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A 2.5-Year Longitudinal Assessment of Naturalistic Driving in Preclinical Alzheimer's Disease

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Abstract

Background: Emerging evidence shows that cognitively normal older adults with preclinical Alzheimer's disease (AD) make more errors and are more likely to receive a marginal/fail rating on a standardized road test compared to older adults without preclinical AD, but the extent to which preclinical AD impacts everyday driving behavior is unknown.

Objective: To examine self-reported and naturalistic longitudinal driving behavior among persons with and without preclinical AD.

Method: We prospectively followed cognitively normal drivers (aged 65 + years) with ($n = 10$) and without preclinical AD ($n = 10$) for 2.5 years. Preclinical AD was assessed using amyloid positron emission tomography (PET) with Pittsburgh Compound B. The Driving Habits Questionnaire assessed self-reported driving outcomes. Naturalistic driving was captured using a commercial GPS data logger plugged into the on-board diagnostics II port of each participant's vehicle. Data were sampled every 30 seconds and all instances of speeding, hard braking, and sudden acceleration were recorded.

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Results: Preclinical AD participants went to fewer places/unique destinations, traveled fewer days, and took fewer trips than participants without preclinical AD. The preclinical AD group reported a smaller driving space, greater dependence on other drivers, and more difficulty driving due to vision difficulties. Persons with preclinical AD had fewer trips with any aggression and showed a greater decline across the 2.5-year follow-up period in the number of days driving per month and the number of trips between 1–5 miles.

Conclusion: Changes in driving occur even during the preclinical stage of AD.

Keywords

Alzheimer's disease; automobile driving; biomarkers; motor vehicles

INTRODUCTION

In the United States (US), 38 million drivers are aged 65 years or older; by 2050, this age group will expand to 84 million and will represent 1 in every 4 drivers [1, 2]. In 2015, 19 older adults were killed, and 712 were injured in a crash on a *daily* basis; both numbers will increase as the pool of older drivers continues to grow [3].

Alzheimer's disease (AD) is one of the most prevalent chronic, neurological diseases affecting older adults, and adversely impacts driving [4]. Symptomatic AD affects 11% of older adults (> 65 years), and is associated with more driving difficulties and an increased likelihood of failing a driving test with time [5, 6]. Drivers with symptomatic AD are twice as likely to have a crash compared to healthy older adults [7, 8]. People with symptomatic AD will eventually need to stop driving entirely. An integral part of driving cessation is a period during which older adults actively change their driving behavior, more commonly known as driving reduction [9–11].

However, it is not clear how early driving reduction begins within the pathological process of AD development. In addition to those with symptomatic AD, another 30% of older adults have preclinical AD, the condition in which observable dementia symptoms are not yet present, but the underlying disease process has begun [12]. Preclinical AD can be detected among cognitively normal individuals using positron emission tomography (PET) imaging and cerebrospinal fluid (CSF) biomarkers. Studies have shown that cognitively normal older adults with preclinical AD make more errors and are more likely to receive a marginal/fail rating on a road test compared to older adults without preclinical AD [13, 14]. Furthermore, increases in brain amyloid deposition are associated with a higher frequency of crashes and traffic violations in cognitively normal older adult drivers [15]. Given these changes in driving outcomes, it is therefore possible that driving reduction also occurs early in the AD pathological process.

Due to limitations of road tests and driving simulators in reflecting day-to-day driving behavior [16], naturalistic methodologies using sensors have been increasingly used to passively gather data on daily driving as older adults drive their personal vehicles in their own environment [17–20]. Several naturalistic studies show that drivers with symptomatic AD drive fewer miles, reduce their number of trips, go to fewer unique destinations, and

have a reduced driving space (<10 miles from home) compared to cognitively normal peers [16, 21–23]. To date, hypotheses about the impact of preclinical AD on everyday driving behavior have been primarily based on what is known about driving among individuals with symptomatic AD. To our knowledge, our group is the first to examine naturalistic driving behavior in older adults with or without preclinical AD [24].

Previously, we presented data as a small cross-sectional study to examine driving behaviors in cognitively normal individuals with ($n = 10$) and without preclinical AD ($n = 10$). In this paper, we report on the extension of the data collection and evaluate changes in both self-reported and objective driving behaviors over a 2.5-year period.

