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ORIGINAL ARTICLE

Adverse driving behaviors are associated with sleep apnea severity and age in cognitively normal older adults at risk for Alzheimer's disease

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Abstract

Alzheimer's disease (AD) pathology accumulates for decades before the onset of cognitive decline. Cognitively normal individuals with biomarker evidence of AD brain pathology (i.e. biomarker + or preclinical AD) can be differentiated from individuals without AD brain pathology based on naturalistic driving data, such as hard acceleration or braking and speeding, measured using in-vehicle dataloggers. Older adults are at increased risk of injury and death from motor vehicle crashes and driving cessation is also linked to negative health outcomes. Identifying potentially modifiable risk factors that increase driving risk may prolong safe driving in old age. Sleep apnea is associated with adverse driving behaviors across the age span. In this study, we hypothesized that high-risk driving behaviors would be associated with increased sleep apnea severity and AD pathology. We found that higher sleep apnea severity measured by a home sleep apnea test was associated with a higher incidence of adverse driving behaviors even after controlling for multiple confounders ($\beta = 0.24 \pm 0.09$, $p < 0.01$). This association was independent of AD biomarker positivity (i.e. increased t-tau/Aβ_{42} ratio). Increasing age was associated with a higher likelihood of high-risk driving behaviors in individuals with AD brain pathology ($\beta = 0.12 \pm 0.04$, $p < 0.01$), but a lower likelihood in individuals without AD brain pathology ($\beta = -0.06 \pm 0.03$, $p < 0.05$). These findings suggest that adverse driving behaviors linked to a higher rate of traffic crashes in older adults are associated with sleep apnea severity and AD pathology even in cognitively unimpaired individuals. Further studies are needed to determine if treatment of sleep apnea decreases high-risk driving behaviors and therefore motor vehicle crashes.

Statement of Significance

Older adults are at increased risk of injury and death from motor vehicle crashes. Driving cessation is also linked to negative health outcomes. Identifying potentially modifiable risk factors that increase driving risk may prolong safe driving in old age. Sleep apnea is associated with adverse driving behaviors across the age span. In this study, we found that higher sleep apnea severity measured by a home sleep apnea test and age in individuals with Alzheimer's disease (AD) brain pathology was associated with a higher incidence of adverse driving behaviors. These findings suggest that adverse driving behaviors linked to a higher rate of traffic crashes in older adults are associated with sleep apnea severity and AD pathology even in individuals without cognitive impairment.

Key words: obstructive sleep apnea; driving; Alzheimer's disease; older adults

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Introduction

The Center for Disease Control and Prevention lists motor vehicle crashes as the second leading cause of deaths by injury in the 65+ age group in 2019 after falls [1]. The age distribution of motor vehicle crashes resembles an inverted bell curve, with rates dropping from ages 16 to 30 before rising again after age 65 [2]. Though this increased risk of crashes does not reach the same level as for younger drivers, older adults are at a much higher risk of death [3], while survivors are more likely to be hospitalized [4] and suffer more severe injuries due to increased frailty [5]. Given the negative health and social outcomes associated with driving cessation [6–9], contrasted with the increased risk of crashes and the associated risks of mortality and/or severe injury, it is important to consider ways to maximize the years of safe driving in older adults while balancing the risks and rewards of access to a personal vehicle.

Alzheimer's disease (AD) is a growing public health crisis. An estimated 5.8 million Americans were living with AD in 2019 [10], and this number is expected to increase to around 14 million by 2060 [10, 11]. Older adults with AD are at a higher risk for motor vehicle crashes [12]. Drivers with cognitive impairment due to AD have 2–5 times the risk of motor vehicle crashes compared with healthy older adults [13, 14], and often progressively limit their driving activities as they become aware of new limitations brought on by the disease [15–17]. In addition, 30%–40% of cognitively normal older adults have biomarker evidence of AD brain pathology and are classified as having preclinical AD [18]. Individuals with preclinical AD are cognitively unimpaired but have detectable underlying disease pathologies and an annual conversion rate to symptomatic AD between 20% and 30% [19–21]. Those with preclinical AD make more errors resulting in a failed road test [22, 23] and have a higher frequency of traffic violations and crashes [24]. Machine learning has been able to differentiate between individuals with and without preclinical AD biomarkers based on measures of naturalistic driving [25, 26], suggesting drivers with preclinical AD experience changes in driving well before any clinical diagnosis criteria are met.

