Acta Neuropsychiatrica

cambridge.org/neu

Relapse of drunk driving and association with traffic accidents, alcohol-related problems and biomarkers of impulsivity

Tõnis Tokko[1], Diva Eensoo[2], Mariliis Vaht[1], Klaus-Peter Lesch[3], Andreas Reif[4] and Jaanus Harro[1]

[1]Division of Neuropsychopharmacology, Department of Psychology, University of Tartu, Estonia, [2]Department of Family Medicine and Public Health, University of Tartu, Estonia, [3]Division of Molecular Psychiatry, Center of Mental Health, University of Wuerzburg, Wuerzburg, Germany, b) Laboratory of Psychiatric Neurobiology, Institute of Molecular Medicine, Sechenov First Moscow State Medical University, Moscow, Russia, c) Department of Neuroscience, School for Mental Health and Neuroscience (MHeNS), Maastricht University, Maastricht, The Netherlands and [4]Laboratory of Translational Psychiatry, Department of Psychiatry, Psychosomatic Medicine, and Psychotherapy, University Hospital Frankfurt, Frankfurt am Main, Germany

Original Article

Cite this article: Tokko T, Eensoo D, Vaht M, Lesch KP, Reif A, Harro J. (2019) Relapse of drunk driving and association with traffic accidents, alcohol-related problems and biomarkers of impulsivity. *Acta Neuropsychiatrica* 31:84–92. doi: 10.1017/neu.2018.30

Received: 17 August 2018
Revised: 4 October 2018
Accepted: 11 October 2018
First published online: 26 November 2018

Key words:
biomarkers, driving under the influence, impulsive behaviour

Author for correspondence:
Jaanus Harro, Division of Neuropsychopharmacology, Department of Psychology, University of Tartu, Estonian Centre of Behavioural and Health Sciences, Ravila 14A Chemicum, 50411 Tartu, Estonia.
E-mail: jaanus.harro@ut.ee

Abstract

Objective: Individual biological predispositions should play a role in risky driving behaviour. Platelet monoamine oxidase (MAO) activity, dopamine transporter gene (*DAT1*) and neuropeptide S receptor 1 (*NPSR1*) gene polymorphisms have been identified as markers of impulsivity, alcohol use and excessive risk-taking. We aimed to find out how this knowledge on neurobiology of impulsivity applies to drunk driving and traffic behaviour in general. *Methods:* We have longitudinally examined the behaviour of drunk drivers (n = 203) and controls (n = 211) in traffic, in association with their alcohol-related problems, personality measures and the three biomarkers. We analysed differences between the subjects based on whether they had committed driving while impaired by alcohol (DWI) violation in a 10-year time period after recruitment or not and investigated further, what kind of predictive value do the different biomarkers have in committing DWI and other traffic violations and accidents. *Results:* The original drunk drivers group had lower platelet MAO activity but further DWI was not significantly associated with this measure. Being a *NPSR1* T-allele carrier contributed to the risk of repeatedly committing DWI. *DAT1* 9R carriers in contrast were involved in more traffic accidents by their own fault (active accidents), compared to 10R homozygotes in the whole sample. All groups with DWI also had significantly more alcohol-related problems and higher scores in maladaptive impulsivity compared to controls without DWI. *Conclusions:* Established biological markers of alcohol use and impulsivity can be reliably associated with everyday traffic behaviour and help in contributing to the understanding of the need for more personalized prevention activities.

Significant outcomes

- Driving while intoxicated tends to re-occur.
- *NPSR1* T-allele carriers were more prone to re-occurrence of drunk driving.
- *DAT1* 9R carriers had more traffic accidents than 10R homozygotes.

Limitations

- The longitudinal design has set limits to the size of the sample and reduces reliability of the findings in stratified analyses.
- Sample size also prevents consideration of dependency of significant relationships on age and driving experience.

