

Leukoaraiosis Predicts Wrong-Way Entry and Near One on Highways for Healthy Drivers

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Abstract

We investigated the correlation between leukoaraiosis (LA) grades and wrong-way entry on highways, main roads, or narrow roads with one-way using a large-scale data of brain healthcare checkups with magnetic resonance imaging (MRI). Multiple and large multiple LA were significantly associated with wrong-way entry and near one on highways, not with wrong-way entry on main and narrow roads. In addition to conventional measures such as legal penalties for drunken driving, lifestyle improvement and medical treatments to suppress LA progress may be useful measures against wrong-way driving on highways.

Keywords: Wrong-way entry • Highways • Leukoaraiosis • Healthy drivers • MRI

Introduction

Traffic crashes caused by wrong-way entry on highways are relatively uncommon. They only make up about 0.3% of all motor vehicle crashes in the USA [1]. However, they have a very high fatality and injury rate. Wrong-way collisions are estimated to comprise roughly 3% of motor vehicle fatalities on highways-about 300-400 deaths a year, according to the National Transportation Safety Board (NTSB) [2]. The majority of wrong-way crashes on highways are destined to be head-on collisions at highway speeds of more than 70 miles per hour, meaning that a head-on collision with higher speeds is extremely damaging and unavoidably fatal. In Japan which has the fastest aging rate in the world, wrong-way crashes on highways or main roads caused by older drivers has been one of the national urgent issues [3]. Since the compulsory implementation of cognitive examinations for older drivers when renewing their licenses, the number of wrong-way crashes caused by dementia drivers has decreased dramatically [4], but there is still no end to hearing the tragic news of wrong-way entry involving drivers without dementia. In general, the wrong-way entry on highways occurs when a driver accidentally enters in the opposite direction to the on-ramp or toll gate and when leaving rest areas on highways. There are several reasons why a driver causes wrong-way entry as follows; drunk or impaired driving with cognition decline, driving while sleepy, unfamiliarity with an area, inexperienced or first-time drivers, and road-infrastructure problems such as poorly marked highway entrance signs and lack of stoplights [5]. However, no study has investigated the brain conditions of drivers which affect dangerous driving behaviors such as the wrong-way entry on highways.

Leukoaraiosis (LA), cerebral white matter hyper intensity, is a common ischemic region in the brain diagnosed by magnetic resonance imaging (MRI) [6]. LA is increasing in frequency according to age and is found in at least 40% of apparently healthy adults over the age of 50, with some reports estimating as high as 95% in the elderly [7,8]. LA can be classified

into four grades, none, single or minimal, multiple, and multiple multiples, according to the degree of LA within the cerebral white matter [9]. Large multiple LA has been clinically reported to be significantly associated with recurrent cerebral stroke and vascular dementia [10]. Nevertheless, it is true that many adults with multiple or large multiples of LA led normal lives without neurological disorders. Most healthy adults with LA live mostly asymptotically. In other words, they keep driving without knowing that LA exists in their brains. In our previous study, traffic crashes at crossroads over the past 10 years were found to be significantly associated with multiple or large multiple LA from 3,930 MRI data of healthy middle-aged drivers [11]. In more recent years, a driving experiment using an actual vehicle on a closed-circuit course showed that older drivers with LA degraded safe driving performance such as appropriate speeding, steering, and signaling [12,13]. Thus, LA may be a candidate for the brain conditions involved in wrong-way entry on highways. In the present study, the correlation between LA and wrong-way entry on highways in comparison with main roads with multiple lines and narrow roads with one-way was investigated using a large-scale sample of brain healthcare checkups with MRI, which have been uniquely developed for the prevention of subarachnoid hemorrhage due to ruptured cerebral aneurysms in Japan.

