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Everyday Driving and Plasma Biomarkers in Alzheimer's Disease: Leveraging Artificial Intelligence to Expand Our Diagnostic Toolkit

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Abstract.
Background: Driving behavior as a digital marker and recent developments in blood-based biomarkers show promise as a widespread solution for the early identification of Alzheimer's disease (AD).
Objective: This study used artificial intelligence methods to evaluate the association between naturalistic driving behavior and blood-based biomarkers of AD.
Methods: We employed an artificial neural network (ANN) to examine the relationship between everyday driving behavior and plasma biomarker of AD. The primary outcome was plasma $A\beta_{42}/A\beta_{40}$, where $A\beta_{42}/A\beta_{40} < 0.1013$ was used to define amyloid positivity. Two ANN models were trained and tested for predicting the outcome. The first model architecture only includes driving variables as input, whereas the second architecture includes the combination of age, *APOE* $\varepsilon 4$ status, and driving variables.
Results: All 142 participants (mean [SD] age 73.9 [5.2] years; 76 [53.5%] men; 80 participants [56.3%] with amyloid positivity based on plasma $A\beta_{42}/A\beta_{40}$) were cognitively normal. The six driving features, included in the ANN models, were the number of trips during rush hour, the median and standard deviation of jerk, the number of hard braking incidents and night trips, and the standard deviation of speed. The F1 score of the model with driving variables alone was 0.75 [0.023] for predicting plasma $A\beta_{42}/A\beta_{40}$. Incorporating age and *APOE* $\varepsilon 4$ carrier status improved the diagnostic performance of the model to 0.80 [0.051].

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Conclusion: Blood-based AD biomarkers offer a novel opportunity to establish the efficacy of naturalistic driving as an accessible digital marker for AD pathology in driving research.

Keywords: Alzheimer's disease, amyloid, artificial intelligence, driving, naturalistic, plasma biomarkers

INTRODUCTION

Alzheimer's disease (AD), the most common type of dementia, is a progressive, debilitating disease and has emerged as an urgent public health crisis given the growing numbers of older adults worldwide [1]. In the United States, it is anticipated that the population of Americans with either symptomatic AD or mild cognitive impairment will reach 15 million in 2060 [2]. A similar trend is expected in Canada as the number of people with symptomatic AD is projected to triple by 2050 [3].

Detection of AD brain pathology is important for diagnosis, prognosis, planning, and development of therapeutic treatments. In fact, current evidence suggests that cognitively normal individuals with AD brain pathology, who are described as having preclinical AD, may benefit from disease-modifying treatments [2]. Recent failures of double-blind placebo-controlled Phase III studies of disease-modifying therapies for AD may result from administering the drugs too late in the disease process [4]. There is an urgent need to diagnose individuals earlier in the disease process so that interventions might slow or prevent further progression [5].

The current "gold-standard" assessments of AD brain pathology are obtained by measuring proteins in cerebrospinal fluid (CSF) or by positron emission tomography (PET) [6], which presents challenges in widespread use due to cost, burden, and availability [7, 8]. More recently, several studies have shown that blood-based biomarkers could aid in AD diagnosis by identifying individuals with brain amyloid pathology, and had relatively high agreement with amyloid PET [9, 10]. Plasma biomarkers may enable more cost-effective and less burdensome evaluation of AD brain pathology compared to conventional AD biomarkers.

At the same time, increasing evidence suggests that the preclinical stage of AD may have a subtle functional signature that is reflected in changes in everyday behavior [11]. These subtle everyday behaviors, when captured continuously using wearable and mobile technology, may serve as non-invasive behavioral markers to track changes in preclinical AD. Our previous work indicates that changes in driving, a complex activity that involves both cognitive and functional abilities, can identify preclinical AD and precedes the emergence of dementia symptoms [12–17]. These previous studies assessed AD brain pathology using a variety of CSF or PET biomarkers among older adults who are cognitively normal. One study using on-road driving tests found that older drivers with higher values of CSF tau/$A\beta_{42}$ and phosphorylated tau/$A\beta_{42}$ ratios were much faster to receiving a time to a rating of marginal or fail on the driving test [12]. Another study of driving cessation over a 24-year period showed that older drivers with more abnormal CSF biomarker measurements predicted a faster time to driving cessation [17]. A pilot study using in-vehicle data loggers reported individuals with positive amyloid-PET status were likely to take fewer trips overall, drive more miles per trip on average, and have fewer trips with aggressive behaviors [14]. More recently, we developed a machine learning-based neurobehavioral digital marker, based on a combination of everyday driving behavior and age that was able to predict preclinical AD as determined by CSF $A\beta_{42}/A\beta_{40}$ with high recall (84%), precision (94%), accuracy (86%), and area under the curve score (0.94) [16].

