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Alzheimer's & Dementia ■ (2017) 1-7

Alzheimer's & Dementia

Featured Article

Driving cessation over a 24-year period: Dementia severity and cerebrospinal fluid biomarkers

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Abstract

Introduction: With 36 million older adult U.S. drivers, safety is a critical concern, particularly among those with dementia. It is unclear at what stage of Alzheimer's disease (AD) older adults stop driving and whether preclinical AD affects driving cessation.

Methods: Time to driving cessation was examined based on Clinical Dementia Rating (CDR) and AD cerebrospinal fluid biomarkers. 1795 older adults followed up to 24 years received CDR ratings. A subset (591) had cerebrospinal fluid biomarker measurements and was followed up to 17 years. Differences in CDR and biomarker groups as predictors of time to driving cessation were analyzed using Kaplan-Meier curves and Cox proportional models.

Results: Higher CDR scores and more abnormal biomarker measurements predicted a shorter time to driving cessation.

Discussion: Higher levels of AD biomarkers, including among individuals with preclinical AD, lead to earlier driving cessation. Negative functional outcomes of preclinical AD show a nonbenign phase of the disease.

Ms. Stout reports no conflicts of interest. Dr. Babulal reports no conflicts of interest. Mr. Ma reports no conflicts of interest. Dr. Carr receives support from NIA (R01 AG043434; Roe-PI and K23; Betz-PI), NEI (R01 EY026199-01; Bhorade-PI), Missouri Department of Transportation (16-M2PE-05-002; Carr-PI, 16-DL-02-002; Carr-PI and 16-DL-02-003; Barco-PI), State Farm Insurance (Carr-PI), and HealthSouth (Carr-PI) and has past Consulting Relationships in the last 2 years with The Traffic Injury Research Foundation, Medscape, the AAA Foundation for Traffic Safety and the American Geriatric Society. Dr. Head reports no conflicts of interest. Dr. Grant reports no conflicts of interest. Dr. Williams reports no conflicts of interest. Dr. Holtzman receives funding from C2N Diagnostics SAB, Genentech SAB, and Neurophage SAB. He is a consultant for AbbVie. His laboratory receives grants from the NIH, the JPB Foundation, Cure Alzheimer's Fund, the Tau Consortium, Eli Lilly, and C2N Diagnostics. Dr. Fagan is on the scientific advisory boards of IBL International and Roche and is a consultant for AbbVie, Novartis, and DiamiR. Dr. Fagan reports no conflicts of interest. Dr. Morris and his family do not own stock or have equity interest (outside of mutual funds or other externally directed accounts) in any pharmaceutical or biotechnology company. Dr. Morris has participated or is currently participating in clinical trials of antidementia drugs sponsored by the following companies: Janssen Immunotherapy, Pfizer, Eli Lilly/Avid Radiopharmaceuticals, SNIFF (Study of Nasal Insulin to Fight Forgetfulness) study, and A4 (Anti-Amyloid Treatment in Asymptomatic Alzheimer's disease) trial. Dr. Morris has served as a consultant for Lilly, USA, and Charles Dana Foundation. He receives research support from Eli Lilly/Avid Radiopharmaceuticals and is funded by NIH grants #P50AG005681; P01AG003991; P01AG026276; and UF1AG032438.

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https://doi.org/10.1016/j.jalz.2017.11.011
1552-5260/

Keywords: Alzheimer's disease; Biomarker; Driving; Driving cessation; Older adults; Aged; Preclinical; Cerebrospinal fluid; Amyloid β; Tau; ptau

1. Introduction

The decision to stop driving is a difficult one for older adults (OAs), their families, and their clinicians. Many OAs are optimistic that they will continue to drive into the foreseeable future [1]. However, there is an elevated crash risk and fatality rate for drivers aged over 65 years [2,3]. Importantly, concerns about driving safety must be balanced with potential negative effects linked to driving cessation [4]. OAs who stop driving have higher rates of depression, faster decline in overall health, higher rates of admission to long-term care, and higher overall rates of mortality [4–6].