METHODS

Participants

Participants were recruited from longitudinal studies conducted at the Washington University Knight Alzheimer's Disease Research Center. All participants were cognitively normal (Clinical Dementia Rating [CDR] = 0) [25], 65 years old, had a valid driver's license, drove at least once per week, and had *in vivo* imaging of brain amyloid using PET with Pittsburgh compound B (PIB) [26].

Participants were divided into those without ($n = 10$) or with ($n = 10$) preclinical AD, based on a previously defined mean cortical binding potential (MCBP) using PIB (> 0.18) [27]. The 20 participants recruited for data logger installation were drawn from the larger sample [28, 29]. We first identified all participants who indicated on the Driving Habits Questionnaire (DHQ) that they were always the driver when they went out in their vehicle and determined whether they were PIB positive or negative. PIB positive participants were recruited until 10 agreed to data collection using the data logger, and these 10 participants were then frequency-matched on age with 10 PIB negative participants who also agreed to data logger installation. Of 22 individuals approached, only two participants (9.1%; one who was PIB positive and one who was PIB negative) refused participation in this study. Additional information concerning amyloid PET imaging and matching procedures has been previously published [24]. Lumbar puncture was used to obtain CSF for determination of fluid brain levels of A β_{42} , tau, and ptau $_{181}$. Study protocols were approved by the Washington University Human Research Protection Office, and written informed consent was obtained from all participants.

Driving performance and behavior

A commercial global positioning system (GPS) data logger (G2 Tracking Device™, Azuga Inc, San Jose, CA) was plugged into the vehicle's onboard diagnostics–II (OBD-II) port and data collected every 30 s. This methodology, termed the Driving Real World In-Vehicle Evaluation System (DRIVES) [30], collected data each time a vehicle was driven. Aggressive actions (hard braking, sudden acceleration, and speeding) were recorded anytime they occurred during a trip, regardless of the 30 s sampling that occurred for other data logger measures. Speeding was determined based on the data logger's GPS, specifically the latitude and longitude and the posted speed limit in the vehicle's location. The device

compared the vehicle's speed to the posted speed limit and if the driver was going 6 miles per hour or more above the posted speed limit in that area, an occurrence of speeding was recorded. Data were collected between July 1, 2015 and January 30, 2018 for each participant, although one participant died approximately one year after data collection began. Participants also completed the DHQ [31], a self-report measure of driving behavior over the past year. To maximize the probability that the participant was the driver of the vehicle at all times (as opposed to a spouse, child, friend, etc.), we only recruited individuals who indicated on the DHQ that they were always the driver when they used their vehicle.

Additional clinical testing

Near and far visual acuity and contrast sensitivity were measured using the King-Devick Variable Contrast Sensitivity Chart (<https://itunes.apple.com/us/app/variable-contrast-sensitivity-chart-by-king-devick/id527148325?mt=8>). Participants also completed the Santa Barbara Sense of Direction Scale [32], the free-recall subtest of the Selective Reminding Test [33], Animal Naming [34], and Trailmaking A and B tests [35].

Statistical analysis

Data were collected and managed securely using a research electronic data capture tool (REDCap) [36]. For data obtained by the DRIVES data logger, a "trip" was defined as data gathered from the period of "ignition on" to "ignition off". For example, an excursion from home to the grocery store and back to home without any other stops would be considered two trips. For each trip, the date of the trip, the distance of that trip, the time spent traveling, and the route were recorded. Data logger data were aggregated by month so that an individual followed for 2.5 years would have 30 data points across time for each data logger variable. As noted earlier, DHQ data were obtained one time per year. Statistical analyses were conducted in SAS version 9.4 (SAS Institute Inc.). Linear mixed models examined whether there was a difference at the y-intercept and over time (i.e., slope) for the preclinical and no preclinical groups for the DRIVES data logger and the DHQ.