Introduction

More than 1.2 million lives are lost each year due to road traffic injuries worldwide (1). Behaviour of drivers contributes to 90–95% of motor vehicle crashes (2). Driving while impaired by alcohol (DWI) is among the key behavioural risk factors in traffic (3). DWI is a high-risk behaviour that is not caused only by drinking problems but influenced by concurrent basic behavioural tendencies, temperament and personality (4). DWI offenders have been

shown to have higher rates of alcohol use disorders, and indeed most of them meet the criteria of alcohol dependence some time during their life (5).

Due to riskier environment, mistakes that accompany impulsive behaviour tend to be more dangerous in traffic, compared to other aspects of our daily lives. While risk-taking may be necessary in some situations, it can be dangerous and inappropriate in others. Dickman (6) distinguished between functional (adaptive) and dysfunctional (maladaptive) impulsivity, first being the willingness and ability to take risks in situations where it is mostly appropriate, and the second expressing the tendency for thoughtlessness and inability to plan, leading to negative consequences. The concept of functional and dysfunctional impulsivity applied to traffic has suggested that different types of violations go with distinct aspects of impulsivity: While speeding has been found to be associated more with adaptive impulsivity, DWI was mostly associated with maladaptive impulsivity (7,8).

Obviously, individual biological predispositions should play a role in risky driving behaviour, but while there is a vast literature on the neurobiology of impulsivity little is known on how such findings apply to everyday behaviours involving higher risk. We have previously found that drunk drivers had lower platelet monoamine oxidase (MAO) activity (7,9). While dopamine is the preferred substrate for the MAO-B isoenzyme that is the form present in platelets, platelet MAO activity is a reliable peripheral marker of serotonergic activity in the CNS, and low levels of platelet MAO activity have been associated with social maladaptation, impulsivity, sensation seeking and monotony avoidance (10–12). Platelet MAO activity is also lower in alcohol-dependent subjects (13) and low-platelet MAO is common in victims of severe trauma (14). Furthermore, low-platelet MAO activity has also been associated with criminal behaviour and suicidality, especially in adolescents who come from an unfavourable psychosocial environment (15–17). Despite the large body of evidence on the association of platelet MAO activity and low serotonergic activity with impulsivity (18), evidence for everyday life significance of such measures from longitudinal observations is scarce.

Another candidate for impacting traffic behaviour is the dopaminergic system that is critically involved in behavioural activation, motivated behaviour and reward processing (19). People with elevated dopaminergic functioning behave more impulsively (20). Dopaminergic dysfunction and elevated impulsivity occur in attention-deficit/hyperactivity disorder (ADHD) (21), and it has been shown that ADHD is associated with traffic accidents and violations (22,23). Different pharmacological, biochemical, lesion and knockout studies in animals provide evidence that impulsivity is causally related to striatal dopamine (24,25). Pharmacological studies in healthy humans have provided similar results (26,27). The dopamine transporter (DAT) plays a critical role in terminating dopamine neurotransmission and in maintaining dopamine homeostasis in the CNS by taking up synaptic dopamine into neurons (28). The *DAT1* gene (SLC6A3) bears a rather widely studied variable number of tandem repeats (VNTR) polymorphism of a 40-base pair sequence in the 3′-untranslated region of the gene (29). It has been shown that the *DAT1* VNTR 9-repeat (9R) allele carriers have higher striatal DAT availability than do the 10-repeat (10R) allele homozygotes (30,31). A significant association of 9R carriers has been found with alcohol dependence, withdrawal seizures and delirium tremens (32). Although being a 10R homozygote is thought to be a risk factor for ADHD in children, a differential association of *DAT1* with ADHD has been suggested in children and adults and being a 9R homozygote has been associated more with persistent ADHD in adults (33), which might be explained by differential functional consequences of the polymorphism in the matured dopamine system. In addition, compared to 10R homozygotes, 9R carriers have reported higher impulsivity in studies on adult healthy subjects (e.g., 34). Because impulsive behaviour has been associated with traffic accidents and violations (35), the 9R carriers may also be more inclined towards risk-taking behaviour in traffic.

