

Received: 2018.01.29 Accepted: 2018.05.02 Published: 2018.08.10

e-ISSN 1643-3750 © Med Sci Monit. 2018: 24: 5566-5572 DOI: 10.12659/MSM.909245

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Relationship Between the Incidence of Road **Traffic Accidents, Psychological Characteristics,** and Genotype in Bus Drivers in a Chinese **Population**

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Corresponding Author: Source of support: This work was supported by The Nature Science Foundation of China (NSFC) (Grant No. 81560528), Innovation Project of Guangxi Graduate Education (Grant No. YCBZ2017046) and Open Research Project from Key Laboratory of High Incidence Diseases Prevention

and Control of Guangxi Universities and Colleges (Grant No. 02402214003-1604)

Background:

The aim of this study was to determine the association between the incidence of road traffic accidents, psychological characteristics, and genotype in bus drivers in a Chinese population.

Material/Methods:

Bus drivers who had been involved in road traffic accidents (n=106) (the study group), and bus drivers with no history of road traffic accidents (n=106) (the control group) completed demographic questionnaires, the Eysenck Personality Questionnaire (EPQ) and the Type-A behavior pattern (TABP) evaluation. Serum 5-hydroxytryptamine (5-HT) (serotonin), and 5-hydroxytryptophan (5-HTP) levels were measured by high-performance liquid chromatography-fluorescent detection (HPLC-FLD). Serotonin transporter promoter-linked polymorphism region (5-HTTLPR) and the 521 C/T single nucleotide polymorphism (SNP) in the regulatory region of the dopamine D4 receptor gene (DRD4-521 C/T) were measured using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Results:

After accounting for potential confounders, extroversion, psychopathy, neuroticism and time hurrying (impatience) were significant factors associated with road traffic accidents in bus drivers (adjusted OR: 1.268, 95% Cl: 1.133-1.419; adjusted OR: 1.177, 95% Cl: 1.028-1.347; adjusted OR: 1.092, 95% Cl: 1.005-1.187; adjusted OR: 1.123, 95% CI: 1.025–1.230, respectively). Reduced serum levels of 5-HT and 5-HTP were significantly associated with the incidence of road traffic accidents (adjusted OR: 0.985, 95% CI: 0.973-0.997; adjusted OR: 0.982, 95% CI: 0.969-0.994, respectively).

Conclusions:

Psychological characteristics associated with the 5-HTTLPR and DRD4-521 C/T genotypes, including extroversion, psychopathy, neuroticism, and time hurrying (impatience), and low serum levels of 5-HT and 5-HTP in bus drivers were associated with an increased risk of road traffic accidents.

MeSH Keywords:

Accidents, Traffic • Genetic Association Studies • Psychology

Full-text PDF:

https://www.medscimonit.com/abstract/index/idArt/909245











Background

Road traffic accidents and fatalities from these accidents represent a serious public health problem in China. Although risk factors for road traffic accidents include factors related to the experience and expertise of the person driving the vehicle, the condition of the vehicle and the road, and environmental factors, driver error is a major contributory factor [1]. A previously published study has shown that the performance of the driver was the most common causative factor in approximately 86% of all road traffic accidents in China [2].

However, previous studies on the causes of road traffic accidents have paid little attention to road traffic accidents and drivers of public transport vehicles, including bus drivers. As a large developing country, buses are the main means of road transport in Chinese cities and are part of the city public transportation system in China. From the few available studies in the literature, the frequency of road traffic accidents involving buses was shown to be common in China [3]. Therefore, a positive contribution to public health associated with the use of public transport might be made if the risk factors associated with accidents caused by bus drivers could be identified.

The psychological characteristics of vehicle drivers, including bus drivers, have previously been recognized to be important individual factors that are closely associated with high-risk driving behaviors and road traffic accidents [4-6]. Previously published studies have shown that certain psychological characteristics in bus divers could predict the occurrence of road traffic accidents [7,8]. Also, a recent meta-analysis of 47 studies concluded that the psychological characteristics of the drivers, including having an extrovert personality and increased neuroticism, were significantly associated with an increased incidence of road traffic accidents [9]. In drivers of urban transportation systems, the main risk factors resulting in accidents have been reported to include driving for long periods of time, driving conditions that required high levels of concentration, driver fatigue, and stressful working conditions [10]. These findings might suggest that impatience, anger, hostility, anxiety, and depression are important considerations in the cause of road traffic accidents, including in bus drivers [10].

