have consistently clustered subjects into two episodic memory trajectories (EMTs): Stable and Decliner. We will stratified the study's participants into four different groups based on their LOAD and TBI clinical status: Group 1 corresponding to subjects with TBI and LOAD, Group 2 corresponding to subjects with TBI but not LOAD, Group 3 corresponding to subjects with LOAD but not TBI and Group 4 corresponding to subjects without TBI and without LOAD. We hypothesize that episodic memory trajectories signatures will be different across the different groups. We anticipate that study participants within Group 4 (non-demented subjects without TBI) will show a sustained memory performance over time, while study participants within Group 1 (subjects with both TBI and LOAD) will exhibit the most prominent decline in episodic memory. We will test whether the interaction between genetic variants and TBI may modify the risk of LOAD using genome-wide SNP data. We will validate the nominally significant genes ($p<0.001$) in the extreme-phenotype sub-sample including Groups 1 and Group 4. Genes achieving statistical significance in their interaction effects with TBI , will be further follow-up using available whole exome sequencing data in WHICAP and NIA-LOAD cohorts to investigate whether rare genetic variants may underlie these signals.

2. KEYWORDS

Episodic memory trajectories (EMTs), longitudinal evaluations, late onset Alzheimer's Disease, Traumatic Brain Injury (TBI), dementia

3. ACCOMPLISHMENTS

- **What were the major goals of the project?**

The overall goals of the project were i) to identify trajectories of episodic memory performance using a longitudinal data from subjects with available clinical diagnosis of LOAD and TBI, and ii) to identify genes that interact with TBI and as consequence modify the risk of developing LOAD. Please see below our approved SOW for the project detailing the specific tasks for period of the grant proposal.

Tasks	YEAR 1				YEAR 2				YEAR 3			
	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4	Qtr 1	Qtr 2	Qtr 3	Qtr 4
SA1. To characterize trajectories of memory change in subjects stratified by AD and TBI status using the longitudinal data in 4,878 samples from the National Institute of Aging Late-Onset Alzheimer's Disease (NIA-LOAD) and Alzheimer's Disease Genetic Consortium (ADGC) cohorts.												
Task 1. Prepare and harmonize longitudinal phenotype data on memory performance from NIA-LOAD and ADGC cohorts												
a) Compute demographically adjusted z-scores of Logical Memory IA and IIA (sex,age and education adjusted)												
Task 2. Prepare and harmonize the NIA-LOAD and ADGC GWAS datasets												
a) Quality control of genome-wide genotype data in both ADGC and NIA-LOAD cohorts (missingness, HWE etc.)												
b) Quality control of sample level data in the two cohorts (relationship and sex checks, missingness, etc.)												
c) Joint imputation of the two datasets												
d) Joint Population substructure analyses of the two datasets												
Task 3: Implement GMM nested models to compute trajectories of memory decline in the joint NIA-LOAD and ADGC GWAS datasets												
SA2a. To identify genome-wide TBI-interacting genes that predict risk of AD using the non-stratified sample from the NIA-LOAD and ADGC cohorts.												
Task 1. Implement SREBIA on the NIA-LOAD and ADGC GWAS datasets												
Task 2. Implement special cases on the SREBIA algorithm (case-online and enhanced version)												
Task 3. Explore novel set based GxE gene-based methods to be applied on genome-wide data												
SA2b. To assess nominally significant TBI-interacting genes identified in SA2a in the stratified sample from the NIA-LOAD and ADGC cohorts.												
Task 1: To select the genes that are nominally significant at $P<10 \times 10^{-3}$ for TBI genotype interaction in predicting LOAD risk												