Another, recent candidate for regulation of impulse control and alcohol use is the neuropeptide S (NPS) system (36) that in turn can stimulate dopaminergic neurotransmission (37). Much of this research has been carried out in animals, but in humans, a functional polymorphism of the gene that encodes for the neuropeptide S receptor 1 (*NPSR1*) (38) has been associated with the development of personality, hyperactivity, alcohol use and alcohol use disorders (39–42). *NPSR1* gene carries a functional A/T single-nucleotide polymorphism (SNP, rs324981) coding for an Asn-Ile exchange at position 107. NPS has up to 10 times higher potency at the receptor encoded by the T-allele (107Ile) compared to the A-allele-encoded receptor, leading to more effective signal transduction with mobilization of intracellular Ca^{2+}, stimulation of cyclic adenosine monophosphate synthesis and induction of mitogen-activated protein kinases phosphorylation (43). Recently Taranov and colleagues (44) found in a study with bus drivers that *NPSR1* was associated with increased risk of a road accident. The T-allele of the *NPSR1* rs324981 polymorphism has been associated with increased impulsivity and ADHD-related traits (39,42). Further, an impulsivity-related early-onset pathway to alcohol use disorder was revealed in male T-allele carriers, particularly in T/T homozygotes: already in adolescence, they exhibit more ADHD symptoms and impulsivity that could make them more vulnerable to alcohol use (41).

Aims of the study

In 2001, we conducted a study of police-referred drunk drivers (7,8), and we could follow-up the driver records about 10 years later. Thus, in the present analysis we enquired whether baseline markers of impulsivity, alcohol use and risk-taking behaviour have any predictive value in traffic in a 10-year time period.

Materials and methods

Sample

The longitudinal Estonian Psychobiological Study of Traffic Behaviour (EPSTB) started with the sample of drunk drivers in 2001; the sample has been described in detail previously (9). The group of drunk drivers comprised male subjects who were identified by the police driving drunk at least once during the previous year (n = 203; mean age ± SD, 33 ± 11 years). The control group was formed by computerised random choice of the male subjects in the driving licence database of the Estonian Motor Vehicle Registration Centre. Subjects were contacted by telephone, the description and aims of the study were provided, and they filled in self-reported questionnaires during a visit to laboratory where they donated venous blood samples. The control group consisted of 211 individuals, with a mean age of 36 ± 12 years. The study was approved by the Research Ethics Committee of the University of Tartu (No 229/T-15).

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

Socio-economic background, tobacco smoking and alcohol use

Subjects reported their socio-economic status, tobacco smoking and alcohol use habits in a self-report questionnaire. Questions about socio-economic background included relationship status, education and monthly income. The latter was dichotomized according to the mean income in the country in 2001. Tobacco smoking status was categorized to non-smokers, ex-smokers, ≤10 cigarettes/day, 11–19 cigarettes/day, ≥20 cigarettes/day (7) and was used in data analysis both as a categorical variable (current smoker vs. non-smoker) and as a continuous variable (5-point scale). The alcohol consumption questionnaire contained items about the frequency of using strong and light alcoholic drinks during the previous year on a 6-point scale (none, some-times during the year, one to three times per month, one to two times per week, three to four times per week, almost every day) (9). The frequency of using alcoholic drinks was used in data analysis both as a categorical (at least once a week vs. less than once a week) and as a continuous variable. The score of alcohol-related problems was obtained by summing up five questions based on the Diagnostic and Statistical Manual of Mental Disorders IV criteria for alcohol abuse, relating to specific life events ('turned aggressive while drunk', 'had longer periods of alcohol use', 'had conflicts with friends and family', 'been absent from work' and 'lost one's job'; reported as present or not, total score 0–5).

Personality measures

Adaptive and Maladaptive Impulsivity Scale (AMIS) was used to measure different facets of impulsivity (fast decision-making, thoughtlessness, disinhibition and excitement seeking) as previously described (45). AMIS is based on the concept of functional and dysfunctional impulsivity as described by Dickman (6). Subjects were asked to assess how much the 24 different impulsivity-related statements applied to them on a scale of 1 to 5. All of the 414 subjects filled in AMIS.