There is also published evidence for genetic influences on psychological characteristics, which mean that genotype analysis may predict individual behavior when driving. Recent studies have focused on investigating the relationship between common genetic polymorphisms and specific psychological characteristics for distinct candidate genes, with some studies showing that the neurotransmitters 5-hydroxytryptamine (5-HT) (serotonin), 5-hydroxytryptophan (5-HTP), and dopamine play an important role in personality traits [11,12]. Psychological characteristics have been mainly studied in association with

the serotonergic system because neurotransmission mediated by 5-HT contribute to several psychological functions, such as emotional instability, anxiety, and depression [13]. Previously published studies have also shown that low levels of platelet 5-HT, and 5-HT metabolites, are associated with forms of impulsive or psychopathic behavior [14].

Among the genes of the 5-HT system, the *5-HTT* gene has received attention, because the 5-HTT protein is involved in the reuptake of 5-HT from the synaptic cleft. The *5-HTT* gene has several polymorphisms, with the most frequently studied being the serotonin transporter promoter-linked polymorphism region (5-HTTLPR), due to its association with negative psychological traits [15]. Also, 5-HTTLPR plays an important role in serotonergic neurotransmission by facilitating the reuptake of 5-HT. The most recent meta-analysis data on studies of the role of 5-HTTLPR have confirmed a strong correlation between the S/S genotype of the 5-HTTLPR, depression, and anxiety [16]. However, the association between the S/S genotype of 5-HTTLPR and psychological characteristics has been reported to have varied associations in subsequent studies [17,18].

The psychological characteristics of psychopathy, including extrovert behavior, impulsivity, and novelty-seeking behavior, have been linked to dopaminergic systems. The dopamine receptor is expressed in limbic areas of the brain involved in cognition and emotion and is shown to modulate motivational behaviors [19]. Variations within the dopamine D4 receptor gene, DRD4, have been associated with the psychological characteristics of extraversion. Recently, some evidence has emerged from published studies that the DRD4 gene promoter region polymorphisms contribute to personality and that the DRD4-521 C/T single nucleotide polymorphism (SNP) was and associated with psychological traits of novelty-seeking and extrovert behaviors [20,21]. The Japanese population was found to have a significant association between the CC genotype of the -521 SNP in the DRD4 gene promoter region and the human psychological characteristic of novelty-seeking, which is a personality trait associated with the need for novel stimulation, a low boredom threshold, impulsive decision making, loss of control of temper [22]. The DRD4-521 C/T polymorphism might have potential functional importance because it occurs in a region regulating transcriptional activity.

Heritability studies have shown that genetic determinants can contribute substantially to changes in levels of anxiety and depression, but there remains no clear consensus on the role of any individual gene variant in the modulation of psychological characteristics, even though 5-HTTLPR and the *DRD4-521* C/T promoter variant appear to be related to anxiety and impulsivity, respectively [22].

Therefore, the aim of this study was to determine the relationship between the association of road traffic accidents, psychological characteristics, and genotype in bus drivers in a Chinese population. The study was designed to compare the psychological characteristics, serum levels of 5-HT and 5-HTP, and the gene polymorphisms, 5-HTTLPR and *DRD4-521* C/T, in bus drivers who experienced road traffic accidents with bus drivers who had no history of road traffic accidents.

Material and Methods

Study design and participants, the study group and the control group

Road traffic accidents data for this study were obtained from the Traffic Police Corps of Guangxi, China, a large database of retrospectively collected primary records that contained the date and details of road traffic accidents from March 2014 to November 2016. This study was approved by the Ethical Committee of Guangxi Medical University (Approval Number: 2015/ethics/SPH/124).

The study participants were bus drivers working in public transportation companies from Guangxi Province. A case-controlled study design was used. In the study group of bus drivers (n=106), the inclusion criteria were a history of ≥3 road traffic accidents in the previous three years, which were associated with driver factors that included speeding, rear-ending, and bus crashes [23]. Episodes of drunk driving were excluded. The control group of bus drivers (n=106) had no road traffic accidents in the same period.

Data collection for the study group and control group

Data were collected through a self-reported questionnaire that consisted of three components: demographic characteristics, the Eysenck Personality Questionnaire (EPQ), and the Type-A behavior pattern (TABP) evaluation. The demographic characteristics of the bus drivers included gender, age, driving experience, the level of education, and the number of road traffic accidents. The psychological characteristics of the bus drivers were assessed by the EPQ and TABP evaluation methods, which were used to examine the relationship between the participant psychological characteristics and driving behavior. The EPQ scale included four personality traits that have been demonstrated to be related to driving safety in China [24]. These four traits were the degree of extrovert behavior, psychopathy, neuroticism, and dishonesty (lying). The TABP evaluation included the characteristics of time hurrying (impatience), competitiveness, hostility, and dishonesty; all the bus drivers who were involved in the study completed the TABP evaluation [25].

