16th Road Safety on Four Continents Conference
Beijing, China 15-17 May 2013

GENOMEWIDE ASSOCIATION STUDY ON FALLIBLE BEHAVIOR OF ACCIDENT-REPEATED DRIVERS IN CHINA

Hui-qing Jin Shu-lin Zhang Yang Song Wan-sheng Yu
Chinese National Center of Engineering and Technology for Vehicle Driving Safety.
Anhui Sanlian University,
No. 47, He'an road, Economic Development Zone, Hefei, 230601, China.
Hui-qing Jin 86-551-63830766 E-mail: jhq@sanliangroup.com.cn
Shu-lin Zhang 86-551-63682616 E-mail: zsl@sanliangroup.com.cn
Yang Song 86-551-63831977 E-mail: songyang@sanliangroup.com.cn
Wan-sheng Yu 86-551-63831995 E-mail: yws@sanliangroup.com.cn

ABSTRACT

Driving behavior of a driver is closely related to traffic accidents, and is controlled by nervous system. Gene expression in the nervous cells may indirectly affect people's behavior. In order to explore genetic basis of fallible behavior of the accident-repeated drivers, in accordance with the Chinese national standard "Physical qualifications for automobile drivers and their test protocol" (GB18463-2001), these drivers whose indexes were all abnormal were chose as candidates of case, and those whose indexes were all normal were chose as candidates of control. A total of 232 matching pairs of drivers were selected. We chose above case candidates who had three or more accidents at the level of more than equal-responsibility within 5 consecutive years (2005-2009) as case group. The control candidates who did not have liability for accidents over the same years (2005-2009) as control group, 179 matching pairs of drivers has been chosen as sample. GWAS (Genome-wide association study) are applied to 179 pairs of matching samples on fallible behavior of drivers. The result showed that 31 SNPs loci in 3 linked genes (SMAD5，TRPC7（$P<10^{-4}$）and CBLN4 ($P<10^{-5}$)) are associated with fallible behavior of drivers .The current study suggested for the first time the potential association between the fallible behavior and the potential susceptible genes.

1 INTRODUCTION

The driving behaviors of a driver play an important role in traffic safety[1,2], which means that drivers respond to a variety of internal and extrinsic environment for safe and fast moving while steering vehicle, including visible overt behavior and invisible covert behavior. Fallible behavior refers to bad driving characterized by that the probability of accident is higher arising from far deviation of operation between actual and normal. Some drivers account for higher frequency of accident than other drivers, named as accident-repeated drivers, and the majority of their traffic accidents are always closely related to fallible behaviors (e.g., violation of laws, over speeding[3,4,5], according to the traffic accident data of The American National Highway Traffic Safety Administration (NHTSA), driver error was by far the most common reason for crashes (95.6%), as opposed to vehicle or environmental factors. Among crashes attributed to a driver error, a teen made the error 79.3% of the time (75.8% of all teen-involved crashes), recognition errors (e.g., inadequate surveillance, distraction) accounted for 46.3% of all teen errors, followed by decision errors (e.g., following too

closely, too fast for conditions) (40.1%)[6]. Accident-repeated driver is more fallible and has a personality characteristics of recurrent accidents, such as aggression, exceeding speed, running red lights, drunk driving etc[7,8,9]. It has been found that accident-repeated driver has some fallible behavior characteristics in our previous research, such as extraversion, neuroticism, error response, low performance and so on[10]. However, the immanent causes of recidivism accident behaviors of accident-repeated driver have not been fully understood, especially from genetic perspective, Human behaviors have a genetic basis[11], behavior genetics suggests that behaviors are not only indirect regulated by genes, but also directly influenced by environment, most human behaviors are regulated by many microeffective genes[12]. If fallible behavior traits of drivers and its genetics track can be revealed, it is possible to provide a new pattern for the selection, safety training and behavior modification of occupational drivers, e.g., The Health Behaviour Research Centre of University College London in UK launched a BCW(behaviour change wheel) trial of "frameworks of behaviour change interventions"at 2010[13]; The Carolina Center for Genome Sciences of University of North Carolina in America attempted on the 9R/9R genotype in the VNTR of the dopamine transporter gene (DAT1)exerts a general protective effect against a spectrum of risky behaviors in comparison to the 10R/9R and 10R/10R genotypes[14]; The Department of Psychiatric Medicine of University of Virginia in America implemented a experiment that taking controlled-release methylphenidate improves attention during on-road driving by adolescents with attention-deficit/hyperactivity disorder(ADHD)[15]; Because accident-repeating drivers frequently or repeatedly cause traffic accident in certain time period, they have become high risk population. Traffic accident has become the largest social disaster world wide, and an enormous effort and great strategy have been put into place in many countries to prevent traffic accidents caused by accident-repeated drivers. Therefore, exploration on fallible behaviors and their genetics basis of accident-repeated driver is significant social impact and scientifically relevant. Accident-repeated drivers cause increased cost for medical and public services[16], once the recrudescent causes of traffic accident of the accident-repeated driver can be under control, rational prediction and monitoring of those accident-repeated drivers would be possible, therefore action can be taken in protecting them from traffic accidents. This will make great contribution to the control of traffic accidents which have brought huge disasters to human beings.