Poor sleep quality or sleep deprivation is also associated with a higher likelihood of motor vehicle crashes [27–29]. Obstructive sleep apnea (OSA) is a common sleep disorder affecting an estimated 54 million Americans [30] and often causes daytime sleepiness (DTS) [31, 32]. Individuals with OSA are at risk for impaired driving and increased risks of crashes [33–36]. As with AD, the prevalence of OSA increases with age [37–40]. OSA is also associated with an increased risk of developing cognitive impairment [41]. Previous research has separately investigated the effects of OSA, aging, and preclinical or symptomatic AD on driving. In the current study, we investigated the effects of OSA and preclinical AD status on driving behaviors that have been shown to increase the risk of motor vehicle crashes such as hard braking, hard acceleration, and speeding [42, 43]. While both OSA and preclinical AD have been found to affect driving performance, it is unknown whether these effects are additive or interactive, or how age may moderate these effects. While amyloid-lowering therapeutics are still being developed and refined [44, 45], treatment of OSA through positive airway pressure (PAP) therapy has been shown to counteract sleep-related driving difficulties [33, 46] and improve overall cognitive function [47], including in individuals with MCI and symptomatic AD [48]. We hypothesize that older adults with both OSA and preclinical AD will have an increase in adverse or high-risk driving behaviors, and that these effects will be additive such that those with preclinical AD will show an increased effect of OSA severity on the incidence of high-risk driving behaviors that are linked to increased risk of motor vehicle crashes. If the relationship between aging, preclinical AD, OSA, and driving can be better understood, interventions may be identified that prolong safe driving in older age.

Methods

Participants

Study participants consisted of 96 older adults aged 65 and older (47 female and 49 male) enrolled in studies of aging, AD, and driving behavior at the Washington University Knight Alzheimer Disease Research Center (ADRC). Participants are community-dwelling adults who are followed at the Knight ADRC for research studies only. All participants in Knight ADRC studies undergo annual clinical and cognitive assessments by a clinician. For inclusion in the current study, participants needed to meet the following inclusion criteria: (1) be cognitively normal based on a Clinical Dementia Rating (CDR) [49] of "0"; (2) have undergone lumbar puncture for the collection of cerebrospinal fluid (CSF) biomarker data within 1 year of the sleep study date; (3) have a valid driver's license and drive at least once a week; (4) have both sleep apnea data and sleep quality data collected; and (5) have one full year of naturalistic data collected with overlapping dates within 1 year of the sleep apnea and sleep quality data collection. Studies were approved by the Washington University Institutional Review Board and each participant signed informed consent.

CSF biomarkers

CSF was collected as previously described [50]. CSF amyloid-beta$_{42}$ (Aβ_{42}) and total tau (t-Tau) were measured using an automated electrochemiluminescence immunoassay (Lumipulse G1200, Fujirebio). The diagnostic biomarker ratio of total Tau to amyloid-beta$_{42}$ (t-Tau/Aβ_{42}) was used to detect preclinical AD. Participants were classified based on cutoffs that have high concordance with amyloid PET [51]. Participants were classed as "positive" and coded as "1" for the analysis, if their t-Tau/Aβ_{42} ratio was over 0.488 they were coded as "0" otherwise.

Driving

Naturalistic driving data were captured using a commercial GPS data logger ("G2 Tracking Device," Azuga Inc, San Jose, CA) plugged into the onboard diagnostics-II (OBDII) port of the participants' personal vehicles. The OBDII port is a standardized port present in all vehicles built and sold in the United States after January 1, 1996 [52]. The ports are primarily located on the driver's side of the vehicle under the dashboard. The chips use the vehicle's battery for power, are a minimally invasive means of collecting naturalistic driving data, take approximately 20 s to install, and elicit no behavioral change in the participants. The Driving Real-world In-Vehicle Evaluation System (DRIVES) samples data every 30 s anytime a vehicle is driven, and provide a wide range of data including date, time, speed, latitude, and

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longitude, as well as a number of driving behaviors including hard braking, sudden acceleration, and speeding. The use of this system has been described in detail in previous publications [53–56]. Speed data are collected every 30 s unless a hard braking or sudden acceleration event occurs, which are logged immediately. Sudden acceleration and hard braking are defined as acceleration/deceleration in excess of 8 mph/s. Speeding is defined as a speed at least 6 mph over the posted speed limit. Driving data were captured over a 12-month period for each participant.