Study personnel, participant blood sampling, questionnaires, and interviews

The investigators were postgraduates in medicine, and nurses in the Guangxi Workers' Hospital (the designated hospital of the medical examinations for the bus drivers), who assisted in the study and collected blood samples. All study personnel underwent a training period conducted by the research team prior to the survey.

Initial interviews took place with the bus drivers during their leisure time, to minimize any work-related stress. A collective explanation of the study aims, financing, and methods was given to all bus drivers who agreed to participate in the study. All study participants signed an informed consent form. For each study participant, their anonymity and confidentiality were respected and their answers used solely for research purposes. All study participants were instructed to answer questions carefully and honestly, without spending too much time on them. Financial compensation of RMB¥30 was provided to the participants for their time, effort with the questionnaire, and for providing blood samples. Finally, 212 completed questionnaires were collected.

High-performance liquid chromatography-fluorescent detection (HPLC-FLD) and polymerase chain reaction (PCR)

The levels of platelet 5-hydroxytryptamine (5-HT) and 5-hydroxytryptophan (5-HTP) from the peripheral blood were measured by high-performance liquid chromatography-fluorescent detection (HPLC-FLD). DNA was extracted from peripheral blood mononuclear cells using a whole-blood genomic DNA extraction kit (Aidlab Biotechnologies Co., Ltd, Beijing, China) according to the manufacturer's protocol.

The serotonin transporter promoter-linked polymorphism region (5-HTTLPR) was amplified by polymerase chain reaction (PCR) using the following primers of the *5-HTT* gene 5'-flanking regulatory region:

forward (stpr5, 5'-CCG CTC TGA ATG CCA GCA CCT AAC-3') and, reverse (stpr3, 5'-AGA GGG ACT GAG CCG ACA ACC AC-3'). The *DRD4-521* C/T primers used were: 5'-CCT AAC TAG CTC ACG GTC TTG -3', and 5'-CAC CCT AGT CCA CCT GGT ATC-3'.

The PCR reactions were conducted in 25 μ l volumes, containing 1 μ l genomic DNA, 0.5 μ l of each primer, 13 μ l Master Mix (Qiagen, Guangxi, China), and 10 μ l double-distilled water (ddH $_2$ O). The PCR products were separated on a 1.2% agarose gel at 110 V for 40 min. DNA cycle sequencing was conducted by standard techniques, using a gel imaging system for photographic observation of the fragment size and genotype analysis.

Table 1. Demographic information between case and control groups.

Characteristics	Cases (n=106)	Controls (n=106)	t/ χ²	Р
Age	38.25±5.57	37.63±4.75	0.86	0.39
Driving experience	13.49±5.12	13.73±4.47	0.36	0.72
Education level				
Primary	36	27	1.83	
Junior middle school	57	64		0.40
Senior middle school or above	13	15		
Alcohol use				
Yes	26	33	1.15	0.20
No	80	73		0.28

Statistical analysis

The Hardy-Weinberg equilibrium was verified using the chisquared (χ^2) test. All variables, including the levels of 5-HT and 5-HTP, the allele and genotype frequencies, and the psychological characteristics of the study participants were identified using the chi-squared (χ^2) test or an independent sample t-test. To estimate the impact of different predictor variables on the possibility of road traffic accidents, a conditional multiple logistic regression analysis was performed for each significant factor in the univariate analysis, while controlling for age, driving experience, and the level of education. Data were analyzed using SPSS version 19.0. All statistical analysis was conducted with the level of significance of P<0.05.

Results

Comparison of the demographic data and driving experience between the study group and the control group

All bus drivers included in the study were men, as the number of female bus drivers was too small. The average age and driving experience of the study group (n=106) were 38.25±5.57 years and 13.49±5.12 years, respectively. The average age and driving experience of the control group (n=106) were 37.63±4.75 years and 13.73±4.47 years, respectively. No differences in age, driving experience, alcohol use and the level of education were observed between the two groups (P>0.05) (Table 1).