In this context, both everyday driving behavior and blood-based biomarkers show enormous potential for developing a widespread solution for the early identification of AD. The objective of the present study is to use artificial intelligence methods to evaluate the association between naturalistic driving behavior and blood-based biomarkers of AD.

METHODS

Study population

Data was collected as part of the longitudinal studies on aging and dementia conducted at the Washington University Knight Alzheimer Disease Research Center and in longitudinal driving studies (R01AG056466, R01AG067428, R01AG068183). Participants were required to be age 60 years or older. cognitively normal as determined by the Clinical Dementia Rating® (CDR® = 0) [18], have a valid driving license, and a compatible vehicle. Participants had no significant chronic disease at baseline such as

cancer, mood disorders, or neurological disease that would otherwise interfere with this ability to drive.

Collection of everyday driving data

Continuous naturalistic driving data were collected using the global positioning system and accelerometer-based Driving Real-world In-Vehicle Evaluation System (DRIVES) as individuals drove daily in their own vehicle and in their own community environments [14, 19]. The DRIVES methodology has been previously published [14, 20, 21]. The "chip" used in this passive data collection system is small and unobstructive. It plugs into the On-Board Diagnostic II port of each participant's vehicle and within 30 s after installation, it starts capturing data on date, time, speed (MPH), longitude/latitude of where a vehicle is driven, and adverse behavior (speeding, hard braking, sudden acceleration). Data transmission occurs from the moment ignition is turned on until it is turned off, with a collection interval set at 30 s. For each participant, one year of driving data was included for analysis in this study, to account for seasonal variability in driving patterns. The one-year driving monitoring period for each participant was selected to start from the month following the participant's plasma collection date. If driving data was not available for that date, the one-year period closest to and maximum of two years from the plasma collection date was selected. All participants provided written informed consent, and ethics approval was granted by the Washington University Human Research Protection Office.

Driving exposures

The complete list of variables currently obtained from the DRIVES chip is reported in Table 1. This list is an extension of a partial list of variables obtained from the DRIVES chip that has been published [16]. Indicators were selected that were most frequently used in these studies and could be inferred from the DRIVES chip data. Spatial and temporal indicators were selected based on our previous work that used GPS technology to measure older adults' outdoor mobility [22, 23]. To select the driving behavior variables, we searched the literature for articles that studied the on-road driving performance of older adults and individuals with mild cognitive impairment or AD [24–26]. We classified the driving variables into three groups: 1) *spatial* metrics describing spatial patterns of movements such as entropy and radius of gyration, 2) *temporal* metrics describing temporal patterns of movement such as the number of night trips, and 3) *behavior* metrics measuring the on-road performance of the drivers such as speed and acceleration. Finally, all variables are either computed over a trip or a month. Trip-wise measures are then aggregated and averaged monthly.

Plasma collection and analysis

Blood samples from each participant were collected at a single session at approximately 8 AM following overnight fasting [9]. Plasma $A\beta_{42}$ and $A\beta_{40}$ were measured in the C_2 N Diagnostics commercial laboratory with immunoprecipitation–mass spectrometry assay [27]. All assays were performed by personnel who were blinded to the participant's demographic data.

Other exposures

All participants underwent *APOE* genotyping. The main analysis included *APOE* $\varepsilon 4$ carrier status (i.e., whether an individual carried one or more $\varepsilon 4$ alleles). The *APOE* allele was determined by genotyping rs7412 and rs429358 with TaqMan genotyping technology [28]. All participants also completed a structured interview regarding socio-demographic characteristics and the Mini-Mental State Examination (MMSE) [29].

Outcomes

The primary outcome was plasma $A\beta_{42}/A\beta_{40}$, which is highly concordant with amyloid PET status [10]. $A\beta_{42}/A\beta_{40} < 0.1013$ was used to define amyloid positivity. This cut-off value is determined in an overlapping cohort of research participants at the Knight Alzheimer Disease Research Center. In this cohort, plasma $A\beta_{42}/A\beta_{40} < 0.1013$ has yielded the highest combined sensitivity and specificity (Youden Index) for amyloid PET status (see the Supplementary Methods for more information). Further, in the Supplementary Results, plasma Amyloid Probability Score (APS) was studied as an auxiliary outcome measure. APS is a modelled score incorporating plasma $A\beta_{42}/A\beta_{40}$, age, and apoE prototype, where the APS > 15 has a higher concordance with amyloid PET [8, 27].