In order to examine the effects of both OSA and preclinical AD on driving behavior, we created a composite of adverse or high-risk driving behaviors that included hard braking, sudden acceleration, and speeding. These three variables have been combined into a single measure as in previous research [57], with observed differences in baseline measures of incidences of high-risk driving behaviors between negative and positive biomarker groups. The variable was labeled "adverse driving" and was coded as "1" if there were any incidences of high-risk driving behaviors during a trip and "0" if there were no instances.

Sleep

Participants underwent a one-night home sleep apnea test (HSAT; Alice PDx, Philips Respironics Inc, Murrysville, PA). The Alice PDx is a type III HSAT device that monitors oxygen saturation (SpO2) and pulse rate from an oximeter finger probe, nasal pressure-based airflow monitor and thermistor, thoracic and abdominal effort via inductance plethysmography, and body position. The Alice PDx has been found to have 96.4% agreement with simultaneously recorded in-laboratory polysomnography [58]. Participants pressed the event monitor at lights off and lights on. Bed and rise times were also confirmed with sleep logs and actigraphy as previously described [59]. In the morning, participants checked the "good study" indicator on the device to confirm a minimum of 4 h of recording. A minimum of 4 h of artifact-free recording was obtained for all participants and participants not meeting this criterion were asked to repeat monitoring. Respiratory events were scored by registered polysomnographic technologists using the American Academy of Sleep Medicine (AASM) criteria [60] and were reviewed by a board-certified sleep medicine physician (B.P.L.). Hypopneas were scored using 4% oxygen desaturation criteria. The apnea–hypopnea index (AHI) was calculated per hour of monitoring time for each participant. Participants using PAP therapy or dental devices were asked to use them as usual during the HSAT (PAP: 12 participants in the preclinical AD group, 1 in the non-preclinical AD group; dental device: 1 in non-preclinical AD group, 0 in the preclinical AD group). The same respiratory event scoring criteria were used for all participants (untreated, treated with PAP, and treated with dental device).

Sleep was also assessed over six nights at home using a single-channel electroencephalography (scEEG) device (Sleep Profiler, Advanced Brain Monitoring, Carlsbad, CA). As with the Alice PDx, bed and rise times were confirmed with sleep logs and actigraphy. The scEEG device was worn on the forehead and recorded at 256 samples per second from three frontal sensors placed at approximately AF7, AF8, and Fpz. Only the AF7–AF8 channel was used for scoring by registered polysomnographic technologists using modified AASM criteria [61]. Average total sleep time (TST) and sleep efficiency (SE) were used in the analyses. Participants' self-reported DTS was also assessed via the Epworth Sleepiness Scale [62]. This is an eight-question scale that asks participants to rate how likely they are to fall asleep during a number of different daytime activities, such as watching television, sitting and talking to someone, or while driving a car that has stopped in traffic.

Cognition

Preclinical AD is defined by the presence of biomarkers for AD brain pathology in the absence of cognitive symptoms. In order to ensure that the preclinical AD positive and negative groups did not differ in terms of cognition, their performance on a number of cognitive tasks was compared. Cognition was compared using a composite score [63] that included sub-tests measuring episodic memory (Free and cued selective reminding task: free recall score) [64], semantic category naming (Animal fluency) [65], processing speed (Trail making A) [66], and executive function (Trail making B) [66]. The composite score was calculated by standardizing scores with a z-score using the sample mean and standard deviation of each of the sub-tests and then calculating a mean of the standardized scores.

Statistical analysis

The data used in the analysis included every trip taken by the sample of 96 participants during the 12-month study period—a total of 119 754 trips. Differences in demographics, driving outcomes, sleep metrics, and cognition were examined between biomarker negative and biomarker positive groups to ensure that no confounding group differences were present. The data were then analyzed using binomial generalized linear mixed models (GLMMs). Binomial GLMMs allow the analysis of binary outcomes; in this case, whether a trip had an aggressive driving event or not. This analysis approach was selected since adverse driving events are both rare and highly variable between participants, which means that Poisson regression analyses are inappropriate due to both zero inflation and overdispersion. Also, due to the variability between participants, and because observations (trips) were nested by the participant, the models include a random intercept for participant ID in order to improve model fit. All models controlled for age, sex, and years of education. Age was centered by subtracting the mean from each age value, which is a common method used in aging research to generate coefficient estimates that are based on the mean age of the sample rather than an age of "0" [67]. To avoid convergence issues due to different scales, and to aid interpretation of main effects and interactions [68–70], the AHI, TST, SE, DTS, education, and biomarker variables were scaled by subtracting the mean from each value and dividing by the standard deviation.