Methods

Data

Data were collected between April 2014 and March 2019 from Kochi Kenshin Clinic (KKC), affiliated with Kochi University of Technology. From KKC, we enrolled 5446 healthy participants (male; 3,054, female; 2,392, age; 20-57 years, average age; 52.7 years; median age; 51 years) for wrong-way of entry on main roads with multiple lines and narrow roads with one-way from April 2014 through March 2016, while we enrolled 11170 healthy participants (male; 6,378, female; 4792, age; 20-87, average age; 52.5 years; median age; 51 years) for wrong-way entry and near one on highways from April 2016 through March 2019. Due to the small number of wrong-way entries on highways, the recruitment period for highways was extended more than double to main or narrow roads. All of them underwent MRI examinations for brain healthcare checkups and answered questionnaires regarding wrong-way entry and/or near one. They had no medical history of neurological disorders including cerebrovascular diseases, arachnoid cysts, brain tumors, and hydrocephalus. They lived in Kochi prefecture in Japan and drove at least one time per week. Professional drivers such as taxis and long-distance bus drivers were excluded from the study. The term healthy was defined as the absence of symptoms or gross neurological deficits before and at the time of enrollment in the study.

Detailed information on driving frequency and wrong-way entries including

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near ones experienced during the past 10 years was gathered from personal interviews conducted at KKC by a dedicated assistant. Driving exposure was classified into 4 categories according to total driving hours per week: 1, two hours per week; 2, five hours per week, 3, ten hours per week; and 4, more than ten hours per week. The presence or absence of wrong-way entry and near one on highways, main roads with multiple lines, and narrow roads with one-way during the past ten years were questioned.

Leukoaraiosis grade by MRI

A 1.5-T MRI system (ECHELON Vega; Hitachi Medical Corporation, Tokyo, Japan) was used to perform MRI examinations. The imaging protocol included T2-weighted spin-echo [repetition time/echo time (TR/TE)=5800/96 ms], T1-weighted spin-echo (TR/TE=520/14 ms), and FLAIR (TR/TE=8500/96 ms; inversion time=2100 ms) images. LA was defined as a focal lesion 2 mm in diameter, with hyperintensity on T2-weighted and FLAIR images and without prominent hypointensity on T1-weighted images. The thickness of MRI slices was 4 mm, and 3 sections of the axial, sagittal, and coronal 2D views were used for LA diagnosis. LA grade was classified into four as follows by reference to Hachinski criteria [14]. The single or minimum was defined as a single dot of hyperintensity in the subcortical white matter (SWM) or rim around lateral ventricles, and the multiple was defined as plural dots and patches in the SWM or confluence of periventricular hyperintensity. The large multiple was defined as more extent than the multiple, which is equal to grade 3 of Hachinski criteria. A trained neurosurgeon (K.P.) first diagnosed LA grades and then another radio-neurologist who was blinded to the wrong-way entry and near one data assessed the LA grades. When the two investigators had differing opinions, the final grades were determined by consensus.

Statistical analysis

Multiple logistic regression analysis was applied to examine whether LA was a significant predictor of involvement in

Table 1. Multiple logistic analyses of wrong-way entry and near one on highways, wrong-way entry on roads with multiple lanes, and wrong-way entry on narrow roads with one-way

Explanatory Variables	Wrong-way Entry and Near One on Highways		Wrong-way Entry on Roads with One-way		Wrong-way Entry on Roads with Multiple Lanes	
	Cases/ Participants	Adjusted OR (95% CI)	Cases/ Participants	Adjusted OR (95% CI)	Cases/ Participants	Adjusted OR (95% CI)
Gender and Age						
Male or Female, Age <40	12/842	1.68 (0.86-3.28)	18/424	1.16 (0.68-1.97)	4/424	0.81 (0.28-2.38)
Male, Age=40-59	39/4148	1 [Reference]	73/1985	1 [Reference]	23/1985	1 [Reference]
Female, Age=40-59	47/3332	1.52 (0.99-2.34)†	72/1705	1.15 (0.82-1.61)	27/1705	1.39 (0.79-2.46)
Male, Age ≥ 60	32/1809	1.68 (1.03-2.75)*	21/857	0.65 (0.39-1.08)	8/857	0.82 (0.36-1.86)
Female, Age ≥ 60	23/1039	2.20 (1.30-3.74)**	15/475	0.84 (0.47-1.47)	3/475	0.55 (0.16-1.87)
Leukoaraiosis Classification						
None	80/7047	1 [Reference]	135/3567	1 [Reference]	45/3567	1 [Reference]
Single	18/1130	1.34 (0.79-2.27)	17/537	0.90 (0.54-1.49)	4/537	0.61 (0.21-1.71)
Multiple or large multiple	55/2993	1.48 (1.02-2.14)*	47/1342	1.04 (0.73-1.48)	16/1342	1.05 (0.57-1.93)
Driving Exposure ^a						
1	62/4822	1 [Reference]	95/2514	1 [Reference]	29/2514	1 [Reference]
2	41/3027	1.07 (0.72-1.59)	48/1290	0.98 (0.69-1.39)	14/1290	0.94 (0.49-1.80)
3 or 4	50/3321	1.25 (0.86-1.81)	56/1642	0.90 (0.65-1.26)	15/1077	1.16 (0.66-2.05)
Total	153/11170		199/5446		65/5446	