Table 1
The complete list of naturalistic driving variables

Variable	Description	Category	Aggregation Scale
Num. trips	Number of trips	Spatial	Monthly
Radius of gyration	Typical distance travelled	Spatial	Monthly
Entropy	Entropy of travelled destinations	Spatial	Monthly
Night trips	Number of trips after sunset	Temporal	Monthly
Eve. trips	Number of trips during the evening rush hour (4pm – 6 pm)	Temporal	Monthly
Morn. trips	Number of trips during the morning rush hour (7am – 9am)	Temporal	Monthly
Dist. travelled	Total distance travelled in kilometers	Spatial	Monthly
Hard braking	Base 10 logarithm of number of hard braking events	Behavior	Trip-wise
Hard-core braking	Base 10 logarithm of number of hard-core braking events	Behavior	Trip-wise
Sudden Acceleration	Number of sudden accelerations	Behavior	Trip-wise
Speeding	Number of speeding events where the speed exceeds the speed limit by more than 10 miles per hour	Behavior	Trip-wise
Under-speeding	Number of under-speeding events where the speed falls below the speed limit by more than 10 miles per hour	Behavior	Trip-wise
Duration	Trip duration in minutes	Temporal	Trip-wise
Med. Speed	Median of speed	Behavior	Trip-wise
SD Speed	Standard deviation of speed	Behavior	Trip-wise
Med. Acceleration	Median of acceleration	Behavior	Trip-wise
SD. Acceleration	Standard deviation of acceleration	Behavior	Trip-wise
Med. Jerk	Median of jerk	Behavior	Trip-wise
SD. Jerk	Standard deviation of jerk	Behavior	Trip-wise
Winter trips	Number of winter trips averaged per month	Temporal	Monthly
Waiting time	Average waiting time between two consecutive trips	Temporal	Monthly
Max. dist. from home	Maximum distance travelled from home	Spatial	Monthly
Jump length	Average jump length between two consecutive stops	Spatial	Monthly
Straight line distance	Straight line distance from start point to the destination	Spatial	Monthly

Statistical and artificial intelligence approach

Intergroup differences in demographic and clinical measures were assessed using analyses of variance (ANOVAs), while associations among categorical variables were checked using analyses of contingency tables (χ^2 tests).

We employed an artificial neural network (ANN), through Keras [30] and TensorFlow [31] packages in Python, to examine the more complex relationship between everyday driving behavior and plasma $A\beta_{42}/A\beta_{40}$ status. ANN is a computational model that is inspired by the structure of the human brain. It is made up of many small units termed artificial neurons that are connected by coefficients, also known as weights, which form the network's structure. If the neurons are not directly connected to the inputs or outputs of the network, they are called hidden neurons. The number of hidden neurons in an ANN can be seen as a hyperparameter that can be adjusted to control the capacity of the network and avoid overfitting or underfitting. In this analysis, the ANN technique was selected because of its ability to model complex non-linear relationships and handle large amounts of noisy data. These models are extensively used to make predictions from complex non-linear GPS trajectory datasets [32–34]. Here, two ANN models were trained and tested for predicting the outcome (i.e., plasma $A\beta_{42}/A\beta_{40}$ status). The architectures of these models are depicted in Fig. 1. The first model architecture only includes driving variables as input, whereas the second architecture includes the combination of age, *APOE* $\varepsilon 4$ status, and driving variables. The second architecture includes age and *APOE* $\varepsilon 4$ to improve the model's performance, as they are both well-established risk factors for AD [35]. The values of each feature were standardized by their mean and standard deviation.