Task 2: Select the most homogenous sample of rapid decliners and stable plateaus (Group 1 and 4) as determined in Aim 1	
Task 3: Test TBI genotype interaction comparing rapid decliners and plateaus in nominally significant genes (SA2, Task1)	
SA2c.To validate the TBI-interacting genes identified in SA2b using independent cohorts with genome-wide SNP data available.	
Task 1. Prepare and harmonize longitudinal phenotype data on memory performance from RADC, CHAP and WHICAP	
Task 2. Prepare and harmonize the GWAS data from RADC, CHAP and WHICAP	
a) Quality control of genome-wide genotype data in the cohorts (missingness, HWE etc.)	
b) Quality control of sample level data in the cohorts (relationship and sex checks, missingness etc.)	
c) Joint imputation of the datasets	
d) Joint Population substructure analyses of the datasets	
Task 3. Validate the TBI interacting genes identified in SA2a and SA2b	
Task 4. Report results and evaluate potential manuscripts/conference presentations etc.	
SA3. To investigate whether rare coding variants in the loci identified in SA2 interact with TBI in predicting risk of AD	
Task 1. Prepare WES from WHICAP and NIA-LOAD	
a) Alignment, variant calling and subsequent to determine high quality variant calls	
b) Harmonize variant data in the two datasets depending on capture kits, depth of coverage etc.	
Task 2. Apply set based TBI genotype interaction analyses to determine genes with rare coding variants associated with LOAD in genes that were significant in SA2c	
Task 3. Conduct genotyping in samples without WES in both cohorts and re-assess TBI-genotype interaction in WES and genotype data	
Task 4. Explore other available WES datasets for replication	
Task 5. Report results and evaluate potential manuscripts/conference presentations etc.	

Task 6. Explore possible collaborations with groups with functional expertise (RNA-seq, cell-based methods etc.) to functionally characterize the genes and variants identified in Aims 1 through 3												

100% completed
In progress
Planned

What was accomplished under these goals?

- *Major activities, Specific objectives and significant results*

The major accomplishments under the described goals are as follows:
1. Augmentation of initially proposed sample size to derive episodic memory trajectories.
2. Implementation and optimization of latent class mix model method (LCMM) in a large and ethnically diverse sample.
3. Estimation of trajectories of episodic memory within TBI and LOAD stratified groups.
4. Evaluating different outcomes for its association with TBI: LOAD (dichotomous outcome) and episodic memory function (quantitative outcome).
5. Genomewide single variant and gene-based approaches to TBI*SNP interaction as predictor of LOAD risk.

1. Augmentation of initially proposed sample size. In our original proposal, we aimed to characterize trajectories of episodic memory over time change in a longitudinal sample of 4,878 participants from NIA-LOAD) and ADGC cohorts. To improve the reliability of the parameter estimates derived from the LCMM method in Aim1, we will include CHAP and ROSMAP as additional cohorts. The inclusion of additional cohorts will lead to a final sample of more than 9,000 subjects for whom will be deriving episodic memory trajectories stratified by LOAD and TBI status. All datasets for replication and validation have prepared for analysis and trajectories have been calculated. Gene-environment interactions using set-based methods are ongoing.

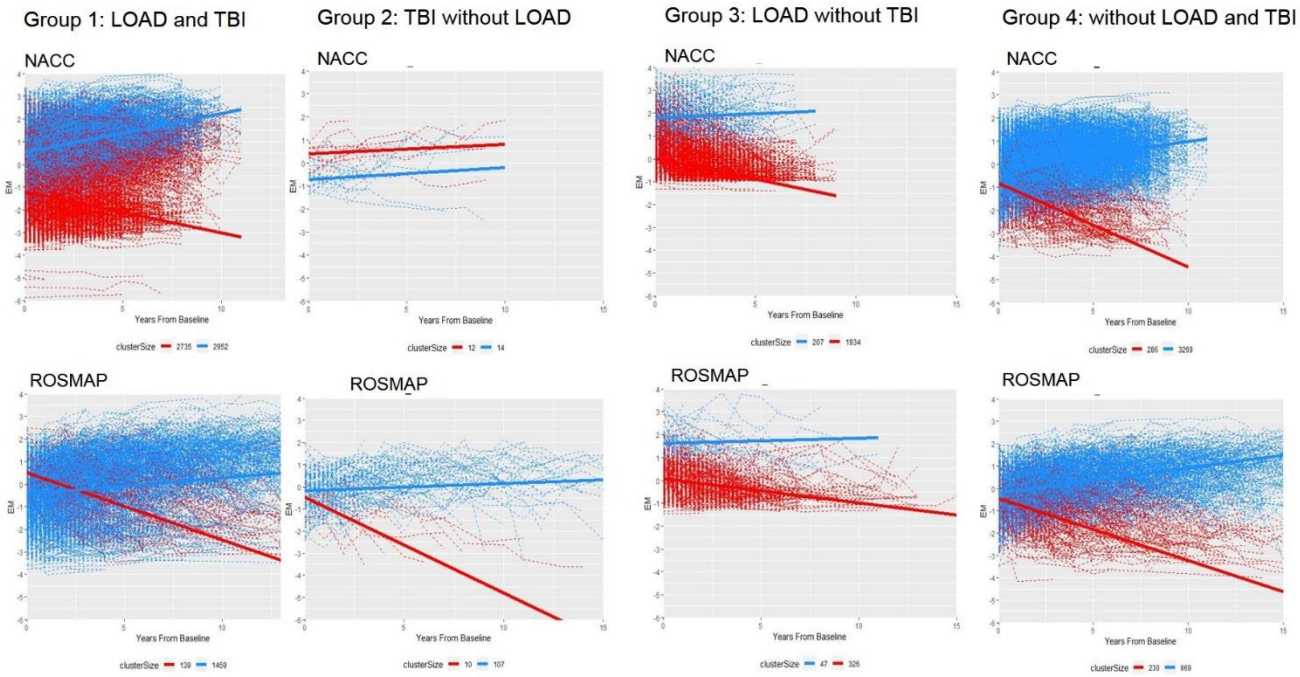
2. Implementation and optimization of LCMM method. Growth curve models represent a powerful analytical framework to model individual differences in cognitive change over time, as well as the variability of patterns of cognitive change between individuals. We used latent curve models to derive growth curve models. The latent model approach allows the possibility of incorporating variables with high degree of inter-individual variability such as the number of follow-up visits. This flexibility becomes especially relevant when participants across study cohorts were enrolled at different ages and/or were followed with different time intervals.