Notes. a: Frequency of driving (1=Two hours or less per week, 2=Five hours or less per week, 3=Ten hours or less per week, 4=More than ten hours per week). †: $p < 0.1$, *: $p < 0.05$, **: $p < 0.01$.

- (i) Wrong-way entry and the near one on highways,
- (ii) Wrong-way entry on main roads with multiple lines
- (iii) Wrong-way entry on narrow roads with one-way.

In analysis (i), the objective variable was defined by allocating a value of 1 to the respondents who had caused at least 1 wrong entry and near one in the last 10 years and a value of 0 otherwise. In analyses (ii) to (iii), a value of 1 was allocated to the respondents who had wrong entries of type (ii), or (iii) in the last 10 years. For each analysis, gender and age, LA grades, and driving exposure were included as explanatory variables. The variables of gender and age were classified into five, male or female less than 40 years old, male with 40-59, female with 40-59, male more than 60, and female more than 60. The variables of LA grade were classified into three, none, single, and multiple or large multiples. The variables of driving exposure were classified into three, two hours or less per week, five hours or less per week, and more than five hours per week. The values of gender and age, LA grade, and driving exposure were categorized into 5, 3, and 3 classes; therefore, 4, 2, and 2 dummy variables, respectively, were defined and included in the models. The program was written in Mathematica version 6.0 (Wolfram Research, Inc., Champaign, IL, USA).

Results

Multiple logistic analyses of wrong-way entry and near one on highways, and wrong-way entry on main and narrow roads

As shown in Table 1, there were 10 cases of wrong-way entry and 143 cases of near-one on highways. In the combination of 10 and 143 cases on highways, men and women aged ≥ 60 years and multiple or large multiple LA showed significant associations. On the other hand, there was no significance on both main and narrow roads.

Gender, age, leukoaraiosis grade, and personal causes of 10 cases having wrong-way entry on highways

In 10 cases, 1 was diagnosed as large multiples and 6 were multiple, while

Table 2. Ten cases of wrong-way entry on highways

Case No	Gender	Age	Wrong-way Entry Type	LA Grade	Personal causes*
1	F	62	A	multiple	first driving out of Kochi prefecture
2	M	64	A	multiple	first driving out of Kochi prefecture
3	M	60	A	none	first driving out of Kochi prefecture
4	F	40	A	none	misunderstood as a main road
5	F	63	A	single	first driving out of Kochi prefecture
6	M	70	B	large multiple	no answer
7	M	63	A	multiple	difficult to understand traffic signs
8	F	61	A	multiple	difficult to understand traffic signs
9	F	57	A	multiple	difficult to understand traffic signs
10	F	57	A	multiple	conversation while driving

F; female, M; male. A; at a toll gate, B; on-ramp. *; the cause why a driver with a wrong entry on highways thinks.