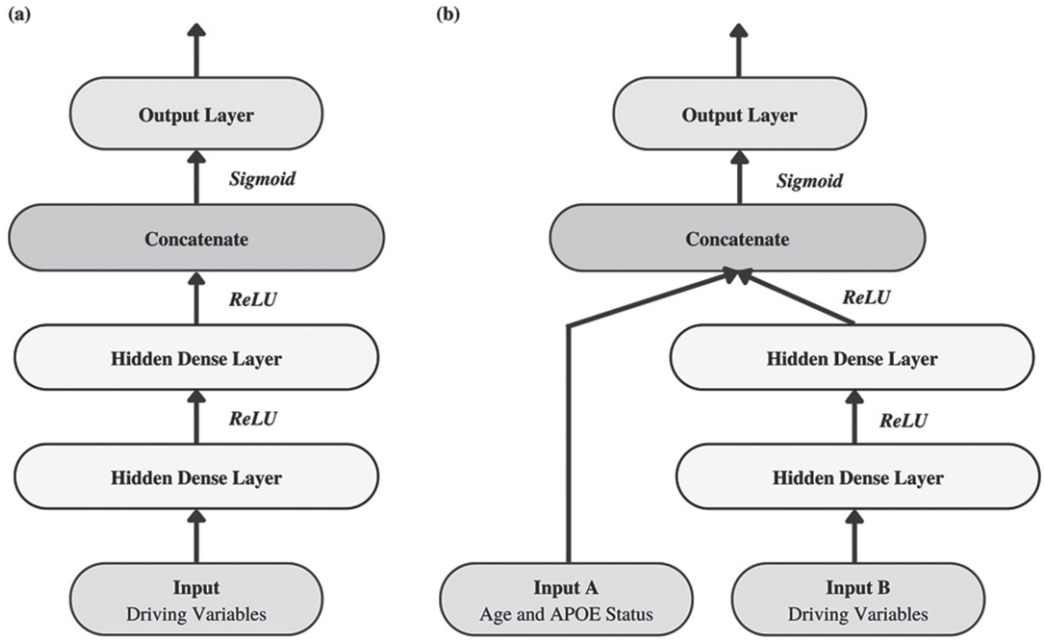

Fig. 1. The architecture of the selected ANN. (a) The architecture of ANN with driving variables as input, (b) the architecture of ANN with driving variables, age, and *APOE* ε4 carrier status.

The neural network architectures consist of up to two densely connected feed-forward hidden layers with sizes ranging from 32 to 16 neurons each. Rectified linear units (ReLU) were set as the activation function for the two hidden layers and Sigmoid was set as the activation function for the output layer. Binary Cross Entropy (i.e., Log Loss) was set as the loss function which computes the negative average of the log of corrected predicted probabilities used for classification problems. Each model training session was limited to 100 epochs, or 100 passes of the input data, and training would be stopped, to prevent overfitting, if there was no improvement to the loss function in 10 consecutive epochs. Each month record for each participant was considered an independent data point. The data was split into 5 partitions and each model was trained 5 times using 4 partitions as training set and the remaining partition as the validation set. To avoid data leakage between the train and validation set, we split the data at participant level and ensured data points from one participant will only be in either the train set, or the validation set, and not both. The best models were defined as the ones with the highest accuracy on the validation sets. Average precision, recall, F1 score, and the area under the receiver operating curve (ROC-AUC) from 5-fold cross-validation were calculated for comparison of the performance of the models. In binary classification, precision, recall, and F1 score are used to evaluate the performance of a model by comparing the predicted labels to the actual labels. The precision score represents the proportion of true positive predictions (i.e., participants with positive plasma $A\beta_{42}/A\beta_{40}$ status that were correctly classified as positive) among all positive predictions made (i.e., all participants classified to have positive plasma $A\beta_{42}/A\beta_{40}$ status by the model), while recall score represents the proportion of true positive predictions among all participants with positive plasma $A\beta_{42}/A\beta_{40}$ status. A high precision means that there are fewer false positive predictions (i.e., cases where a participant has negative plasma $A\beta_{42}/A\beta_{40}$ status but is classified as positive), while a high recall means that there are fewer false negatives (i.e., cases where a participant has positive plasma $A\beta_{42}/A\beta_{40}$ status but is classified as negative). F1 Score represents the harmonic mean of precision and recall, providing a single metric to give an overall measure of a model's performance.

Furthermore, to evaluate the importance of each input feature and perform feature selection, we first addressed the multicollinearity by removing highly correlated driving variables (Pearson correlation coefficient of greater than 0.6). Then, we repeated the 5-fold cross-validation process described above but this time we employed a relief-based feature selection technique to identify features relevant for

each outcome prediction [36]. Features that yielded higher weight were deemed as more important. All the analyses were repeated for APS status. Since the APS score is a proprietary algorithm, results are reported in the Supplementary Results.