Results

Participant characteristics

Participant characteristics are summarized in Table 1. Variables used in the regression modeling are shown in bold. There were no statistically significant differences in age or years of education, or differences in the distributions of sex or race between

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Table 1. Participant characteristics

	Total sample	Biomarker negative (n = 61)*	Biomarker positive (n = 35)*	Test†
Demographics				
Age, years	74.13 ± 5.05	73.46 ± 4.94	75.31 ± 5.11	p = 0.09
Sex, N = female (%)	47 (49.00)	30 (49.18)	17 (48.57)	p = 1.00
Education, years	16.65 ± 2.00	16.72 ± 2.16	16.51 ± 2.32	p = 0.67
Race‡, N = White (%)	84 (87.50)	51 (83.61)	33 (94.29)	p = 0.20
APOE ε4 + carrier, N (%)	41 (42.71)	18 (29.51)	23 (65.71)	p < 0.01**
CSF biomarkers				
t-Tau/Aβ_{42} > 0.488	0.50 ± 0.39	0.284 ± 0.075	0.869 ± 0.444	p < 0.001***
p-Tau/Aβ_{42} > 0.0649	0.07 ± 0.06	0.038 ± 0.011	0.125 ± 0.073	p < 0.001***
Aβ_{42}/Aβ_{40} < 0.0673	0.07 ± 0.02	0.086 ± 0.013	0.048 ± 0.012	p < 0.001***
Driving				
Trips with speeding (%)	9.34 ± 10.44	10.22 ± 9.73	7.82 ± 11.57	p = 0.34
Trips with hard braking (%)	9.38 ± 7.14	9.79 ± 6.36	8.66 ± 8.38	p = 0.49
Trips with hard acceleration (%)	4.70 ± 9.04	5.28 ± 10.49	3.70 ± 5.69	p = 0.31
Trips with any adverse driving events(%)	19.50 ± 13.74	21.13 ± 13.34	16.64 ± 14.16	p = 0.13
Cognition				
Free & cued serial reminding task	29.39 ± 6.11	30.47 ± 5.75	27.50 ± 6.36	p < 0.05*
Animal fluency	20.73 ± 5.62	20.85 ± 5.86	20.51 ± 5.25	p = 0.77
Trail making A	31.31 ± 10.00	32.04 ± 10.74	30.09 ± 8.63	p = 0.35
Trail making B	75.32 ± 26.11	76.86 ± 26.81	72.74 ± 25.08	p = 0.46
Composite score	0.01 ± 0.63	0.028 ± 0.680	−0.012 ± 0.550	p = 0.76
Sleep				
Central apnea index	0.35 ± 0.78	0.28 ± 0.45	0.48 ± 1.14	p = 0.32
Obstructive apnea index	0.62 ± 1.89	0.62 ± 2.00	0.61 ± 1.73	p = 0.97
Mixed apnea index	0.07 ± 0.31	0.05 ± 0.25	0.11 ± 0.41	p = 0.42
Hypopnea index	7.36 ± 7.49	7.45 ± 8.19	7.19 ± 6.2	p = 0.86
Apnea–hypopnea index	8.40 ± 8.46	8.40 ± 9.19	8.39 ± 7.15	p = 1.00
Sleep efficiency (%)	79.39 ± 8.91	80.27 ± 7.66	77.87 ± 10.71	p = 0.25
Total sleep time, min	374.52 ± 52.14	376.98 ± 50.78	370.34 ± 54.92	p = 0.56
Daytime sleepiness	6.54 ± 3.90	6.59 ± 4.25	6.46 ± 3.23	p = 0.86

APOE, apolipoprotein E composite; CSF, cerebrospinal fluid. Variables in bold were included in the models.
*Preclinical AD status was based on t-Tau/Aβ_{42} ratio.
†Means were compared using t-tests. Frequencies were compared using Fisher's exact test.
‡The sample contains only Black and White races.

the biomarker negative and biomarker positive groups. There were also no statistical differences in the mean driving behaviors or any of the sleep measures. While the groups differed on the episodic memory sub-score, there was no statistically significant difference for the composite score. This result was expected since only participants rated as cognitively normal (CDR = 0) were included in the study.