The initial optimization of the LCMM algorithm was conducted using the Washington Heights Columbia Aging Project (WHICAP) as training dataset. The optimized algorithm was subsequently expanded to additional study cohorts: NIA-LOAD, NACC_ADGC, , ROSMAP and CHAP. We were able to gather a final sample size of 13,037 ethnically diverse elderly (ages 72 to 85 years) for whom relevant data was available: episodic memory scores from follow-up clinical visits, dementia status, age, sex, education, and *APOE* genotypes. We identified two major clusters: $EMT_{Stables}$, consisting of individuals whose memory function remains stable or improved over time, and $EMT_{Decliners}$, consisting of individuals whose memory function declined. Consistent with previous studies, the majority of study participants maintain their memory performance over time. Compared to those with Stable trajectory, individuals characterized as Decliners exhibited a significant decline of episodic memory, were more likely to have non-white ethnic background, fewer years of education, a higher frequency of ε4 allele at *APOE* gene and five times more likely to develop dementia. Description of the methodology and its implementation has been summarized in a publication that is currently under its second revision in PLOS One journal. The characterization of EMTs in a large and

ethnically diverse sample with and without late onset Alzheimer's disease and no traumatic brain injury that can be use as reference for future analyses.

3. Estimation of trajectories of episodic memory within TBI and LOAD stratified groups. Using LCCM method in samples from NACC_ADGC and ROSMAP cohorts, we estimated episodic memory trajectories (EMTs) over time within each of the four previously defined groups: Group 1 corresponding to subjects with TBI and LOAD, Group 2 corresponding to subjects with TBI but not LOAD, Group 3 corresponding to subjects with LOAD but not TBI and Group 4 corresponding to subjects without TBI and without LOAD.

Figure 1. EMTs in NACC_ADGC and ROSMAP cohorts stratified by LOAD and TBI status.



Follow-up analyses will consider estimating EMTs in additional cohorts, CHAP and NIA-LOAD. Secondary analysis will consider linear mixed models to evaluate the impact of socio-economic (sex, education and ethnicity) , genetic factor (*APOE* genotype) and TBI in the EMTs. The linear mixed models will use the slope of the residualized episodic memory scores (EM_{res}) as a continuous outcome and the socio-economic, *APOE* gene and TBI as independent variables.

4. Evaluating different outcomes for its association with TBI.

We used a cross-sectional sample of 7,491 participants from NACC_ADGC study to examine the association between a clinical history of TBI and the risk of LOAD. Table 1 summarizes the sample size of the different diagnostic categories for both TBI and LOAD (NCI: non-cognitive impaired, AD: Alzheimer's disease; MCI: mild cognitive impaired). For each of the study participants, the LOAD diagnosis was defined based on the clinical assessment of the most recent evaluation.