In summary, in this study, we hypothesized that the ANN model with driving variables alone and the ANN model with driving variables with age and *APOE* $\varepsilon 4$ status both can distinguish older drivers with a positive plasma $A\beta_{42}/A\beta_{40}$ status from older drivers with negative plasma $A\beta_{42}/A\beta_{40}$ status.

RESULTS

Socio-demographic and clinical data

A total of 142 participants met inclusion/exclusion criteria with one complete year of driving data and plasma collection within two years of their driving data. Table 2 presents the socio-demographic data of the participants in this study divided into two groups according to their amyloid status as determined by plasma $A\beta_{42}/A\beta_{40}$. Participants with positive plasma $A\beta_{42}/A\beta_{40}$ status were older than those with negative status (74.8 (5.4) versus 72.3 (4.4), $p < 0.01$). There were no significant differences in sex, education, race, and MMSE [29] scores between the two groups. As expected, individuals who were plasma $A\beta_{42}/A\beta_{40}$ positive were more likely to be positive for the *APOE* $\varepsilon 4$ allele. The participants made a total of 188,935 trips over the time period.

Selection and ranking of the driving variables

Since the presence of highly correlated features can impede the feature ranking performance, highly correlated features were removed from the list of driving variables. These included median and standard deviation of acceleration. From the reduced set of driving variables, the ranked importance score of each variable for both outputs are presented in Fig. 2. For predicting plasma $A\beta_{42}/A\beta_{40}$ status, the six most important driving features were the number of trips during rush hour, the median and standard deviation of jerk, the number of hard braking incidents and night trips, and the standard deviation of speed. Only the six listed features were included in the ANN model. The violin plots of the six most important driving measures across the 12 months are depicted in Fig. 3.

Results of neural network analysis

By employing ANN, we predicted amyloid positivity status defined by plasma $A\beta_{42}/A\beta_{40}$ using a combination of driving variables, age, and *APOE* $\varepsilon 4$ status as input variables. Automatic architecture training of the network delineated the best model with two layers each consisting of 32 hidden neurons. To prevent overfitting, we employed a 5-fold cross-validation scheme and an early stopping criterion during model training. Overall, the model with driving variables alone achieved 0.68 precision, 0.84 recall, and 0.75 F1 scores for classifying amyloid positive status based on $A\beta_{42}/A\beta_{40}$. Further, the model with driving variables, age, and *APOE* $\varepsilon 4$ status achieved 0.77 precision, 0.82 recall, and 0.77 F1 scores for classifying amyloid positive status based on plasma $A\beta_{42}/A\beta_{40}$. Table 3 shows all the performance metrics for the two models.

DISCUSSION

This study examined associations between daily driving behavior and plasma $A\beta_{42}/A\beta_{40}$ biomarker among cognitively normal older adults. The main finding from studying over 144,000 driving trips among 142 older adults over a year was that the model with driving variables along with age and *APOE* $\varepsilon 4$ status showed moderately high concordance with plasma $A\beta_{42}/A\beta_{40}$ status, with an area under the curve of 0.77.

The predictive ability of the models for identifying plasma $A\beta_{42}/A\beta_{40}$ status significantly improved with the addition of age and *APOE* $\varepsilon 4$ status. In fact, the model with driving variables, age, and *APOE* $\varepsilon 4$ status achieved F1 scores of 0.80 [0.051], while the models with driving variables alone achieved F1 scores of 0.75 [0.023], for predicting $A\beta_{42}/A\beta_{40}$ status. This improvement is expected since age and carrying one or more *APOE* $\varepsilon 4$ alleles are among the strongest risk factors for AD.

The two models achieved higher recall scores than precision for predicting plasma $A\beta_{42}/A\beta_{40}$ status. The higher recall scores indicate that the predictive models performed better in correctly identifying the true positives. That is, the models can accurately identify individuals with positive amyloid status, among all individuals with positive amyloid status. The lower precision score, on the other hand, can be indicative of a higher false positive rate, which are the cases predicted as positive, but were amyloid negative as defined by the biomarkers.