Database search

Data on violations of traffic law, traffic accidents and the status of subjects driver's licences (valid or withdrawn) were obtained from databases maintained by the traffic police, the traffic insurance fund and the Estonian Road Administration for the period of January 1, 2002, to December 31, 2011. The traffic behaviour measures were as follows: speeding (penalties for exceeding the speed limit), DWI (penalties for drunk driving with an estimated blood alcohol level of 0.2‰ or more) and other traffic violations (all the traffic violations besides speeding and DWI). The accidents where the subject was at fault were classified as active accidents, and other accidents were classified as passive accidents.

Platelet MAO activity

Platelet MAO activity was analysed in platelet-rich plasma by a radioenzymatic method with β-phenylethylamine as the substrate according to the procedure described by Hallman et al. (46) after modification (47). Platelet MAO activity was analysed in 405 subjects and used both as a categorical variable (low 25th percentile vs. high) and as a continuous variable in the statistical analyses.

Genotyping

DAT1

DNA was extracted from venous blood and *DAT1* 3′UTR VNTR was genotyped as previously described (48). Altogether 399 subjects were successfully genotyped. As the most common *DAT1* alleles are the 9- (9R) and 10-repeat (10R) forms (49), 8 subjects who had a rare VNTR genotype (10R/11R, 6R/10R) were excluded, leaving 391 subjects for the *DAT1* analyses. Genotype distribution was as follows: 10R/10R 63.7%, 9R/10R 31.5% and 9R/9R 4.8%. Genotype frequencies were in Hardy–Weinberg equilibrium.

NPSR1

NPSR1 rs324981 was genotyped by routine polymer chain reaction followed by restriction enzyme digest and gel electrophoresis as previously described (50). *NPSR1* was successfully genotyped in 402 subjects. Genotype distribution was as follows: A/A 28.1%, A/T 46.3% and T/T 25.6%. Genotype frequencies were in Hardy–Weinberg equilibrium.

Statistical analysis

Data were analysed using SPSS (version 23.0 SPSS, Chicago, IL) and SAS (version 9.4 SAS Inc., Cary, NC) software. Pearson's chi-square test and survival analysis were conducted to compare the differences between control group and drunk drivers group in DWI from 2002 to 2011. Control group and drunk drivers group were additionally separated by whether they had committed a DWI after the initial recruitment (2002–2011) or not. As a result, four subgroups were obtained: controls without DWI (n = 189), controls with DWI (n = 22), drunk drivers without further DWI (n = 136) and drunk drivers with repeat DWI (n = 67). Differences between these subgroups regarding categorical variables (*DAT1* VNTR, *NPSR1,* occurrence of traffic accidents and violations, status of driver's licence, education, relationship status, income, frequency of using alcohol and tobacco smoking) were analysed with Pearson's chi-square test and *post hoc* Fisher test, and for continuous variables (platelet MAO activity, personality measures, alcohol-related problems and age) with ANOVA and *post hoc* Fisher least significant difference test. Kruskal–Wallis test was used to analyse the differences between subgroups by non-parametrically distributed variable (time without drivers licence).

Cox regression analyses were used to investigate the effect of different variables upon the time subjects committed DWI after the initial recruitment to the study. First, the effect of independent variables was analysed one by one, then the analysed variables were adjusted by the occurrence of DWI before recruitment by adding it as a covariate. In order, to investigate the role of *NPSR1* in predicting DWI in combination with other significant variables, the best Cox regression model with *NPSR1* was found.

Logistic regression analyses were used for predicting the occurrence of active traffic accidents in 2002–2011. First, simple logistic regression analyses were used for predicting active traffic accidents by independent variables. Next independent variables predicting the occurrence of active traffic accidents were adjusted by the occurrence of DWI after recruitment. Finally, the variables significantly predicting the occurrence of active traffic accidents independently were entered into a logistic regression model together.