Increased AHI associated with more adverse driving events

The regression analyses for driving and AHI are summarized in Table 2. The table summarizes four models: (1) only main effects; (2) main effects plus an AHI:t-Tau/Aβ_{42} interaction; (3) main effects plus a t-Tau/Aβ_{42}:age interaction; and (4) main effects plus the two interaction terms. An Akaike Information Criterion (AIC) value is included with the models to allow comparisons of model fit. Out of a set of models, the model with the smallest AIC value is considered the best-fitting in terms of under- and over-fitting. For the regressions summarized in Table 2, the best-fitting model is that which includes the t-Tau/Aβ_{42}:age interaction (Model 3).

The coefficients represent changes in the log odds of a trip having an incident of adverse driving given a point increase in the value for each independent variable. It is possible to calculate odds ratios from these coefficients. For example, in Table 2, Model 3, the AHI coefficient is 0.24, meaning that participants were $e^{0.24}$ = 1.27 times more likely to have an adverse driving incident during a trip for every 1 point increase in the scaled AHI variable, which translates to an approximate eight-point increase in the AHI. Conversely, the t-Tau/Aβ_{42}+ group were $1/e^{-0.47}$ = 1.61 times "less" likely to have an adverse driving event during a trip compared with the t-Tau/Aβ_{42}– group. The effects of AHI and biomarkers are shown in Figure 1, which plots AHI against the percentage of trips with an adverse driving event across the three biomarkers.

To confirm that these differences could be attributed to AHI rather than general sleep quality, three additional regression models were run that matched the structure of Table 2, Model 3, except that the AHI factor was replaced with SE, TST, and DTS as measured by the Epworth Sleepiness Scale [75]. None of these sleep variables were statistically significant factors in explaining adverse driving behavior (Table 3).

Relationship between OSA and AD biomarker status

We hypothesized that AHI and biomarker status would have a compounding effect on adverse driving. However, this pattern was not observed in the analysis: the best fitting model (Table 2, Model 3) did not contain an interaction between AHI and

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Table 2. Hierarchical logistic regressions of aggressive driving behavior using CSF t-Tau/Aβ_{42} to define biomarker status

	Dependent variable			
	Adverse driving			
	(1)	(2)	(3)	(4)
(Intercept)	−1.600*** (0.155)	−1.596*** (0.163)	−1.654*** (0.154)	−1.652*** (0.154)
AHI	0.218* (0.097)	0.250* (0.111)	0.242** (0.092)	0.256* (0.107)
t-Tau/Aβ_{42}+	−0.420* (0.213)	−0.421* (0.208)	−0.475* (0.202)	−0.475* (0.192)
Age	−0.019 (0.021)	−0.020 (0.021)	−0.062* (0.026)	−0.062* (0.026)
Sex (F vs. M)	0.108 (0.208)	0.102 (0.220)	0.169 (0.198)	0.166 (0.205)
Education	−0.099 (0.103)	−0.111 (0.109)	−0.143 (0.102)	−0.148 (0.103)
AHI:tTau/Aβ_{42}+		−0.125 (0.219)		−0.057 (0.214)
t-Tau/Aβ_{42}+:Age			0.115** (0.043)	0.114** (0.044)
Observations	119 754	119 754	119 754	119 754
Log likelihood	−51 488.090	−51 487.950	−51 484.690	−51 484.660
Akaike inf. crit.	102 990.200	102 991.900	102 985.400	102 987.300

Coefficient estimates for changes in log odds are displayed, with standard errors. The best fitting model according to Akaike Information Criterion is Model 3.
*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