Table 2
Socio-demographic and clinical data divided according to the amyloid positivity status based on (1) plasma $A\beta_{42}/A\beta_{40}$ and (2) the Amyloid Probability Score (APS) status

Variable	Plasma $A\beta_{42}/A\beta_{40}$ Status				
	Negative (n = 54)	*Positive (n = 88)*	F/χ^2	*df*	*p*
Age (y)	72.3 (4.4)	74.8 (5.4)	8.65	1	0.004
Education (y)	16.6 (2.0)	16.3 (2.4)	0.33	1	0.565
Sex (M/F) (counts)	28/26	38/50	0.69	1	0.405
Race (White/Black or African American)[a] (counts)	43/11	79/9	2.07	1	0.150
MMSE	29.2 (1.2)	29.3 (0.9)	0.77	1	0.383
APOE ε4 status (carriers/ non-carriers) (counts)	9/45	47/41	11.85	1	0.001

[a]The sample only includes Black and White participants. MMSE, Mini-Mental State Examination.

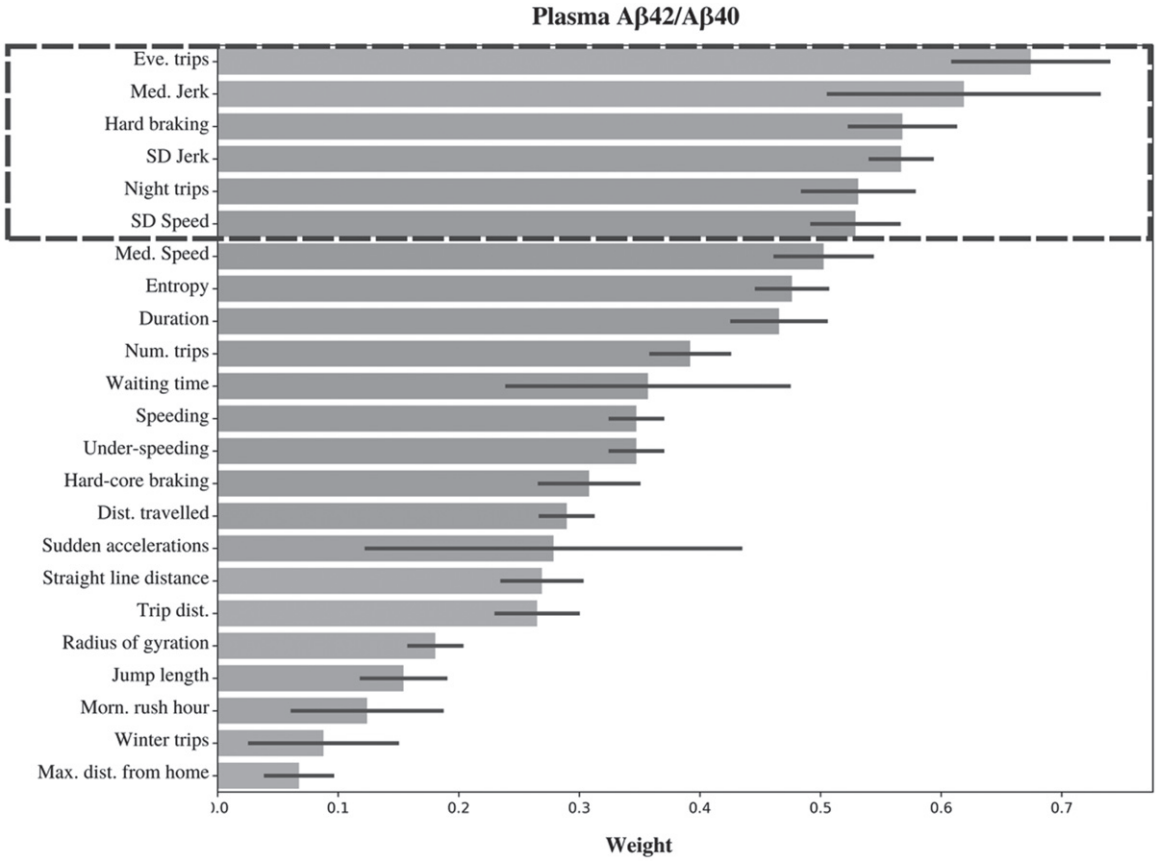

Fig. 2. Relief-based feature importance ranking for Plasma $A\beta_{42}/A\beta_{40}$.