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

Results

In 2002–2011, the members of the original drunk drivers group committed a new DWI with significantly higher probability than the incidence of DWI in controls (33.0% vs. 10.4%, $\chi^2 = 31.3$, $p < 0.001$). Survival analysis (Fig. 1) showed that in years 2002–2007 (500–2000 days after recruitment) there was a rapid reoccurrence of DWI in the drunk drivers group ($p < 0.001$). After that the DWI plateaued, meaning that most of the subjects in the drunk drivers group who committed repetitive DWI did it in up to 6 years after the initial recruitment, and very few of them afterwards.

The initial, new and relapsing drunk drivers

As for platelet MAO activity, *DAT1* VNTR and *NPSR1*, significant differences between the DWI subgroups were only found in platelet MAO activity (Table 1): drunk drivers without further DWI and drunk drivers with repeat DWI had lower platelet MAO activity compared to controls without DWI [$F(3,401) = 4.7$, $p = 0.003$]. Since cigarette smokers have been shown to have reduced MAO activity (51), we controlled for smoking status in the statistical analyses of MAO and with smoking as a covariate significant difference between the subgroups in platelet MAO activity disappeared ($p = 0.19$). When smoking dose-dependent effect on platelet MAO activity was taken into account (7), then among subjects smoking less than 10 cigarettes per day, there was however a significantly higher proportion of subjects with low-platelet MAO activity among drunk drivers without further DWI compared to controls without DWI (respectively, 26.6% (n = 21) vs. 15.1% (n = 23), $\chi^2 = 4.4$, $p = 0.036$), and a tendency for higher proportion of subjects with low-platelet MAO activity in drunk drivers with repeat DWI compared to controls without DWI (respectively, 27.3% (n = 9) vs. 15.1% (n = 23), $p = 0.095$).

There were no significant differences in speeding or traffic accidents in 2002–2011 between the four subgroups separated on the basis of single and repeat drunk driving, but there were significant differences in other traffic violations ($\chi^2 = 21.6$, $p < 0.001$). Controls with DWI and drunk drivers without further DWI had more other traffic violations compared to controls without DWI, and drunk drivers with repeat DWI had more other traffic violations than all the other groups.

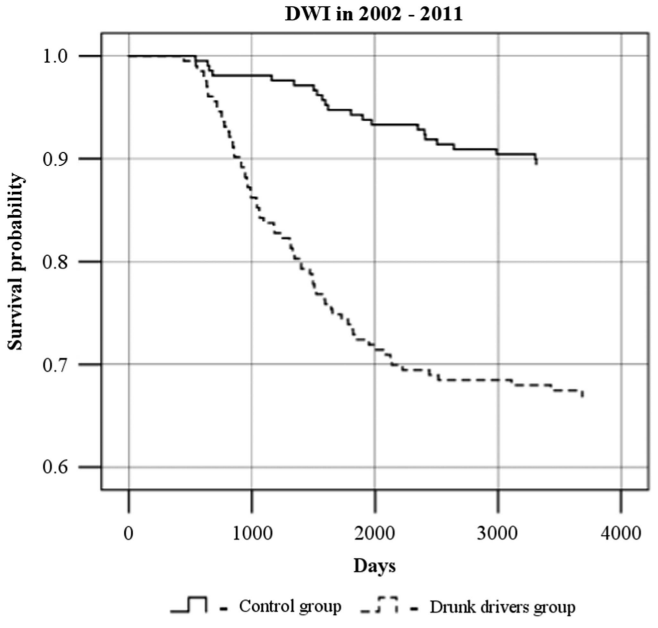

Fig. 1. Occurrence of driving while impaired by alcohol (DWI) in 2002–2011 after recruitment in 2001.

While this is irrelevant for the conducted survival analysis, it can be of interest whether any group differences were observed in suspension of driver's license that could also limit the period of legal driving. There were a few subjects from the original drunk drivers group who had had their drivers licence withdrawn already at the beginning of the observation period (n = 5). During the observation period, drunk drivers with repeat DWI and controls with DWI had more subjects whose drivers licence was withdrawn ($\chi^2 = 118.2$, $p < 0.0001$) and also longer periods of time without a valid drivers licence per person, compared to controls without DWI (Kruskal–Wallis $\chi^2 = 123.6$, $p < 0.0001$). The period of time without a valid licence per person was also higher in drunk drivers with repeat DWI compared to drunk drivers without further DWI.