RESULTS

At the baseline clinical assessment (Table 1), the 20 participants were well educated (Mean = 16.3 y; SD = 2.3), predominately Caucasian ($n = 18$), mostly male ($n = 13$), and ranged in age from 66.4 to 80.8 years (Mean = 73.1 y; SD = 3.9). Seven participants had at least one apolipoprotein $\epsilon 4$ allele and performance on the Mini-Mental State Examination [37] was generally high (Mean = 29.1; SD = 1.1). There were no statistically significant differences between the two groups on any of the aforementioned demographic variables ($p > 0.05$). MCBP values ranged from -0.004 to 0.07 for the PIB negative group and from 0.18 to 1.06 for the PIB positive group. As expected, participants in the preclinical AD group also had more abnormal mean values of MCBP, and CSF $A\beta_{42}$, tau, and ptau₁₈₁ (Table 1). However, participants with preclinical AD at baseline recalled significantly fewer words on the free recall subtest of the Selective Reminding Test [33] ($p = 0.03$), and reported a marginally worse ($p = 0.052$) sense of direction as assessed by the Santa Barbara Sense of Direction Scale (Table 1). Participants with preclinical AD had lower near visual acuity values

compared to those without preclinical AD, although the difference did not reach statistical significance ($p = 0.083$).

All participants were followed for exactly 2.5 years, except for one participant who died approximately one year after data collection began. Because our major interest was change in DHQ and data logger variables across time, and our main analyses were conducted using linear mixed models, there was no “baseline” visit for these variables. Instead, y-intercepts generated by the mixed models, and differences between them, were taken to indicate whether there were statistical differences between the groups on the driving outcomes at the beginning of data collection. The y-intercept estimates yielded by the mixed models indicated that differences existed at the beginning of data collection on multiple driving variables between participants with and without preclinical AD (Table 2). Based on data from both self-report and the DRIVES data logger at the beginning of the follow-up period, participants with preclinical AD traveled more miles, but went to fewer places/unique destinations, drove on fewer days, and took fewer trips than participants without preclinical AD. The DRIVES data also demonstrated that persons with preclinical AD drove more miles per trip and spent more time driving per trip. The preclinical AD group reported a smaller driving space and more difficulty driving due to vision. Despite all participants indicating on the DHQ that they were always the driver when they used their vehicle, individuals with preclinical AD reported greater dependence on other drivers. The data logger indicated that persons with preclinical AD had fewer trips with any aggression (Table 2).

Generally, the linear mixed models showed little difference between the two groups in longitudinal change in driving behaviors over time (Table 3). However, data logger results showed that participants with preclinical AD showed a greater decline over the follow-up period in the number of days driven per month compared to those without preclinical AD (Fig. 1B) and the groups differed in the rate of change of the number of trips between one and five miles (Fig. 1C) This is particularly notable since the majority of trips made by participants across the 2.5-year observation period were below five miles, comprising approximately 70% of all trips (Table 2).

Given the differences between the preclinical and no preclinical groups at the baseline office testing session, we also examined correlations between the free recall and reported sense of direction scores with the driving outcomes. DHQ outcomes at baseline were used in these analyses. For DRIVES data logger outcomes, the mean for each outcome was calculated across all study months and these calculated means were used as dependent variables. Greater self-reported sense of direction was correlated with driving more days per week on the DHQ ($r = 0.46$, $p = 0.040$); and as recorded by the data logger, driving more days per month ($r = 0.46$, $p = 0.041$) and taking a greater number of trips between 5 and 10 miles ($r = 0.49$, $p = 0.030$).

DISCUSSION

Comparison of the estimates yielded by linear mixed models demonstrated that at the beginning of the follow-up period (i.e., y-intercepts) older adults with preclinical AD were

statistically different from those without preclinical AD on both self-reported driving habits and DRIVES daily driving behavior recordings. Furthermore, over time, older adults with preclinical AD experienced greater rates of change (slopes) in selected driving behaviors compared to those without preclinical AD.

These results confirm and extend our cross-sectional findings [24]. Despite a limited sample size, we found that older drivers with preclinical AD have decreased driving space and driving exposure (miles, trips, places visited, days/week) based on both self-report and objective measurement of driving behavior compared to those without preclinical AD. Drivers with preclinical AD also had a lower number of trips with aggressive behavior (especially, hard braking and sudden acceleration). Most notably, older adults with preclinical AD experience a greater rate of decline over two and one-half years in certain driving behaviors compared to those without preclinical AD, specifically in the number of days driven in a month and number of trips made between one to five miles.