Table 1. Sample size of LOAD and TBI diagnostic categories in a NACC_ADGC sample

	LOAD				TBI		
Sample size	NCI	AD	MCI	total	Absence	Presence	total

N	4,003	2,647	841	7,491	6,089	823	6,912
%	53	35	11	100	88	12	100

Multivariable relative risk regression models were used to determine if the association between LOAD (outcome) and TBI (predictor) was robust to potential confounding effects of sex, age, self-reported ethnic background, education and *APOE* genotype. As shown in Table 2, our results did not show significant association (p=0.698) between Alzheimer diagnosis (defined as disease presence/absence after having excluded MCI subjects).

Table 2. Adjusted association between LOAD and TBI

predictors	deviance	df	ChiSq	P
TBI	12376.58	1	0.15	**0.698**
sex (men)	12261.89	1	114.69	<.0001
age	11919.67	3	342.22	<.0001
ethnicity	11910.01	2	9.66	0.008
education	11572.35	3	337.66	<.0001
*APOE*_E4	10828.31	1	744.04	<.0001

In secondary analyses we considered a diagnosis of TBI based on its severity. We defined four different diagnostic categories: 1) absence of TBI, 2) TBI with brief loss of consciousness, 3) TBI with extended loss of consciousness and 4) chronic. For analysis purposes, we further collapsed diagnostic categories 4 and 5 into a new category, "severe TBI". The results (Table 3) did not show significant LOAD and TBI association.

Table 3. Adjusted association between LOAD and severe TBI

predictors	deviance	df	ChiSq	P
TBI_severe	12226.44	3	1.25	**0.741**
sex (men)	12116.9	1	109.54	<.0001
age	11774.43	3	342.47	<.0001
ethnicity	11764.7	2	9.74	0.0077
education	11436.26	3	328.43	<.0001
*APOE*_E4	10694.9	1	741.36	<.0001

Finally, using linear regression models, we investigated episodic memory function as clinical outcome and its possible association with TBI. In addition to the previous described socio-demographic and genetic covariates, we also adjusted the model for LOAD diagnosis (defined as presence/absence of the disease) and the number of visits where the participant was assessed. As summarized in Table 4, our results showed a significant association of TBI with episodic memory. As expected, we also observed a significant association between decline in memory performance and LOAD. Follow-up analyses will consider the association between TBI and over-time change in episodic memory performance.

Table 4. Adjusted association between episodic memory function and TBI

predictors	B	SE	P
TBI	0.12	0.04	***0.001***
sex (men)	-0.23	0.02	<.0001
age	-0.01	0	<.0001
education	0.06	0	<.0001
*APOE*_E4	-0.31	0.03	<.0001
AD	-2.45	0.03	***<.0001***
number visits	0.11	0.01	<.0001

5. Genomewide single variant and gene-based approaches to TBI*SNP interaction as predictor of LOAD risk. We conducted preliminary analysis using a genome-wide single variant approach, i.e., individual SNPs in a genome-wide screen are tested for their interaction with TBI and the SNP*TBI interaction term is investigated as predictor of LOAD risk. Analyses were performed using PLINK software 1.07. In a sample of 5,713 participants from NACC_ADGC cohort, we found that the interaction of TBI with SNP variant rs1015290455 significantly increased the risk of LOAD, OR=5.2, $p=3 \times 10^{-6}$. The variant is an intronic SNP within Astrotactin-1 gene (*ASTN1*) located in chromosome 1. Astrotactin gene codifies for a neuronal adhesion molecule required for glial-guided migration of neuroblasts in cortical regions of developing brain, including among others, hippocampus. Replication in a sample of 950 participants from ROSMAP cohort, showed that interaction of TBI with SNP rs1015290455 was not associated with LOAD risk (p=0.417). Our preliminary results suggested that different SNPs in the same gene might be modulating risk of LOAD, further supporting the rationale for using gene-based approaches in the context of gene-environment interaction (i.e., multiple SNPs will be aggregated within a gene).

In the original project, we proposed the use of the algorithm implemented in SBERIA software to conduct set-based gene-environment interactions. However, we encountered substantial lack of information to successfully implement the program. As an alternative methodology, we have evaluated the performance of gene–environment set association test (GESAT). The software, publically available through R, tests for SNP-set by environment interactions using a variance component test, and estimates the main SNP effects under the null hypothesis using ridge regression. Gene-based analyses of *ASTN1* candidate gene using samples from NACC_ADGC and ROSMAP cohorts are being conducted to test the performance of GESAT software. Once implementation and optimization of GESAT method is completed, gene-based analyses will be escalated to the genome-wide level.