While there were no significant differences in excitement seeking and fast decision-making (the facets of adaptive impulsivity), both original drunk driver groups and controls with DWI had significantly higher scores in disinhibition compared to controls without DWI [$F(3,410) = 9.1$, $p < 0.001$] and both original drunk driver groups had also significantly higher scores in thoughtlessness, compared to controls without DWI [$F(3,410) = 6.6$, $p < 0.001$].

Statistically significant differences between DWI subgroups were found in education ($\chi^2 = 22.4$, $p < 0.001$), tobacco smoking status ($\chi^2 = 49.9$, $p < 0.001$) and alcohol consumption ($\chi^2 = 15.2$, $p = 0.002$, $\chi^2 = 11.8$, $p = 0.008$, for light and strong alcohol, respectively); compared to all the other three groups, controls without DWI had more subjects with higher education, less subjects who were smokers and less subjects who consumed light and strong alcohol more than once a week. Both original drunk driver groups and controls with DWI also reported more alcohol-related problems compared to controls without DWI [$F(3,410) = 21.9$, $p < 0.001$]. There were however also differences in mean age between the groups: drunk drivers with repeat DWI were significantly younger than controls without DWI and drunk drivers without further DWI [$F(3,410) = 4.8$, $p = 0.003$]. There were no significant differences in relationship status or income between the DWI subgroups.

Predicting DWI

Next, using Cox regression, models were found that predicted the occurrence of DWI in the 10-year time period. Table 2 presents the variables predicting DWI in 2002–2011 independently, and models predicting DWI in 2002–2011 with analysed variables adjusted by DWI before recruitment. The following variables predicted DWI in the years 2002–2011 independently: age, education, AMIS disinhibition, AMIS thoughtlessness, frequency of using light alcoholic beverages, alcohol-related problems, tobacco smoking, *NPSR1* genotype, active traffic accidents and other traffic violations (in 2002–2011) and drunk driving before recruitment. Adjusting these associations by drunk driving before recruitment, models with age, education, alcohol-related problems, tobacco smoking, *NPSR1* and other traffic violations predicted DWI in 2002–2011 significantly. Because our focus was on biological mechanisms behind behaviour, and *NPSR1* was the only biological marker significantly predicting DWI, we ran Cox regression models with *NPSR1* and other significant variables to

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

Table 1. Comparison of different variables between DWI subgroups

Variable	Controls without DWI (n = 189)	Controls with DWI (n = 22)	Drunk drivers without further DWI (n = 136)	Drunk drivers with repeat DWI (n = 67)
Age, mean (SD)	36.1 (12.4)	31.3 (9.1)	34.0 (12.0)	30.1 (9.2)**¤
Excitement seeking, mean (SD)	20.1 (5.3)	20.9 (6.8)	20.9 (5.4)	20.6 (5.5)
Fast decision-making, mean (SD)	19.4 (4.5)	20.8 (5.8)	20.5 (4.1)	20.0 (4.1)
Disinhibition, mean (SD)	16.5 (4.3)	19.7 (5.2)*	18.6 (4.1)**	18.5 (4.4)*
Thoughtlessness, mean (SD)	14.3 (4.4)	16.1 (6.2)	16.4 (4.9)**	16.7 (5.6)*
Alcohol-related problems, mean (SD)	0.7 (1.1)	1.5 (1.3)*	1.6 (1.4)**	2.0 (1.5)**¤
Platelet MAO activity, mean (SD)†	8.1 (4.1)	7.4 (2.8)	6.5 (2.8)**	6.9 (5.9)*
Education – higher, %	37.6	13.6*	19.9**	13.6**
More frequent light alcohol users, %	46	72.7*	63.2*	65.7*
More frequent strong alcohol users, %	10.1	27.3*	22.8*	19.4*
Tobacco smokers, %	30.2	72.7**	59.6**	70.1**
DAT1 10R/10R homozygotes, %	62.1	61.9	65.6	65.1
DAT1 9R allele carriers, %	37.9	38.1	34.4	34.9
NPSR1 AA homozygotes, %	30.3	9.5	30.8	22.2
NPSR1 T allele carriers, %	69.7	90.5	69.2	77.8
Other traffic violations, %	60.8	72.7*	70.6*	91.0**#¤
Drivers licence withdrawn, %‡	7.9	54.6**	8.8	61.2**¤¤
Mean time without drivers licence per person, in months (SD)	0.5 (2.7)	5.6 (8.1)**	1.1 (4.5)	8.4 (12.1)*¤¤