Previous studies examining naturalistic driving behavior among persons with normal cognition and those with cognitive impairment have typically used in-car cameras [16–18, 38, 39], although use of OBD II-connected data loggers, as in this study, is increasing [19, 20]. The differences found in this study are consistent with previous studies comparing persons with symptomatic AD and controls [16], but provide further insight demonstrating that differences in naturalistic driving behavior are evident even during the long preclinical stage of AD. Participants with preclinical AD may be already self-limiting their daily driving behavior as evidenced by a lower number of overall trips and number of unique places from the DRIVES data logger and DHQ data. It has been suggested that changes in executive function would lead to later recognition of dangerous situations, and this might lead to more last-minute braking.

However, as in symptomatic AD, we found a lower rate of aggressive behaviors in participants with preclinical AD. This may suggest an active process of internal behavior monitoring [16, 39]. However, although participants with preclinical AD made fewer trips, they traveled more miles per trip than those without preclinical AD. The overall lower scores on the Santa Barbara Sense of Direction Scale [32], a self-report measure of environmental spatial ability, suggests that persons with preclinical AD may have more difficulty navigating their environment.

Emerging research is beginning to establish that changes in sensory (e.g., vision, hearing, olfaction) and motor function occur in the preclinical stage of AD, and may precede any measurable cognitive decline [40]. An increase in vision problems like cataracts and macular degeneration has been associated with preclinical AD [40]. Additionally, decline in strength, range of motion, and reaction time have been shown in individuals with preclinical AD [41, 42]. The visual system is the primary sensory skill used in driving and directly influences the motor system; deficits in one or both of these crucial systems will impact driving behavior. Thus, there may be an effect of vision problems linked to preclinical AD impacting driving space and exposure in our sample. Screenings of the visual system (e.g., visual acuity, contrast sensitivity) and motor system (grip strength, range of motion) are common in medical settings and Departments of Motor Vehicles for licensure renewal. Since function of

the sensory and motor systems are also age-dependent, understanding their individual and combined functions (e.g., reaction time) on driving in the context of preclinical AD may help to better understand driving decline and eventual driving retirement. The findings that greater self-reported sense of direction is associated with both driving on more days, as well as not having preclinical AD, suggest that larger samples should explore the comparative predictive ability of AD biomarkers and self-reported sense of direction on driving outcomes.

There are several limitations to this study. The sample size was small, and despite having results that were statistically significant, not all may be clinically meaningful. PET-PIB imaging is not readily available to the public nor is it reimbursable by health insurance. Since an objective method to detect the driver of the vehicle was unavailable, self-report of being the only driver of a vehicle may not always be accurate, and another driver (e.g., spouse, family, friend) may have made a small percentage of trips. Given the length of the longitudinal follow-up period, this is not expected to affect the study results. Finally, this study occurred in the greater St. Louis metropolitan area, therefore our findings may not be generalizable to regions with different geography or traffic density.

In conclusion, this study suggests that changes in driving behavior appear in preclinical AD and progress through conversion to dementia. Driving reduction during the preclinical stage may reflect awareness by the individuals of subtle intra-individual differences in driving skills and associated efforts to reduce driving risk. With progression of the AD pathological process, as executive function declines, drivers may take longer to anticipate dangerous situations and show increases in outcomes such as hard braking and crashes. Future longitudinal studies with larger samples and additional participant populations are needed to test these hypotheses.