It is well known that active dementia is associated with worse driving performance [7–10], and that persons with dementia will eventually need to stop driving altogether. However, little is known about how dementia severity relates to when an OA needs to cease driving.

In addition, driving difficulties have recently been linked to preclinical Alzheimer's disease (AD) [11–13]. Preclinical AD is signified by abnormal AD biomarkers in the presence of cognitive normality [14,15]. Cerebrospinal fluid (CSF) AD biomarkers reflect the accumulation of amyloid and tau lesions and provide a measure of actual underlying pathology [16,17]. In particular, CSF tau/amyloid β $(A\beta)_{42}$ and phosphorylated tau $(ptau)_{181}/A\beta_{42}$ ratios are believed to be strong predictors of the presence of preclinical AD [16,17]. Cognitively intact OAs with more abnormal biomarker values make more driving errors on a standardized road test and are more likely to have poorer performance on that test longitudinally than those with normal values [11–13]. Because AD biomarkers are linked to driving performance, early driving cessation may also be a functional outcome of preclinical AD.

Given the safety and public health implications of driving cessation among OAs, there is an urgent need to better understand the link between driving cessation and the factors that predict it. We examined the time from baseline to driving cessation as a function of AD CSF biomarker ratios in 591 participants and Clinical Dementia Rating (CDR) scores in 1795 participants, over a period of up to 24 years. We hypothesized that individuals with higher baseline CDR scores would stop driving earlier, and that CSF biomarkers would predict time to driving cessation independent of CDR score.

2. Methods

2.1. Participants

OAs (age ≥55 years) were enrolled in studies conducted at the Knight Alzheimer's Disease Research Center at Washington University. Participants, along with a required collateral source (CS), were enrolled in studies without knowledge of whether or not they had abnormal biomarkers. Participants completed an annual clinical assessment in which experienced clinicians classified participants using the CDR [18] based on information from the participant, as well as a CS who knew the participant well and who can discuss intraindividual changes in the participant's cognition. CSs have been shown to be highly accurate and were individuals who generally interacted with the participant on a daily basis; had known the participant for 30–60 years; and were most often a female (70%), adult child (38%), or a spouse (46%) [19].

The CDR has well-documented reliability and validity [20–22]. A global CDR, which can be used to compare intraindividual change over time, is derived from scores in the areas of memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care [18,22]. Participants were given an annual CDR of 0, 0.5, 1, 2, or 3, representing cognitively normal, very mild dementia, mild dementia, moderate dementia, and severe dementia, respectively. During each annual clinical assessment, which lasts approximately 90 minutes, as part of the Initial Subject Protocol [23], the CS was asked whether the participant ever drove, whether they drive now, and if so, whether there are problems or risks because of poor thinking. CDR data were available from October 14, 1991, through December 31, 2015.

CSF was acquired after an overnight fast via standard lumbar puncture by experienced neurologists using a 22-gauge Sprotte spinal needle to draw 20–30 mL of CSF [24]. CSF analytes ($A\beta_{42}$, tau, and $ptau_{181}$; Innotest, Fujirebio [formerly Innogenetics], Ghent, Belgium) were measured using enzyme-linked immunosorbent assays. CSF samples are gently inverted and centrifuged at low speed to preclude gradient effects. They are then frozen at −84°C after aliquoting into polypropylene tubes. All biomarker assays include a common reference standard, within-plate sample randomization and strict standardized protocol adherence [16]. CSF data were available from May 26, 1998, through December 31, 2015.

All research protocols were approved by the Washington University Human Research Protection Office, and signed informed consent was obtained from all participants.

2.2. Statistical analysis

Kaplan-Meier curves were used to examine whether individuals with higher baseline CDR scores stop driving earlier compared with those with lower CDR scores. Because only three participants had a CDR ≥2, the analyses were restricted to those with baseline CDRs of 0, 0.5, and 1. All