- **What opportunities for training and professional development has the project provided?**

The project has provided two significant opportunities for professional development: 1) a solid collaboration with Dr. Seonjoo Lee and 2) mentoring of students.

Dr. Lee is an Assistant Professor of Clinical Biostatistics in the Department of Psychiatry and the Department of Biostatistics at Columbia University Medical Center. Under the leadership of Dr. Lee, we have gained a deeper knowledge of statistical methodology and analysis of longitudinal data. The project has also allow us to create an educational setting in which we

have mentored students from diverse academic backgrounds: master students in Epidemiology and Mathematics.

- **How were the results disseminated to communities of interest?**
  Manuscript describing the optimization of the LCMM method to estimate episodic memory trajectories along with its implementation for the analysis of a sample of more than 13,000 subjects is currently under review (second revision) in PLOS One journal.

- **What do you plan to do during the next reporting period to accomplish the goals?**

We anticipate the completion of the genome-wide gene-based SNP*TBI interaction analyses (Specific aim 2a) using GESAT software for the next period.
Below, there is a summary of the specific tasks planned for the next reporting period:
1. Narrow TBI phenotype definition based on severity. We will refine the definition of TBI by accounting for degree of severity. We will create four different categories: no history of TBI, mild TBI (head injury with loss of consciousness lasting less than 10 minutes), moderate TBI (head injury with loss of consciousness lasting between 10 to 30 minutes), and severe TBI (head injury with loss of consciousness lasting more than 60 minutes).

2. EMTs will be derived using the new TBI definition to update the qualitative description of the trajectories of memory performance within each of the defined groups

3. Incorporate additional study cohorts: WHICAP, , a cohort of Caribbean-Hispanic families with TBI and LOAD diagnosis, Estudio Familiar de la Influencia Genetica Alzheimer (EFIGA).

4. **IMPACT**

- **What was the impact on the development of the principal discipline(s) of the project?**

Characterization of EMTs in a sample of 13,037 subjects from different ethnic backgrounds with and without Late Onset Alzheimer's Disease and no Traumatic Brain Injury that can be use as reference for future analyses.

- **What was the impact on other disciplines?**

Nothing to Report

- **What was the impact on technology transfer?**

Nothing to Report

- **What was the impact on society beyond science and technology?**

Nothing to Report

5. **CHANGES/PROBLEMS**

- **Changes in approach and reasons for change**

The algorithm to be implemented SREBIA is no longer supported and the implementation is missing in the literature. We identified two independent methods- GESAT (https://rdrr.io/github/lin-lab/iSKAT-GESAT/man/GESAT.html) and rareGE

(https://www.ncbi.nlm.nih.gov/pubmed/25060534) implemented in R. We are in the process of evaluating and optimizing GESAT software.

- **Actual or anticipated problems or delays and actions or plans to resolve them**

NA

- **Changes that had a significant impact on expenditures**

Hiring of the post-doctoral research scientist is being more difficult than anticipated and it explains why there is large carryover into the second year. In an attempt to broader our options to find a suitable candidate, we have contacted the Division of Neurology Clinical Outcomes Research and Population Science (NeuroCORPS) at Columbia University Medical Center. NeuroCORPS receive requests from a number of data science/computer science students at Columbia University looking for analytic opportunities. Therefore, we interviewed master students who have strong background in statistics or/and bioinformatics data analysis. We hired a Masters student for conducting analyses. We also hired a Staff Associate who is actively contributing to tasks in Aims 2 and 3 of the proposed project.

- **Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

Nothing to Report

- **Significant changes in use or care of human subjects**

Nothing to Report

- **Significant changes in use or care of vertebrate animals**

Nothing to Report

- **Significant changes in use of biohazards and/or select agents**

Nothing to Report

6. PRODUCTS

- **Publications, conference papers, and presentations**

Manuscript describing methodology to derive the episodic memory trajectories (EMTs) in the study cohorts and corresponding findings is being under revision in PLOS ONE journal.