2 SUBJECTS AND METHODS

2.1 SUBJECTS:

We chose all bus drivers as the object population at The Public Transportation Incorporation in some coastal city in China, who live stably in the city and have a long time driving exposure in this study, the city is characterized by high incidence of traffic accidents. The subjects were screened by at least two researchers through analysis and quality control. we diagnosed the fallible behavior of drivers in accordance with the Chinese national standard " Physical qualifications for automobile drivers and their test protocol " (GB18463-2001). The drivers whose testing indexes were all abnormal were candidate of cases group, and those whose testing index were all normal were candidate of control group (see table 1.).

Table 1. subject's screening conditions

Index	control candidate	case candidate
Speed anticipation (ms)	800-2500	< 800 or >2500
Multiple relation judgment Response time (ms)	≤1600	>1600
Reaction times by mistake (times)	≤5	>5
Attention distribution and duration (times)	≤110	>110
Night acuity (s)	≤35	>35
Depth perception (mm)	±22	< -22 or >22
Dynamic acuity	≥0.2	〈0.2

(* from GB18463-2001)

To eliminate bias of confounding factor including age, gender, driving experiences, this study used matched case-control samples. The matching conditions include similar age, driving duration (difference less than 2 years), same nationality, gender, residence, education and marital status, similar driving route and driving training, etc.(see Table 2). Subjects are all healthy drivers, and those drivers who have the history of genetic diseases, psychiatric disorders, cardiovascular diseases and driving contraindications were excluded. A total of 232 matching pairs of drivers were selected in this study.

Table2 Matching conditions of the case and control

matching conditions	Case group	Control group
Age	+	Similar（difference less than 2 years）
Gender	+	Same
Nationality	+	Same(Han Chinese)
Residence	+	Same
Education	+	Same
Driving duration	+	Similar（difference less than 2 years）
Driving training	+	Same
Driving route	+	Same
Marital status	+	Same
Accident records	Three times or more accidents in 5 years	Zero accidents during the same period

After five years following up study(2005-2009) ,according to accident record of drivers,we chose these case candidates who had three or more accidents at the level of more than equal-responsibility within 5 consecutive years are as case group. Some control candidates who did not have liability for accidents over the same years (2005-2009) are as control group. A total of 179 matching pairs of candidates were selected.

3 METHODS:

2 ml of blood was taken from each subject of the 179 pairs of matching samples into tubes encapsulated with EDTA anticoagulation and stored in -80 ° C refrigerator pending analysis. DNA was extracted from whole blood after thawing. All subjects in this research are volunteers after being informed, and all the information of the drivers are collected from the original materials of the Safety Division of the Bus Company by the trained investigators with uniform questionnaire. This study is performed under the approval of the local ethical committee.

DNA extracted from the whole blood of 179 pairs of matched samples were utilized for the GWAS. SNPs tests with the Affymetrix Genome-Wide Human Mapping.SNP 6.0 Array (Affymetrix, Santa Clara, CA, US). SNP analysis was performed by Chinese National Engineering Center for Biochip in Shanghai.