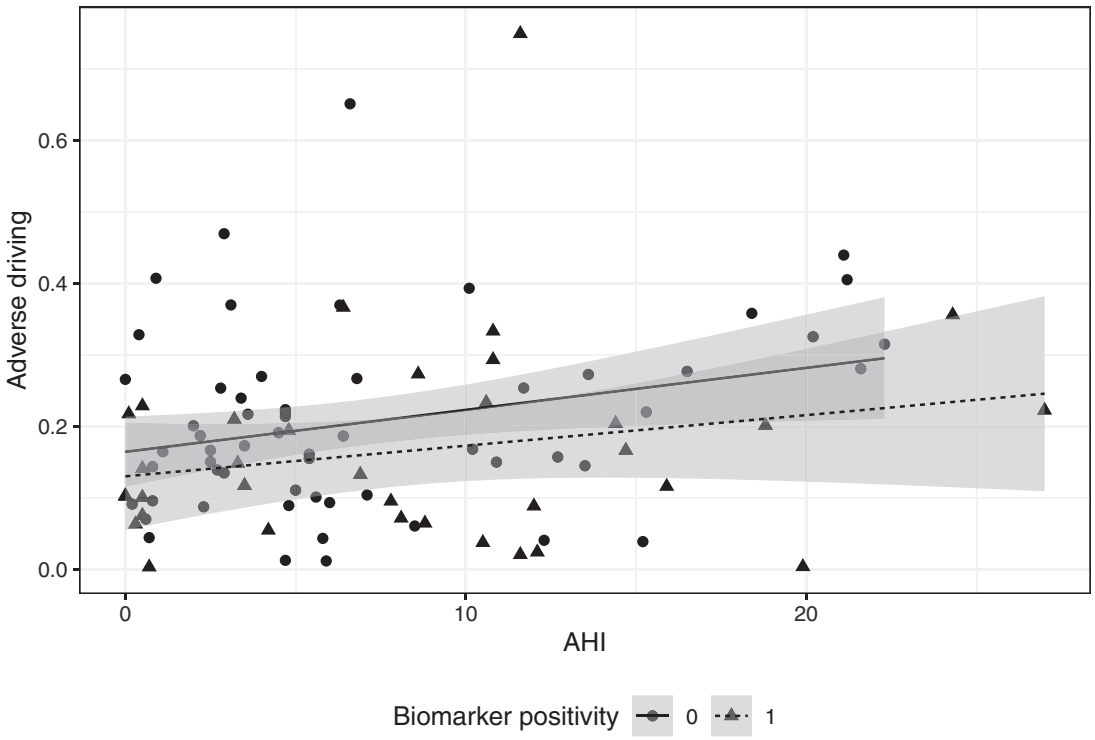

Figure 1. Comparison trips with adverse driving plotted against the apnea–hypopnea index (AHI) and grouped by biomarker status. Greater AHI results in increased mean number of trips with adverse driving behavior in both groups, although the mean number of adverse driving events was lower for the biomarker negative group. Note: To increase legibility of the plots two outliers have been excluded from the data. These participants were included in the data used to construct the statistical models as they did not meet any a priori exclusion criteria.

biomarker status, and when the interaction term was included (Table 2, Model 4) it was not statistically significant. It appears, therefore, that AHI and biomarker status have independent effects on adverse driving behavior.

Relationship between age and adverse driving differs by AD biomarker status

The decreased overall risk of adverse driving in the biomarker positive group also did not match our predictions. However, there is a statistically significant interaction between age and t-Tau/Aβ_{42} in the best-fitting model (Table 2, Model 3). To interpret this effect, we first examined the main effect of age. Focusing on Table 2, Model 3, for every 1-year increase in age, adverse driving events are $1/e^{-0.47} = 1.61$ times "less" likely. Since this coefficient estimate is based on all other factors being set to zero, this 1.61 figure represents the decrease in the odds of an adverse driving event in the negative biomarker group (which was coded as "0"). Conversely, the t-Tau/Aβ_{42}+:age interaction represents a 1.17 "increase" in the probability of an adverse driving event with every

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Table 3. Supplementary regression models investigating measures of sleep quality

	Dependent variable		
	Adverse driving		
	(1)	(2)	(3)
(Intercept)	−1.601*** (0.153)	−1.599*** (0.166)	−1.819*** (0.233)
Sleep efficiency	0.008 (0.105)		
Total sleep time, min		0.047 (0.105)	
Daytime sleepiness			0.032 (0.026)
t-Tau/Aβ_{42}+	−0.462* (0.208)	−0.457* (0.211)	−0.460* (0.210)
Age	−0.062* (0.027)	−0.062* (0.027)	−0.065* (0.027)
Sex (F vs. M)	0.051 (0.198)	0.038 (0.216)	0.057 (0.203)
Education	−0.137 (0.106)	−0.133 (0.110)	−0.135 (0.109)
t-Tau/Aβ_{42}+:Age	0.105* (0.045)	0.104* (0.045)	0.112* (0.044)
Observations	119 754	119 754	119 754
Log likelihood	−51 487.670	−51 487.570	−51 486.960

*$p < 0.05$.
**$p < 0.01$.
***$p < 0.001$.