- **Journals publications**

Nothing to Report

- **Books or other non-periodical, one-time publications**

Nothing to Report

- **Other publications, conference papers, and presentations**

Nothing to Report

- **Website(s) or other Internet site(s)**

Nothing to Report

- **Technologies or techniques**

Nothing to Report

- **Inventions, patent applications, and/or licenses**

Nothing to Report

- **Other Products**

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

- **What individuals have worked on the project?**

- *Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change."*

***Example**:*

Name:	Badri Vardarajan
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2.4
Contribution to Project:	Dr. Vardarajan has contributed to the preparation and harmonization of the data from the different study cohorts, and reviewed/edited the manuscript
Funding Support:	N/A

Name:	Sandra Barral
Project Role:	Principal Investigator
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	2.4
Contribution to Project:	Dr. Barral performed the statistical analyses, supervised research assistant analyses, interpreted the data, and wrote the manuscript.
Funding Support:	N/A

Name:	Yizhe Gao
Project Role:	Research Associate
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	6 months
Contribution to Project:	Ms. Gao integrated data from the study cohorts and performed the latent class mix models analyses, as well as implementation and optimization of additional statistical software needed for analyses purposes.

Funding Support:	N/A

- **Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

Vardarajan, Badri (PI): Dr. Vardarajan contributes efforts to additional projects: U01AG057659, R01AG058918, R56AG059756, and R56AG061837.

Barral, Sandra (PI): Dr. Barral contributes efforts to R01AG056387 and R56AG059756 in addition to active other support previously reported.

- **What other organizations were involved as partners?**

Nothing to Report

8. **SPECIAL REPORTING REQUIREMENTS**

- **COLLABORATIVE AWARDS**

Nothing to Report

- **QUAD CHARTS**

Nothing to Report

9. **APPENDICES**

Nothing to Report

10. ***THE APPENDICES.***

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List of abbreviations

Alzheimer's Disease (AD)
Alzheimer Disease Research Centers (ADCs)
Apolipoprotein E (APOE)
The Alzheimer's Disease Genetic Consortium (ADGC)
Binary Sequence Alignment/Map (BAM)
Bootstrap likelihood ratio test (BLRT)
Base pairs (bp)
Base Quality Score Recalibration (BQSR)
Burrows-Wheeler Aligner (BWA)

The Children’s Hospital of Philadelphia (CHOP)
Combined Annotation Dependent Depletion (CADD)
The Center for Inherited Disease Research (CIDR)
Copy Number Variation (CNVs)
Database of Single nucleotide polymorphism (dbSNP)
Deoxyribonucleic acid (DNA)
The Department of Defense and Veterans Brain Injury Center (DVBIC)
Genome Analysis Toolkit (GATK)
Gigabites (Gb)
Glasgow Coma Scale (GCS)
Gene environment interaction (GXE)
Genomic Evolutionary Rate Profiling (GERP)
Growth mixture modeling (GMM)
Genome-Wide Association Studies (GWAS)
Human Gene Mutation Database (HGMD)
Hardy-Weinberg Equilibrium (HWE)
Identity-by-descent (IBD)
Latent Class Growth Analysis (LCGA)
Linkage disequilibrium (LD)
Late Onset Alzheimer’s Disease (LOAD)
Minimum Allele Frequency (MAF)
Rush Memory and Aging Project (MAP)
Microtubule-Associated Protein Tau (MAPT)
The Minority Aging Research Study (MARS)
Megabases (Mb)
Maximum Likelihood Algorithms (MLE)
The National Alzheimer's Coordinating Center (NACC)
The National Heart, Lung, Blood Institute Grand Opportunity Exome Sequencing Project (NHLBI GO ESP)
National Insitutes of Aging (NIA)
The National Institute of Aging Late-Onset Alzheimer's Disease Family Study (NIA-LOAD)
The National Institute of Neurological and Communicative Diseases and Stroke–Alzheimer’s Disease and Related Disorders Association (NINCDS-ADRDA)
Nanograms (ng)
Online Mendelian Inheritance in Man (OMIM)
Polymorphism Phenotyping (POLYPHEN)
Principal Components (PCs)
Polymerase Chain Reaction (PCR)
Quality Control (QC)
The Rush Alzheimer’s Disease Center Cohorts (RADC)
The Religious Orders Study (ROS)
Sorting Intolerant From Tolerant (SIFT)
Single nucleotide polymorphism (SNP)
Traumatic Brain Injury (TBI)
Uniform Data Set (UDS)
Variant Call Format (VCF)

The Washington Heights Inwood Columbia Aging Project (WHICAP)
Whole Exome Sequence (WES)
Whole Genome Sequence (WGS)