Comparison of the psychological factors and serum levels of 5-hydroxytryptamine (5-HT) and 5-hydroxytryptophan (5-HTP)

Table 2 shows the comparative data of the psychological characteristics and the levels 5-HT and 5-HTP between the bus drivers who had a history of road traffic accident (study group) and the control group. For the study group, the degree of extroversion,

psychopathic traits, neuroticism, Type-A behavior pattern (TABP), and time hurrying (impatience) scores were significantly greater when compared with the control group (P<0.05), but competitiveness and hostility did not seem to have a significant effect on the risk of road traffic accidents (P>0.05). Significant decreases in the levels of 5-HT and 5-HTP were found in the bus drivers who had road traffic accidents (study group) when compared with the control group of bus drivers (P<0.05).

Allele and genotype frequencies of the serotonin transporter promoter-linked polymorphism region (5-HTTLPR) and dopamine D4 receptor gene (*DRD4*) *DRD4-521* C/T

As shown in Table 3, two different alleles, the common S allele (484 bp) and the L allele (528 bp), were detected. There were three genotypes of the DRD4 gene: TT (366 bp), CT (366 bp, 245 bp, and 121 bp) and CC (245 bp and 121 bp). The Hardy-Weinberg equilibrium was determined on the original serotonin transporter promoter-linked polymorphism region (5-HTTLPR) and DRD4-521 C/T database, showing that the genotype frequencies of S/S, L/L, and S/L and CC, CT, and TT did not depart from the Hardy-Weinberg equilibrium (χ^2 =0.65, P=0.421 and χ^2 =0.83, P=0.363, respectively). The distributions of genotype and allele were significantly different between the study group and the control group for 5-HTTLPR (χ^2 =6.08, P=0.048 and χ^2 =6.39, P=0.011, respectively) but there were no significant differences between the study group and the control group in the DRD4-521 C and T alleles and the respective genotypes (χ^2 =0.96, P=0.619 and χ^2 =0.01, P=0.922, respectively).

Risk factors associating with road traffic accidents caused by bus drivers

Table 4 shows the adjusted odds ratio (OR), corresponding to the 95% confidence interval (CI) and P-values for each factor. Extroversion, psychopathic traits, neuroticism, and time hurrying (impatience) were identified as significant factors associated

Table 2. Psychological factors and the contents of 5-HT and 5-HTP between case and control groups (mean ±SD).

	Cases (n=106)	Controls (n=106)	t	р
EPQ (scores)				
Extroversion	14.46±4.26	12.34±3.78	3.84	<0.001
Psychoticism	6.66±2.92	5.27±2.27	3.86	<0.001
Neuroticism	9.86±5.04	7.89±3.36	3.35	0.001
Lie	11.21±3.62	11.81±3.58	1.22	0.223
ABP (scores)				
TABP	25.19±6.10	22.85±5.57	2.92	0.004
Time hurry	12.98±3.86	11.38±3.64	3.11	0.002
Competition and hostility	12.21±3.06	11.47±2.89	1.79	0.074
5-HT and 5-HTP contents				
5-HT	119.76±50.82	150.28±68.44	3.67	<0.001
5-HTP	225.76±54.42	254.14±62.78	3.52	0.001

Table 3. 5-HTTLPR, DRD4-521 C/T allele and genotype frequencies for case and control groups [n (%)].

	Genotype frequency			Allele frequency		
5-HTTLPR	L/L	S/L	S/S	L	S	
Cases	20 (18.87)	49 (46.22)	37 (34.91)	89 (41.98)	123 (58.02)	
Controls	32 (30.19)	51 (48.11)	23 (21.70)	115 (54.25)	97 (45.75)	
DRD4-521 C/T	CC	СТ	TT	С	Т	
Cases	27 (25.47)	46 (43.40)	33 (31.13)	100 (47.17)	112 (52.83)	
Controls	23 (21.70)	53 (50.00)	30 (28.30)	99 (46.70)	113 (53.30)	

 Table 4. Adjusted OR and 95% CIs in multiple logistic regression analysis of risk factors associating with traffic accident in bus drivers.

Factor	Adjusted OR	95% CI		р
EPQ(scores)				
Extroversion	1.268	1.133	1.419	0.000
Psychoticism	1.177	1.028	1.347	0.018
Neuroticism	1.092	1.005	1.187	0.038
TABP(scores)				
TABP	1.003	0.878	1.145	0.970
Impatience	1.123	1.025	1.230	0.013
5-HT and 5-HTP contents				
5-HT	0.985	0.973	0.997	0.017
5-HTP	0.982	0.969	0.994	0.004
5-HTTLPR genotype				
SS	1			
LS	0.784	0.294	2.096	0.628
LL	0.583	0.263	1.289	0.182

with road traffic accidents (P<0.05). Also, the serum levels of 5-HT and 5-HTP were significantly associated with the number of road traffic accidents in bus drivers in the study group, indicating that the drivers with low levels of 5-HT and 5-HTP were more likely to be involved in road traffic accidents (P<0.05).