4 STATISTICS

SNPs association analysis was performed on the 179 pairs of matched samples. MAF analysis of all SNP locus and Hardy-weinberg equilibrium test were performed with the Genespring software. Genotype – Phenotype associated analysis was performed using three methods of the Cochran-Armitage tests: Pearson's χ^2 test, and Fisher's exact test.

5 RESULT

We carried out GWAS on 179 pairs of matched samples, and found that there are significant associated SNPs loci ($P < 10^{-4}$) located at genome variant regions by comparing fallible behavior of drivers (case group) with the normative behavior of drivers (control group). The potential association signals between case group and control group were determined by using Cochran-Armitage trend test. Significant 31 SNPs loci concentrate on position of 10^{-5}～10^{-3} of the genome wide *P* values of the Cochran-Armitage trend test, and SNP peak locus reached to 10^{-6}(see table 3,fig.1).

The expected *P* value($-\log_{10} P$) and the observed *P* value($-\log_{10} P$) between case group and control group all locate within 95% CL(fig.2). We can rule out the false positive results coming from samples stratifying according to condition of "IF < 1". There is a deviation at the tail of the distribution from null distribution(fig.2), which showed the deviation possibly caused by really genetic association.We found two blocks of linkage illequilibrium through haploid analysis of associated SNPs loci (red block A and red

Table 3 SNPs significant information site genotype and gene locus information table

dbSNP RS ID	Chr	Physical Position	Allele A/B	Association Gene	p-value	OR	OR (9)
rs2033581	chr8	69264902	A/G	DEPDC2	2E-06	0.4629	0.3365-0.6368
rs6978138	chr7	16856893	A/G	AGR2	5E-05	0.5443	0.4011-0.7385
rs1019621	chr7	135000000	A/G	CNOT4///STRA8	1E-05	0.4485	0.3047-0.6603
rs292661	chr7	135000000	C/T	CNOT4///STRA8	9E-05	0.4972	0.3317-0.7452
rs2972106	chr7	148000000	C/T	CNTNAP2	9E-05	0.5272	0.3748-0.7414
rs2717741	chr8	18490786	C/G	PSD3	2E-05	3.2696	1.7794-6.0078
rs2634449	chr8	18488730	A/G	PSD3	2E-05	0.2772	0.1489-0.5161

rs6069499	chr20	53973735	A/G	CBLN4	9E-05	0.2857	0.1478-0.5521
rs6035200	chr20	18970894	A/T	C20orf79///SLC24A3	1E-04	0.5884	0.4395-0.7879
rs7732110	chr5	135547908	C/T	TRPC7	6E-04	0.6058	0.4505-0.8148
rs11242316	chr5	135547747	C/G	TRPC7	5E-04	1.6866	1.256-2.2648
rs3734125	chr5	135551643	C/T	TRPC7	4E-04	1.73	1.2873-2.325
rs10045073	chr5	135557803	C/T	TRPC7	6E-04	1.712	1.274-2.3006
rs10041689	chr5	135565676	A/G	TRPC7	2E-04	1.7676	1.3141-2.3776
rs171101	chr5	135646103	C/G	TRPC7	3E-04	0.5696	0.4155-0.7809
rs7701815	chr5	135649997	A/C	TRPC7	4E-04	1.7555	1.2805-2.4067
rs1392170	chr5	135659201	A/C	TRPC7	4E-04	0.5806	0.4229-0.797
rs950715	chr5	135708138	C/T	TRPC7	2E-04	0.5317	0.3784-0.7471
rs3777150	chr5	135705746	A/C	TRPC7	3E-04	0.524	0.3655-0.7513
rs12515628	chr5	135712924	C/T	TRPC7	1E-04	1.8919	1.3443-2.6624
rs346644	chr5	135746033	A/G	TRPC7	3E-04	0.5538	0.3955-0.7755
rs2548979	chr5	135481392	C/T	SMAD5	5E-04	0.5924	0.4408-0.7962
rs2906830	chr5	135481829	C/T	SMAD5	9E-04	1.6487	1.2284-2.2128
rs2548978	chr5	135492030	C/T	SMAD5	4E-04	1.7065	1.2701-2.2928
rs9327743	chr5	135495208	C/G	SMAD5OS	3E-04	0.5714	0.4243-0.7695
rs13187638	chr5	135500093	C/G	SMAD5	9E-04	1.6324	1.2146-2.194
rs6596288	chr5	135512462	C/T	SMAD5	4E-04	1.706	1.2702-2.2915
rs10056474	chr5	135519295	C/G	SMAD5	4E-04	1.7061	1.2702-2.2915
rs10064147	chr5	135533740	A/G	SMAD5	2E-04	1.7823	1.3249-2.3976
rs6886699	chr5	135543637	C/T	SMAD5	2E-04	1.7546	1.3037-2.3614
rs7719008	chr5	164000000	A/G		1E-04	0.548	0.4086-0.7348