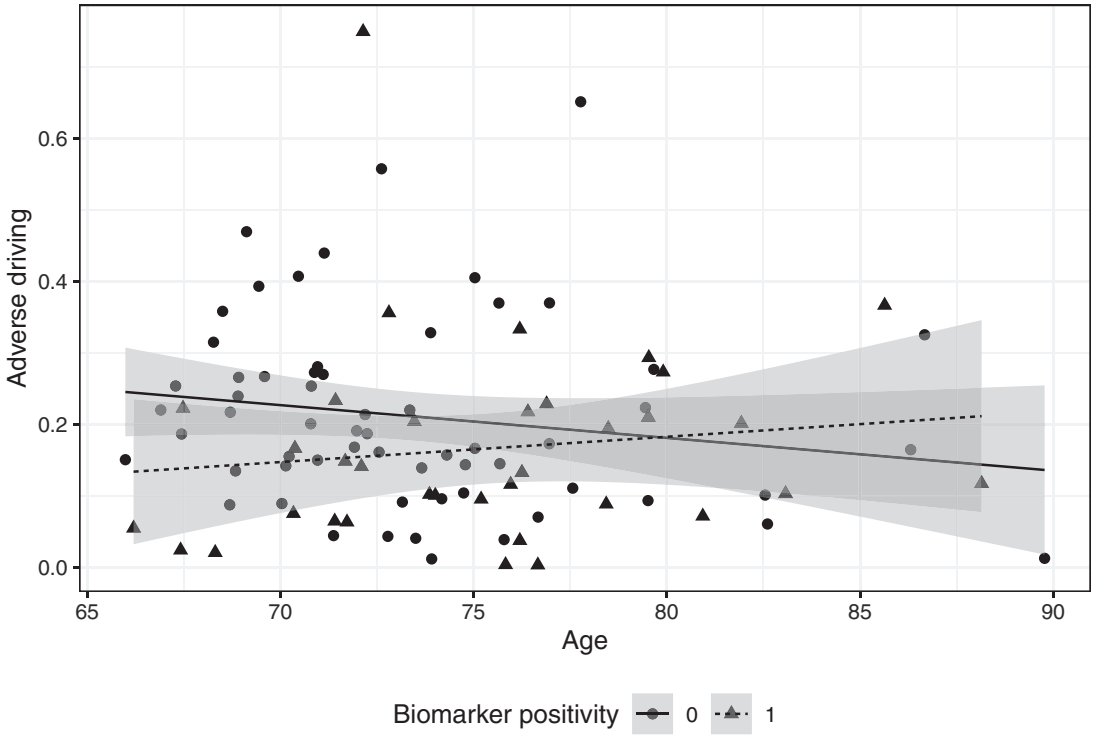

Figure 2. Mean number of trips with adverse driving plotted by age and biomarker status. The biomarker negative group demonstrates a decrease in adverse driving with age, while the biomarker positive group demonstrates an increase in adverse driving with age.

1-year increase in age in the t-Tau/Aβ_{42}+ group. To help visualize this interaction, the percentage of trips with adverse driving is plotted against age and biomarker group in Figure 2.

Discussion

The effect of OSA on driving has been explored largely by comparing mean performance between different groups or performance in the same group pre-/post-treatment [46, 71] rather than how the severity of sleep apnea is related to driving behaviors, and/or have relied on driving simulators to measure driving performance rather than real-world driving [72, 73]. Additionally, previous research has investigated the effects of dementia and preclinical AD [22–24, 53, 54, 74] on driving [12, 15–17], the contributions of comorbidities have not been thoroughly investigated. Links between sleep quality and AD risk have also been the focus of recent research [75, 76], but little work has investigated their combined effects on real-world behaviors such as driving. This study combines these areas of research and provides novel findings in the sleep, AD, and driving fields of research.

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The effects of sleep apnea and preclinical AD biomarker status on driving

In this study, we found that OSA, as measured by AHI, increased the likelihood of a participant having an adverse driving event during a trip, with around a 1.25 times increase in the odds of an event for each approximate eight-point increase in the AHI. This increase in AHI is meaningful given the typical clinical cutoffs of <5: no sleep apnea; 5–15: mild sleep apnea; 15–30: moderate sleep apnea; and >30: severe sleep apnea [77]. This finding adds to the existing sleep apnea and driving literature as it supports previous findings comparing participants with sleep apnea with healthy controls, while also providing evidence that more severe sleep apnea as measured by the AHI is associated with a higher likelihood of adverse driving events.