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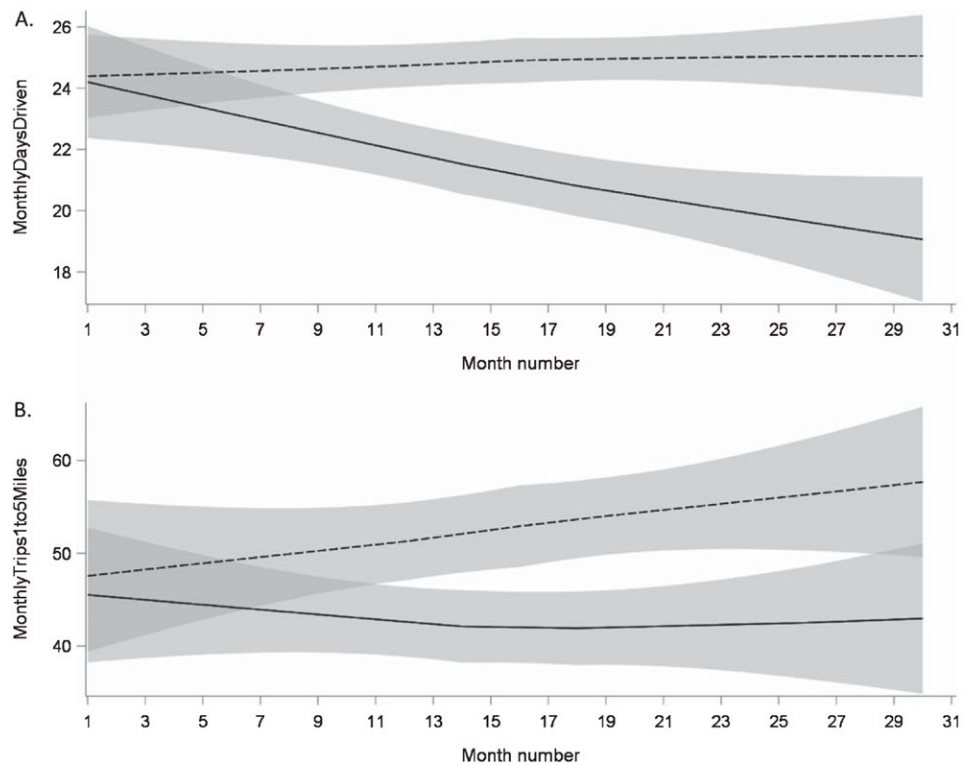


Fig. 1. Longitudinal change in selected DRIVES data logger outcomes for the preclinical (solid line) and control (dashed line) groups, showing A. differences in both intercept ($p > 0.001$) and slope ($p = 0.026$) for days driven per month; and B. differences in both intercept ($p < 0.001$) and slope ($p = 0.040$) for monthly trips between 1 and 5 miles.

Table 1

Demographics and baseline testing

	PIB Negative		PIB Positive		p	Total	
	N/Mean	%/SD	N/Mean	%/SD		N/Mean	%/SD
Age, y	71.9	3.1	74.5	4.3	0.139	73.2	3.9
Women, N	5	50.0%	2	20.0%	0.160	7	35.0%
APOE ε4, N	3	30.0%	4	40.0%	0.639	7	35.0%
Education, y	16.6	1.7	16.0	2.8	0.565	16.3	2.3
MCBP for PIB	0.03	0.03	0.46	0.26	<0.001	0.25	0.28
CSF Aβ ₄₂ , pg/mL	840.4	221.8	524.5	206.6	0.004	682.5	264.2
tau, pg/mL	227.9	64.3	523.5	285.1	0.001	375.7	251.9
p-tau ₁₈₁ , pg/mL	45.2	8.5	85.7	36.4	0.007	65.5	33.1
Selective Reminding Test - Free Recall	34.6	5.1	28.1	7.2	0.031	31.4	6.9
Animal Naming	23.0	5.8	19.6	4.6	0.166	21.3	5.4
Trailmaking A, s	27.7	7.4	32.7	10.7	0.240	30.2	9.3
Trailmaking B, s	79.4	39.8	92.1	41.1	0.516	85.8	39.8
Santa Barbara Sense of Direction	5.8	1.0	4.7	1.2	0.052	5.2	1.2
Near acuity	68.0	1.8	65.5	3.9	0.083	66.8	3.2
Far acuity	48.6	7.3	48.4	43.6	0.950	48.5	6.8
Contrast sensitivity	21.8	8.5	21.0	8.4	0.834	21.4	8.2

PIB, Pittsburgh Compound B; SD, standard deviation; MCBP, mean cortical binding potential; s, seconds.