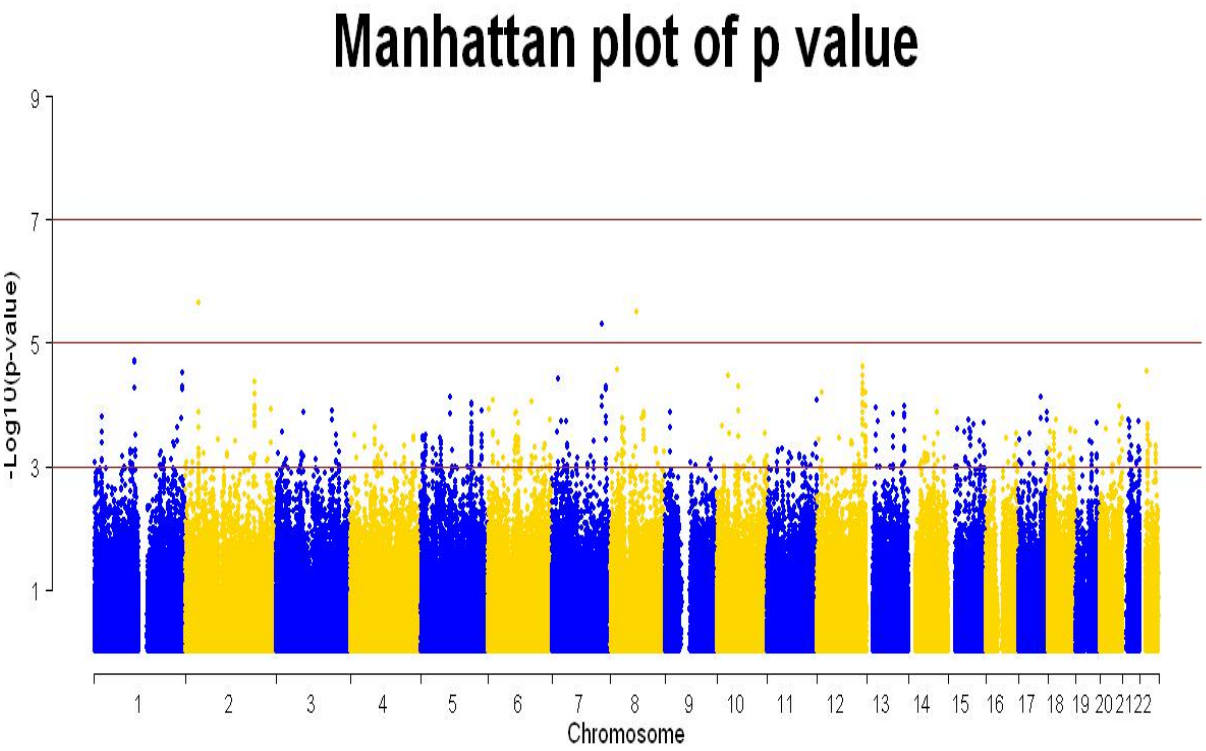

Fig.1 P value of all SNPs loci distribution on each chromosome

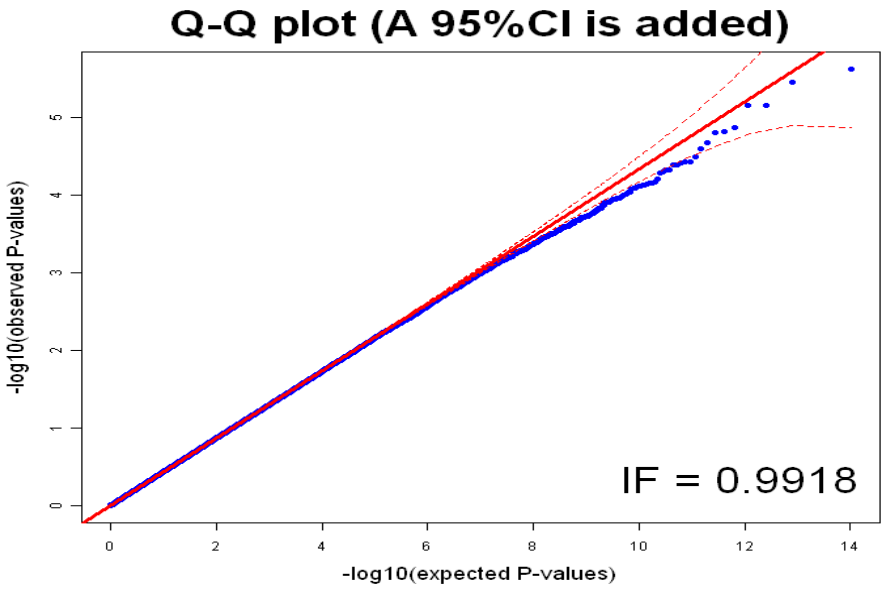

Fig.2 QQ-plot

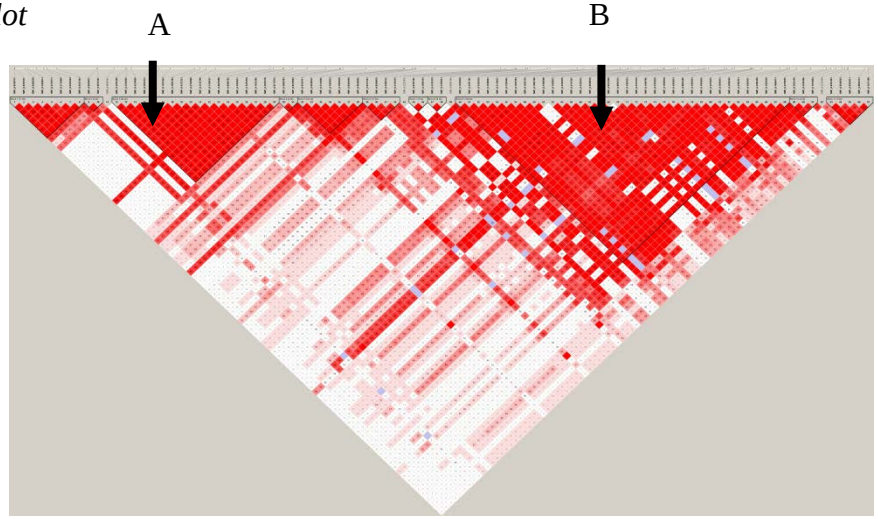

Fig.3 LD-plot linkage illequilibrium distribution

block B of fig.3). which indicated combination of allele genes each SNP locus is non-random.

The GWAS showed that genome variation frequency of the SNPs in fallible behavior drivers is higher than that in control group, and three genes SMAD5（rs6886699） on chromosome 5，TRPC7（rs10041689,rs3777150）on chromosome 5，CBLN4（rs6069499）on chromosome 20 are strongly associated with fallible behavior of Chinese drivers ($P < 10^{-4}$）.

6 DISCUSSION

The fallible behaviors of drivers have a tendency to induce more traffic accidents than the general population. Studies have showed that accident-repeated drivers have some fallible behavior characteristics such as low motion perception, error judgement, attention deficit、depth perception deviation. These results suggest that processing capability of accident-repeated drivers on driving information is lower than that of safe drivers in general, consequently, more accidents are caused by these drivers. That is the chance for an accident-repeating is not a statistical phenomenon, rather it is likely to be a result of those genetic traits. This implies that the accident-repeating drivers possess certain psychological and behavioral characteristics of cognition and processing capability on information, especially for motion perception, reaction, attention, performance on dynamic objects. Ergun Y. Uc and Matthew Rizzo compared older drivers who suffered from neurodegenerative disorders with control drivers. They found that driving errors of the drivers with neurodegenerative disorders were more than that of control drivers in driving task experiment, because the behavior function of the drivers with neurodegenerative disorders was impaired in their cognition, visual perception, attention and motor function etc[18]. The experiments showed that drivers with low motion perception prone to anticipate judgement on moving object, and their error judgement lead to error operation, and their attention deficit (i.e. to care for the left but lose the right) easily neglect the potential risk, therefore, any fault or error on a chain of driving processing behavior could cause accident (fig.4).