Discussion

Based on our research strategy “The brain controls driving, therefore, we need to examine the brain directly”, we are investigating the relationship between driving behaviors and brain MRI data [11-13]. In general, MRI examination is very expensive and difficult to use for research data, but it is relatively easy to collect MRI data from brain healthcare checkups in Japan [11]. However, a big problem exists because dangerous cases such as the wrong-way entry on highways are extremely uncommon in ordinary drivers who undergo brain healthcare checkups. Only 10 cases were obtained even after a five-year recruitment period (Table 2). The incidence of multiple and large multiple LA was high in 7 of 10 cases. It is, however, too small to analyze statistically. Only when combining 10 cases and 143 cases of near wrong-way entry, we found a significant association. Further accumulation of data is necessary for validation. From previous research results [11-13], we believe that LA is one of the brain factors of dangerous driving performance. Japan's police authorities have not released the traffic accident database for research purposes. Confirmation is strongly awaited by direct MRI investigation of drivers involved in traffic crashes from all over the world.

Recent functional MRI studies have shown correlations between LA and brain dysfunction. This is because the damaged vessels in LA yield an insufficient blood supply in the white matter including neuronal fibers, which can lead to dysfunction of the neuronal network [15,16]. LA is regarded to reduce executive functioning such as planning, prioritization, risk management, processing speed, and attention that are necessary for safe driving performances through the rapid and accurate exchange of information in the white matter [17,18]. More recently, the driving performance of 101 older drivers using actual vehicles on a closed circuit has shown that the LA volume values in the parietal lobe being involved in spatial cognition and the occipital lobe in dynamic visual cognition are significantly correlated to the degradation of safe driving performance [19]. In the present study, we used qualitative LA assessment and obtained relatively lower values of the adjusted odd ratios (Table 1). The next study needs quantitative LA evaluation per lobes of the brain for more accurate and reproducible results.

A significant relationship with LA was found only for highways, not for main roads including multiple lines or narrow roads with one-way. We often drive faster on highways than on other roads. We may be strangers around highways as compared with other roads. These situations may interfere with quick decisions for driving entry through the brain function.

1 was single and 2 as none (Table 2). With regards to the sites of wrong-way entry, nine cases occurred at toll gates and one case on-ramp where multiple lanes intersect. Most of the males and females were more than 60 years old.

LA generally increases with aging but the LA development varies greatly between individuals and depends on healthcare and medical treatments regardless of age [14]. LA is greatly affected by disordered lifestyles such as smoking and metabolic syndrome, and lifestyle-related diseases such as hypertension and diabetes [6-8]. Especially, people who have hypertension are up to 14 times more likely to develop LA than those who have no hypertension [20]. Comprehensive countermeasures include blood pressure and sugar control with or without drug treatment, suppression of excessive salt intake, regular physical exercise, dietary control, and a cessation of smoking. On the other hand, conventional countermeasures for traffic crashes including wrong-way entry are as follows; heightened awareness of traffic rules, punitive approaches to drunk drivers, improved road infrastructure, increased use of seatbelts, and enhanced vehicle safety [5,21]. All of them lead to no countermeasures against LA. The present study showed the possibility that LA measures such as lifestyle improvement and drug treatment may lead to the prevention of wrong-way entry and traffic crashes. Therefore, MRI examinations may enable the identification of potentially dangerous drivers through LA grading or LA volume values and may contribute to preventing wrong-way entry on highways through LA management with healthcare guidance and medical practice.

Conclusion

The study findings demonstrated the impact of LA on wrong-way entry and near one on highways. Whether living in urban or in rural areas, driving a car on highways is an essential activity for modern people. The early detection of LA in the brain using MRI and the subsequent treatment of LA may be useful for avoiding fatal crashes by wrong-way driving.

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Author Contributions

K.P. is the lead author, and made the research design, recruited all

participants, collected all the data, and wrote the manuscript text. Y.N. conducted all the analyses, prepared the figures and tables, and partially wrote the manuscript text.

Conflicts of Interest

The authors declare no conflict of interest.

Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki, and approved by the ethics committee of the Kochi University of Technology.

Informed Consent Statement

Each participant gave written informed consent to participate in the study which was conducted following the Declaration of Helsinki and approved by the ethics committee of Kochi University of Technology.

Data Availability Statement

After publication, data will be available to any researcher who provides a methodologically sound study proposal to the corresponding author that is approved by the central study team.

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