Discussion

The psychological characteristics of vehicle drivers, including bus drivers, can result in risky driving behavior resulting in road traffic accidents [26]. Ulleberg and Rundmo [27,28] found that certain psychological characteristics, especially the attitudes of the drivers to traffic safety, were related to self-reported road traffic accidents. Studies have shown that the attitude of the drivers towards traffic safety is difficult to change, because it is influenced by other psychological characteristics such as ease of distraction [29], Type-A behavior patterns [30], and extrovert characteristics [31,32]. Previously published studies have also shown that an extrovert personality and neuroticism were significantly associated with an increased risk of being involved in road traffic accidents [24,33].

The findings of the current study are supported by the findings of previously published studies that have shown that some psychological characteristics, including an extrovert personality, psychopathic traits, neuroticism, and time hurrying (impatience) were significantly associated with road traffic accidents. These findings may be because individuals who have more negative psychological characteristics are more likely to suffer from anxiety, impatience, stress, and irritation, and may be more easily distracted from their driving, resulting in an increased risk of road traffic accidents [24]. Although the results of the present study support the hypotheses that certain psychological characteristics can predict risky driving behaviors in bus drivers that contribute to road traffic accidents, different findings have been reported by some other studies [4,34]. The reasons for the different study findings in this area may include the varied sample sizes of the studies, the different ethnic and cultural populations studied, and different genders studied, and the influence of these factors should be investigated in future studies.

In a previous study, serum 5-hydroxytryptamine (5-HT) (serotonin) levels were found to be negatively correlated with impulsivity, aggression, and depression [14]. Also, in a previous study, it was reported that reduced 5-HT levels and reduced 5-hydroxytryptophan (5-HTP) levels were associated with increased impulsivity [35]. The findings of the present study showed that platelet 5-HT and 5-HTP levels in bus drivers with a history of road traffic accidents (the study group) were significantly lower when compared with bus drivers with no history of road traffic accidents (the control group), indicating that

the low levels of 5-HT and 5-HTP may be potential risk factors for road traffic accidents in bus drivers. This finding might be because low levels of 5-HT and 5-HTP are associated with the psychological symptoms such as extroversion, psychopathic traits, neuroticism, and impatience, all of which increase the incidence of road traffic accidents when driving. The findings of the present study are supported by the growing evidence of the effects of 5-HT and 5-HTP levels on psychological characteristics and risk-associated behaviors [36].

In this study, there were no significant differences in the serotonin transporter promoter-linked polymorphism region (5-HTTLPR) and the dopamine D4 receptor gene (*DRD4*) *DRD4-521* C/T genotypes between the study group and the control group by multivariate logistic regression analysis, but differences were found by univariate analysis. A possible explanation for this phenomenon is that road traffic accidents are related to the psychological factors of the driver [37], and that the 5-HTTLPR genotype is also associated with psychological factors [38]. Larger study population samples and more detailed research into these genetic mechanisms are needed to investigate this hypothesis.

This study had several limitations. First, bus drivers were asked to recall their experience of road traffic accidents during the past three years, which may have resulted in some inaccuracies in data, due to recall bias. The methods used to minimize recall bias in this study included standardized investigation, the use of an anonymous survey, and repeated confirmation of the events of the road traffic accidents for bus drivers. Also, although good rates of study compliance and good response rates were achieved, the study sample size was small, which limited the power of the statistical analysis of effects and associations, which may have resulted in exaggeration by confounders and bias. Despite these study limitations, the findings of this preliminary study to explore the psychological characteristics associated with the 5-HTTLPR and *DRD4-521* C/T genotypes, highlight important directions for future research on this topic.

Conclusions

The present study constructed a conditional multiple logistic regression model to analyze the psychological and genotypic factors that influenced the occurrence of road traffic accidents in bus drivers. The present study confirmed that extroversion, psychopathy, neuroticism, time hurrying (impatience), and decreased serum levels of 5-hydroxytryptamine (5-HT) (serotonin) and 5-hydroxytryptophan (5-HTP) might be risk factors for road traffic accidents for bus drivers. These findings may have implications for future selection of bus drivers, or provide support for the development of psychological interventions for bus drivers who may be at increased risk of road traffic accidents.

Acknowledgments

The authors gratefully acknowledge the Traffic Police Corps of Guangxi, the Guangxi Workers' Hospital and staff for their help in collecting data, and all of the participants who made this research possible.

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Conflict of interest

None.

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