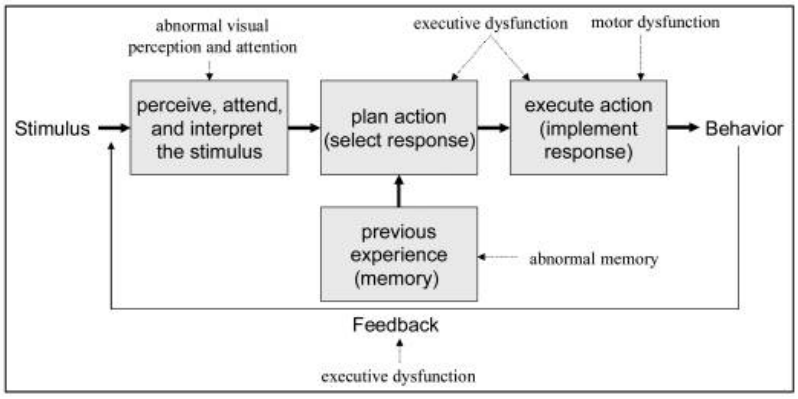

Fig 4 Information processing model for driver error

Previous studies have dispersedly reported the fallible behavior traits or clues of drivers from different districts[7,19,20], which were basically identical with the present study, it showed that fallible behavior of accident-repeated drivers may have certain common individual idiosyncracy. Some researchers have reported the relationship between traffic accident and personality of driver behavior such as anxiety, drinking, aggressing, violation, etc[21-23].

Based on fallible behavior traits of drivers in Chinese population, we conducted GWAS on genetic foundation of fallible behavior traits. Result showed that there is significant difference in SNPs genome variation frequency between case group (fallible behavior of drivers) and control group(normative behavior of drivers). We found that there are three genes (SMAD5，TRPC7 and CBLN4) located in significant SNPs genome variant region that are particularly associated with fallible behavior of drivers（$P<10^{-4}$）.

Behavioral genetics has demonstrated that human behavior has a genetic basis, behavior is the combination of heredity and environment and has genetic polymorphisms[24]. M Nelen and XO Breakefield found that a point mutation was identified in a termination codon of the eighth exon of the MAOA structural gene, which is intimately associated with a recognizable abnormal behavior, including impulsive aggression, arson, attempted rape, and exhibitionism[25]. A recent study in British Medical Council (BMC) showed the genetic contribution to aggressive behavior in Drosophila animal model [26]. Studies on the relationship of genes and behavior have just sprung up, there exists some directly or indirectly association between intricate behavior traits and genes[27]. Driving behavior is one of the human special occupational behaviors involving complicated information processing including information cognition, judgment, decision and operation etc., and also has genetic foundation. Fallible behaviors of drivers are mainly revealed in information cognition and processing, once genome variation/ gene function abnormity involved in driving information cognition pathway (e.g. signal translation) or processing take place, driving behavior of drivers would be out of control.

Based on GeneBank database, SMAD5 is a kind of cytoplasm protein gene, mainly plays a certain regulating role in tissue dynamic development through the signal transduction pathways. It is reported that, 2/3 of the SMAD protein signal directly promote expression of Nanog , moderate repression of SMAD5 may inhibit expression of Sox2[28]. However, Sox2 plays a primary regulating role in the potential ability and self-refreshing by adjusting transcription of embryo stem cells, such as the reaction to environmental stimuli[29]. It is for the first time that we found that SMAD5 has certain association with the behaviors of accident prone drivers, however further studies are warranted. TRPC7 gene is mainly involved in cell calcium and magnesium ion channel regulation, and highly expressed in peripheral organs such as heart, lung, eye etc, and sensitivity to cognition from visual and tactual information, TRPC7 plays important roles in regulating balance of intracellular Ca^{2+} and transferring extracellular signal[31-32]. We consider that significant linked SNPs located at TRPC7 gene probably associated with functional modulation of visual cognitive channel for drivers, in case its function would be abnormal, the omen of accident as “brain blank” likely appear due to interrupt cognitive channel. In the current GWAS, above 2associated genes all involve in neural signal transduction, cell differentiation and nervous function regulation, therefore, there is a strong functional coherence between their biological understanding and molecular mechanism of fallible behavior of drivers.