We did not find a significant relationship between adverse driving and either TST, SE, or DTS. This may be due to a limitation of data collection in our study. Adverse driving scores were measured over 1 year of driving monitoring, while TST and SE were the averages of six nights of monitoring. Further, TST, SE, and an Epworth Sleepiness Score may not be optimal markers for daytime impairment in individuals with sleep apnea. The effect of night-to-night sleep variability on driving behavior cannot be determined in this study. However, these results are promising in that they support the hypothesis that AHI has a specific effect on driving behavior.

Our hypotheses regarding a compounding effect of OSA and preclinical AD on adverse driving behaviors were not supported by the analysis, suggesting that (at least for participants without cognitive symptoms) these two factors have independent effects on adverse driving.

While not an initial hypothesis, there was an interaction between age and biomarker status which revealed that older participants in the biomarker positive group have an increased risk of adverse driving events compared with both younger positive biomarker participants and older negative biomarker participants. This finding is also important when interpreted alongside the lack of interaction between OSA and biomarker status. It appears that for a sample who are not showing cognitive symptoms (as measured by CDR and the combined cognitive index score), sleep apnea, and biomarker status have independent effects on driving behavior. It is unclear at this stage what causes this different pattern in the preclinical AD group, but one potential hypothesis is that younger individuals with preclinical AD have some awareness of change in their driving abilities and so are self-regulating their behavior (as has been observed in previous research [70]). However, older individuals with preclinical AD appear to be less effectively self-regulating their driving—particularly when contrasted with the negative group.

One possible confound may have been trips with aggression were longer on average (mean duration for trips without aggression was 11.33 min, while the mean duration for trips with aggression was 27.71 min). However, biomarker positive participants' average trip lengths were not statistically different from biomarker negative participants' (13.53 min vs. 15.24 min, $t(58.34) = -1.70$, $p = 0.09$). Additionally, age did not correlate with trip duration for either the positive ($r = -0.15$, $p = 0.36$) or negative ($r = -0.12$, $p = 0.36$) groups, despite the latter having higher incidences of adverse driving with age. These additional findings support the initial interpretation that age had a different effect on the risk of adverse driving behaviors in individuals with preclinical AD biomarkers compared with those without.

Limitations and future research

The main limitation of our study was the relatively low number of participants in our sample. While we were able to include over 100 000 trips in our analysis, the fact that adverse driving events remain relatively uncommon means a large amount of data are required to detect effects—trips without adverse driving incidents were approximately five times more likely than trips with incidents. One result of this limitation was that all of our analyses dichotomized the biomarker data into positive and negative groups. However, the DRIVES project has ongoing recruitment and so it may be possible to investigate how the full range of biomarker ratios relate to driving behavior, for example, does adverse driving increase as ratios tend toward the preclinical AD cutoffs, and do more extreme values show larger effects.

A related limitation, again due to the sample size but also the long timescale of the ongoing project, is that all comparisons were cross-sectional. The interaction between age and biomarker status suggests that age plays a different role in driving behavior in the positive and negative groups. Future research aims to track participants' changes in sleep, driving behavior, and biomarker status over time to investigate how these factors interact across the span of old age.

Another caveat was that the sleep assessments were performed at home and not via gold standard attended polysomnography. However, the HSAT and scEEG have a high agreement with polysomnography, and using these methods, we were able to measure sleep in the more naturalistic home environment. A further limitation of the participant sample is that only a subset of study participants had moderate-to-severe OSA. We found significant associations between adverse driving behaviors despite this limitation suggesting that even mild OSA has adverse effects on driving behaviors. However, OSA severity may be underestimated since HSATs do not monitor sleep and rely on monitoring time [58].

By design, our sample was limited to participants with no cognitive impairment (i.e. CDR = 0) and this may be why we did not observe any interaction between OSA and preclinical AD factors. There is also value in understanding how OSA affects individuals further along with the AD pathology. This would also allow for a wider range of biomarker values for the investigation described earlier. An ongoing recruitment process is recruiting participants with CDR > 0.

Conclusion

In this study, we show that OSA increases the likelihood of adverse driving behaviors that have been linked with a higher rate of road traffic crashes, and this risk increases with OSA severity. Older individuals with biomarker evidence of AD are especially likely to have these adverse behaviors. When discussing self-regulated driving and/or driving cessation with participants who are at an increased risk of developing dementia, clinicians may wish to consider potential comorbidities that could have independent effects on driving behavior and whose treatment could prolong safe driving in old age. Although future studies are needed, these findings suggest that treatment of OSA could decrease adverse driving and therefore motor vehicle crashes in cognitively normal older adults.

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