Table 3
Assessment of the model performance. Values in parentheses represent the standard deviation across the 5 folds

Outcome	Input	Precision	Recall	ROC-AUC	F1-score
Plasma $A\beta_{42}/A\beta_{40}$ Status	Driving features	0.68 (0.021)	0.84 (0.046)	0.68 (0.061)	0.75 (0.023)
	Driving features, age and *APOE* ε4 status	0.77 (0.025)	0.82 (0.081)	0.77 (0.043)	0.80 (0.051)

Prior studies have found driving behavior can be indicative of preclinical AD determined by CSF and PET biomarkers, among cognitively intact older adults. More specifically, preclinical AD is associated with more driving errors during an on-road driving test [37], can predict the time at which an individual will fail a driving test in the future [12, 13, 38], spatial navigation abilities [39], and time

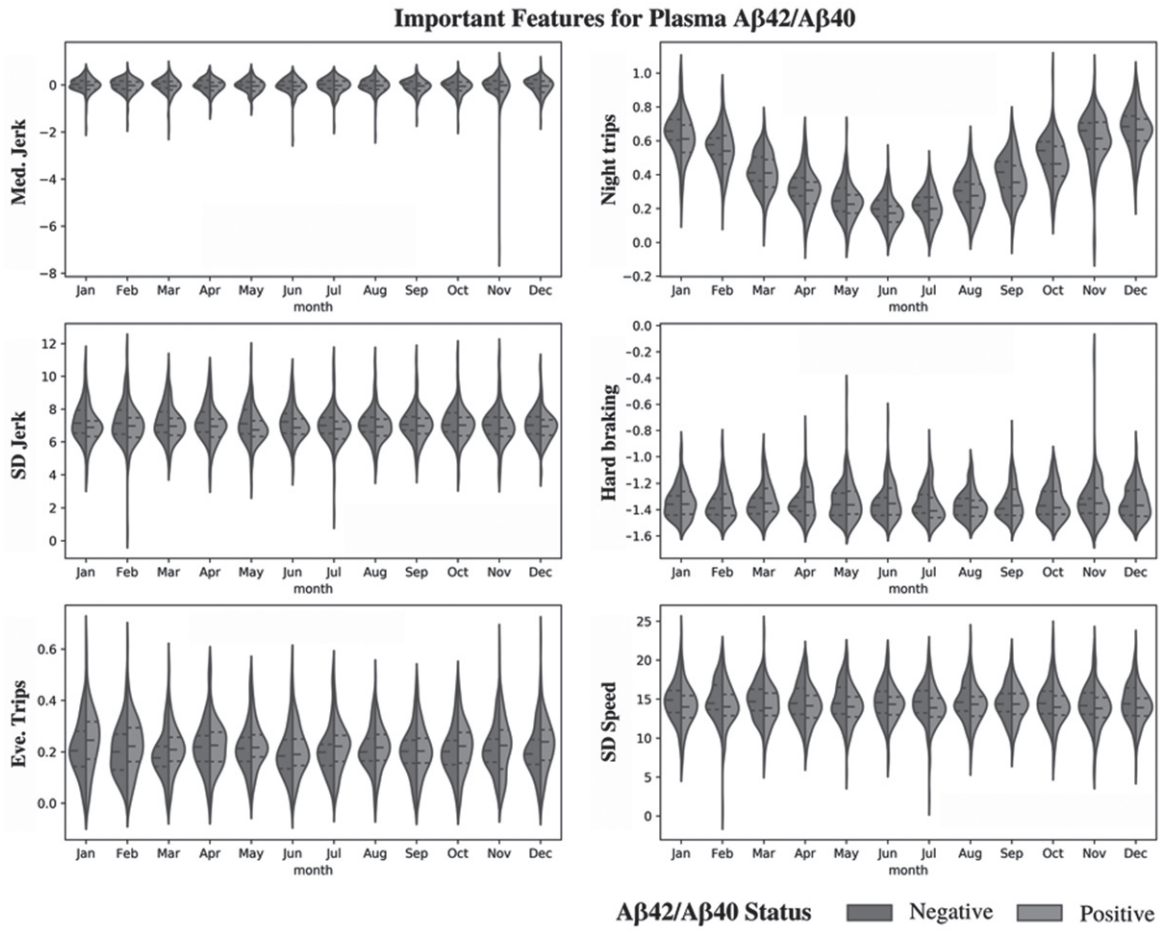

Fig. 3. Violin plots of the six most important driving measures across 12 months grouped by plasma $A\beta_{42}/A\beta_{40}$ status.