In the GWAS, we found that there exists stronger SNP signal located at CBLN4 gene（$P<10^{-5}$）. CBLN4 genes mainly involve in adrenal development and regulation of secretion[33-34], which plays important roles in the regulation of main hormone and neurotransmitter of the stress system. Previous studies showed that the neurotransmitter levels of dopamine (DA), 5 - hydroxytryptamine (5-HT) of the accident-repeated drivers are lower than that of the safe drivers. Bergomi M et al in Italy investigated the relationships between young driver behaviour and personality factors as well as to assess the neuroendocrine correlation of psychological and behavioural factors, and found that the subjects are prone to adopt safe driving behaviour, a positive correlation was observed between DA levels and the frequency of driving violations while a negative relationship was found between adrenaline(NE) levels and frequency of driving errors[35]. Whether or not the changes in these neurotransmitters are caused by regulating variation of CBLN4 gene still needs further study.

7 CONCLUSION

Fallible behavior of the accident-repeated drivers have internal traits and their typical behavioral properties in motion perception, reaction, attention, depth perception, etc. These traits and behavior may be associated with genome structure variations involved in cell signal translation pathway. Our Genome-wide Association Study demonstrated that CBLN4 genome structure variations could be related to the genetic susceptibility of fallible behavior of drivers, and suggest for the first time the potential association between the accident-repeated drivers and their fallible behavior and the potential susceptible genes.

REFERENCES

1. Leonard Evans(1996). The dominant role of driver behavior in traffic safety. *American Journal of Public Health*. 86,784-786.

2. John D. Lee(2005). Driving Safety. Reviews of human factors and ergonomics.1, 172 -218.

3. Burgut HR, Bener A, Sidahmed H, Albuz R, Sanya R, et al(2010). Risk factors contributing to road traffic crashes in a fast-developing country: the neglected health problem. *Ulus Travma Acil Cerrahi Derg*.16, 497-502.

4. Nabi H, Consoli SM, Chastang JF, Chiron M, Lafont S, et al(2005). Type a behavior pattern, risky driving behaviors, and serious road traffic accidents: a prospective study of the GAZEL cohort. *Am J Epidemiol*.161, 864-870.

5. Williams N(1964). Traffic accidents-epidemiology and medical aspects of prevention. *Can Med Assoc J*.90, 1099-1104.

6. Curry AE, Hafetz J, Kallan MJ, Winston FK, Durbin DR(2011). Prevalence of teen driver errors leading to serious motor vehicle crashes. *Accid Anal Prev*.43, 1285-1290.

7. Pauline G, Dorothy B(2007). Personality factors as predictors of persistent risky driving behavior and crash involvement among young adults. *Inj Prev*.13, 376-381.

8. Nabi H, Louis Rachid Salmi, Sylviane Lafont, Mireille Chiron, Marie Zins, et al(2007). Attitudes associated with behavioral predictors of serious road traffic crashes: results from the GAZEL cohort. *Inj Prev*. 13,26–31.

9. Parker D, West R, Stradling S, Manstead AS(1995). Behavioral characteristics and involvement in different types of traffic accident. *Accid Anal Prev*.27, 571-581.

10. H.Q. Jin, S. Araki, X.K. Wu, Y.W. Zhang, K(1991). Yokoyama, Psychological performance of accident-prone automobile drivers in China: a case-control stuty. *Int J Epidemiol*.20, 230.

11. Plomin R, Owen M J, Guffin P M(1994). The genetic basis of complex human behaviors. *Science*. 5166, 1733-1739.

12. Mann CC(1994). Behavioral genetics in transition . *Science*. 5166, 1686-1689.

13. Michie S, van Stralen MM, West R(2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci*. 6, 42.

14. Guo G, Cai T, Guo R, Wang H, Harris KM(2010). The dopamine transporter gene, a spectrum of most common risky behaviors, and the legal status of the behaviors. *PLoS One*.5, e9352.