Table 2

Y-intercept values yielded by the mixed models for driving outcomes

	PIB Negative		PIB Positive		p
	Mean	SE	Mean	SE	
Self-report on the DHQ (per average week)					
# miles	174.43	55.60	186.71	55.47	0.002
# trips total	10.03	1.17	9.22	1.65	<0.001
# places visited	5.19	0.71	4.73	0.71	<0.001
Driving space	5.38	0.28	4.95	0.28	<0.001
Dependence on other drivers	1.00	0.12	1.18	0.12	<0.001
Average days/week usually drive?	6.35	0.59	5.73	0.58	<0.001
Difficulty driving due to vision	95.96	3.82	98.69	3.82	<0.001
DRIVES data logger (per month)					
# miles	847.69	250.09	891.57	250.38	<0.001
# trips total	122.04	14.92	106.79	14.95	<0.001
# trips <1 mile	26.88	5.89	21.43	5.90	<0.001
# trips 1–5 miles	46.83	7.26	44.97	7.27	<0.001
# trips 5–10 miles	25.20	2.99	14.97	3.00	<0.001
# trips 10–20 miles	13.44	3.57	15.88	3.57	<0.001
# trips 20 + miles	9.56	5.19	10.14	5.19	0.032
# hours driven	29.81	5.79	27.04	5.80	<0.001
# days driven	24.33	1.33	24.03	1.33	<0.001
Mean miles/trip	6.37	1.49	8.35	1.49	<0.001
Mean hours/trip	0.23	0.03	0.26	0.00	<0.001
Mean trips/day	4.91	0.42	4.34	0.32	<0.001
Mean trips at night	0.06	0.01	0.05	0.01	<0.001
# unique destinations	44.42	5.47	39.40	5.48	<0.001
Mean trips with speeding	3.83	1.98	4.19	1.98	0.036
Mean trips with sudden acceleration	17.20	6.26	10.09	6.27	0.020
Mean trips with hard braking	13.11	2.28	10.91	2.29	<0.001
Mean trips some aggression	27.44	6.38	20.75	6.38	<0.000

AD, Alzheimer's disease; DHQ, Driving Habits Questionnaire; DRIVES, Driving Real-World In-Vehicle Evaluation System.

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Table 3

Slope (change/year) values yielded by the mixed models for driving outcomes

	No preclinical AD		Preclinical AD		Prob.
	Mean	SE	Mean	SE	
Self-report on the DHQ (per average week)					
# miles	19.31	28.95	13.61	28.93	0.890
# trips total	0.94	0.85	0.79	0.79	0.898
# places visited	-0.16	0.25	0.20	0.25	0.326
Driving space	-0.17	0.15	-0.31	0.15	0.555
Dependence on other drivers	0.08	0.14	0.11	0.13	0.913
Average days/week usually drive?	-0.07	0.21	0.06	0.21	0.661
Difficulty driving due to vision	-0.38	3.55	-1.69	3.55	0.794
Data logger (per month)					
# miles	-0.28	7.22	-9.08	7.45	0.367
# trips total	0.25	0.43	-0.70	0.45	0.147
# trips < 1 mile	-0.05	0.13	-0.15	0.13	0.307
# trips 1–5 miles	0.36	0.19	-0.22	0.19	0.040
# trips 5–10 miles	-0.01	0.08	-0.14	0.09	0.280
# trips 10–20 miles	0.03	0.07	-0.16	-0.16	0.102
# trips 20 + miles	-0.07	0.14	-0.09	0.14	0.950
# hours driven	-0.003	0.16	-0.22	0.17	0.349
# days driven	0.02	0.05	-0.17	0.06	0.026
Mean miles/trip	-0.01	0.04	-0.04	0.04	0.594
Mean hours/trip	-0.0002	0.001	-0.001	0.001	0.572
Mean trips/day	0.005	0.01	0.001	0.01	0.869
Mean trips at night	-0.0002	0.0004	0.005	0.0005	0.259
Driving area, m ²	8.10E+07	2.63E+08	-4.99E+08	2.72E+08	0.136
Driving perimeter, m ²	2,993.02	4,592.28	-4,947.07	4,852.93	0.252
# unique destinations	0.11	0.17	-0.26	0.18	0.183
Mean trips with speeding	0.00	0.03	0.06	0.03	0.516
Mean trips with sudden acceleration	-0.41	0.14	-0.18	0.14	0.262

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	No preclinical AD		Preclinical AD		Prob.
	Mean	SE	Mean	SE	
Mean trips with hard braking	-0.16	0.06	-0.11	0.06	0.543
Mean trips some aggression	-0.39	0.14	-0.15	0.15	0.259

AD, Alzheimer disease; DHQ, Driving Habits Questionnaire; DRIVES, Driving Real-World In-Vehicle Evaluation System.