to driving cessation [17]. Recently, we reported that machine learning models incorporating naturalistic driving behavior and age can identify amyloid positivity status, as determined by CSF biomarkers, with high accuracy [16]. To our knowledge, this is the first study to investigate the associations between driving behavior and plasma biomarkers of AD. The driving model presented in this study achieved lower performance for predicting plasma $A\beta_{42}/A\beta_{40}$ status, compared to the previous driving machine learning model for predicting CSF $A\beta_{42}/A\beta_{40}$ status. This difference may result from current plasma biomarkers showing lower concordance with amyloid-PET status, compared to CSF biomarkers. The use of $A\beta_{42}/A\beta_{40}$ to define amyloids is a notable limitation in this study. While recent evidence suggests that plasma $A\beta_{42}/A\beta_{40}$ reflects amyloid-β deposition and correlates with brain amyloidosis [9, 40, 41], the prognostic value of plasma biomarkers including $A\beta_{42}/A\beta_{40}$ and whether they can predict future AD pathological and clinical changes remains to be confirmed with continued research for confirmation [42]. Emerging work suggest that plasma biomarkers like p-tau_{217} may also be associated with amyloidosis but this time course with $A\beta_{42}/A\beta_{40}$ needs to be delineated. Additionally, more research needs to be conducted to understand how $A\beta_{42}/A\beta_{40}$ may perform differently across ethnoracial groups in predicting AD pathology. Future studies are required to compare driving behavior with CSF and blood biomarkers to identify amyloid deposition in AD, as defined by the "gold standard" PET-amyloid to establish concordance with driving behavior across the biomarkers. Additionally, accumulation of Aβ alone does not represent AD. In fact, evidence suggests that the molecular phenotype of AD is highly complex, and a variety of changes can differentiate AD from healthy aging [43]. For example, hyperphosphory-

lated tau, neurofibrillary tangles, and synaptic and neuronal loss have been shown to be closely associated with memory deficits in AD [44]. Therefore, future studies will expand beyond Aβ to test the models for predicting other AD pathologies such as tau.

Finally, driving is critical for daily life for many older adults, including those with dementia. Although individuals with dementia have to eventually stop driving, research shows that they may be able to drive safely for a period of time [45–47]. Therefore, the subtle differences in driving behaviors detected by machine learning models among drivers with preclinical AD should not be interpreted as if these individuals are unsafe drivers. In fact, the direction of the patterns (e.g., lower jerk or fewer night trips among individuals with preclinical AD) suggests that older drivers with preclinical AD are more cautious drivers and are more likely to self-regulate their driving behaviors. It is important to assess each individual's ability to drive based on their specific symptoms and ability to operate a vehicle safely. This allows individuals with dementia to maintain their independence and mobility for as long as possible.

Conclusions

The findings of this cohort study demonstrate the high diagnostic power of artificial neural network models incorporating daily driving, age, and *APOE* ε4 status for identifying plasma $A\beta_{42}/A\beta_{40}$ status, which can be considered as a distant proxy for brain amyloid pathology, among cognitively intact older adults. The increasing evidence showing plasma $A\beta_{42}/A\beta_{40}$ ratio has utility in detecting brain amyloidosis is opening new avenues for neurologists and other clinicians to have access to a low-burden, affordable, rapid, and reliable AD biomarker. At the same time, increasing evidence suggests that subtle everyday driving behaviors, when captured continuously using mobile technology, may serve as non-invasive behavioral marker to track changes in AD. When used together, blood-based biomarkers and driving-based digital markers can improve the available diagnostic toolkit of preclinical AD and offer an ideal first step in the multi-stage diagnostic process of AD. More specifically, they offer more scalable, convenient, and cost-effective solutions to meet the requirements for implementation in primary care settings. Digital driving-based markers can provide the means to monitor AD progression continuously and passively and together with blood-based biomarkers, can help determine which individuals should be referred for further assessment, such as diagnostic CSF analysis and amyloid PET diagnostic. The most significant advantage of blood-based biomarkers and digital markers of driving is their accessibility and affordability, making it possible for rural and marginalized communities, who have historically encountered limited access to healthcare systems due to geographic distance and a lack of specialty clinics or hospitals, to receive adequate healthcare.

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CONFLICT OF INTEREST

Drs. Roe and Babulal are Editorial Board Members of this journal but were not involved in the peer-review process nor had access to any information regarding its peer-review.

Dr. Schindler has analyzed data on the PrecivityAD blood test provided by C2 N Diagnostics. She has not received any research funding or personal compensation from C2 N Diagnostics or any other diagnostics or pharmaceutical companies. Washington University may receive royalties from the PrecivityAD blood test.

All other authors have no conflict of interest to report.

DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JAD-221268.

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