15. Cox DJ, Humphrey JW, Merkel RL, Penberthy JK, Kovatchev B(2004).Controlled-release methylphenidate improves attention during on-road driving by adolescents with attention-deficit/hyperactivity disorder. *J Am Board Fam Pract*.17, 235-239.

16. Jansson B, Stenbacka M, Leifman A, Romelsjö A(2004). A small fraction of patients with repetitive injuries account for a large portion of medical costs. *Eur J Public Health*.14, 161-167.
17. People's Republic of China(2003). The Law of Road Triffic Safety, China.
18. Ergun Y. U, Matthew R. (2008). Driving and neurodegenerative diseases. *Curr Neurol Neurosci Rep*. 8, 377-383.
19. Ulleberg P, Rundmo T(2003). Personality, attitudes and risk perception as predictors of risky driving behaviour among young drivers. *Safety Science*.41, 427-443.
20. Schwebel DC, Severson J, Ball KK, Rizzo M(2006). Individual difference factors in risky driving: the roles of anger/hostility, conscientiousness, and sensation-seeking. *Accid Anal Prev.* 38, 801-810.
21. Shahar A(2009). Self-reported driving behaviors as a function of trait anxiety. *Accid Anal Prev.* 41, 241-245.
22. Moore M, Dahlen ER(2008). Forgiveness and consideration of future consequences in aggressive driving. *Accid Anal Prev.* 40, 1661-1666.
23. Ozkan T, Lajunen T, Parker D, Sümer N, Summala H(2010). Symmetric relationship between self and others in aggressive driving across gender and countries. *Traffic Inj Prev.*11, 228-239.
24. Plomin R, John C, DeFries Gerald E, et al(2007). Behavioral Genetics(4th Edition). New York: Worth Publisher, USA.63-80.
25. Brunner HG, Nelen M, Breakefield XO, Ropers HH, van Oost BA(1993). Abnormal behavior associated with a point mutation in the structural gene for monoamine oxidase A. *Science*. 5133, 578-580.
26. Jasinska AJ, Freimer NB(2009). The complex genetic basis of simple behavior. *J Biol.* 8, 71.
27. Genes and behavior . *Science*. 5166:1685-1739(1994).
28. Domyan ET, Ferretti E, Throckmorton K, Mishina Y, Nicolis SK, Sun X(2011). Signaling through BMP receptors promotes respiratory identity in the foregut via repression of Sox2. *Development*. 138, 971-981.
29. Boyer LA, Lee TI, Cole MF, Johnstone SE, Levine SS, Zucker JP, et al(2005). Core transcriptional regulatory circuitry in human embryonic stem cells. *Cell*.122, 947-956.
30. Lee WY, Weber DA, Laur O, Stowell SR, McCall I, Andargachew R, et al(2010). The role of cis dimerization of signal regulatory protein alpha (SIRPalpha) in binding to CD47. *J Biol Chem*. 285, 37953-37963.
31. Miyagi K, Kiyonaka S, Yamada K, Miki T, Mori E, Kato K, et al(2009). A pathogenic C terminus-truncated polycystin-2 mutant enhances receptor-activated Ca2+ entry via association with TRPC3 and TRPC7. *J Biol Chem*. 284, 34400-34412.
32. Abed E, Moreau R(2007). Importance of melastatin-like transient receptor potential 7and cations (magnesium, calcium) in human osteoblast-like cell proliferation. *Cell Prolif*. 40, 849-865.
33. Rucinski M, Ziolkowska A, Szyszka M, Malendowicz LK(2009). Precerebellin-related genes and precerebellin 1 peptide in the adrenal gland of the rat: expression pattern, localization, developmental regulation and effects on corticosteroidogenesis. *Int J Mol Med*. 23, 363-371.

34. Rucinski M, Malendowicz LK(2009). Precerebellin-related genes and precerebellin 1 peptide in endocrine glands of the rat - pattern of their expression. *Int J Mol Med*. 23, 113-119.
35. Bergomi M, Vivoli G, Rovesti S, Bussetti P, Ferrari A, et al(2010). Role of some psycho-physiological factors on driving safety. *Ann Ig*. 22, 387-400.