DWI, driving while impaired by alcohol; MAO, monoamine oxidase; *NPSR1*, neuropeptide S receptor 1.
†With smoking as a covariate significant difference between the subgroups disappeared; ‡Proportion of subjects whose driver's licence was withdrawn at some time during 2002–2011; *$p < 0.05$ statistically significant difference from controls without DWI;**$p < 0.001$ statistically significant difference from controls without DWI; #$p < 0.05$ statistically significant difference from controls with DWI; ¤$p < 0.05$ statistically significant difference from drunk drivers without further DWI; ¤¤$p < 0.001$ statistically significant difference from drunk drivers without further DWI.

see which variables predict DWI best together with *NPSR1*. The final model included drunk driving before recruitment [hazard ratio (HR) = 3.42; 95% confidence interval (CI) = 2.08–5.63], committing other traffic violations (HR = 2.41; 95%CI = 1.30–4.45) and being an *NPSR1* T-allele carrier (HR = 1.85; 95%CI = 1.07–3.18). The Cox regression model was statistically significant, $\chi^2(3) = 42.9$, $p < 0.001$ (−2 log likelihood = 941.6).

DAT1 genotype and active traffic accidents

There were no significant differences between the DWI subgroups when we compared them regarding *DAT1* VNTR genotype. However, there were significant differences with respect to *DAT1* VNTR when we compared the occurrence of active traffic accidents in the whole sample (Fig. 2): a significantly higher proportion of 9R carriers had been involved in active accidents in 2002–2011 ($\chi^2 = 4.5$, $p = 0.033$).

Simple logistic regression analyses showed that in addition to *DAT1,* the following variables predicted occurrence of active traffic accidents from 2002 until 2011 independently: age, income, AMIS excitement seeking, AMIS fast decision-making, committing DWI and other traffic violations in 2002–2011. The associations in the models were adjusted by committing DWI in 2002–2011 to control for the effect of DWI after recruitment: all the variables except age remained significant (Table 3). From significant predictors by simple logistic regression analyses, multiple logistic regression model was found that predicted the occurrence of active traffic accidents: higher income (OR = 2.47; 95%CI = 1.43–4.24), committing DWI (OR = 1.80; 95%CI = 1.08–3.00), committing other traffic violations (OR = 1.83; 95%CI = 1.14–2.93) and being a *DAT1* 9R-allele carrier (OR = 1.58; 95% CI = 1.02–2.44). The logistic regression model was statistically significant, $\chi^2(4) = 29.050$, $p < 0.001$, explained 9.7% (Nagelkerke R^2) of the variance and correctly classified 62.9% of cases.

Discussion

The aim of the current study was to investigate the factors associated with recurrence of drunk driving and whether such factors are also associated with other traffic violations and accidents, with particular focus on established biological markers of excessive risk-taking. People who commit more DWI represent the most hazardous drivers, and police records offer clear advantage of obtaining objective record of behaviour. Previously conducted similar studies on impulsivity and risk-taking

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

Table 2. Cox regression models predicting DWI during 2002–2011

Independent variable	HR (95% CI)	Adjusted HR (95% CI)†
1. Age	**0.96 (0.94–0.99)**	**0.97 (0.95–0.99)**
2. Education, low vs. high	**2.49 (1.35–4.57)**	**1.94 (1.05–3.59)**
3. Relationship status, couple vs. single	1.27 (0.83–1.93)	1.20 (0.79–1.82)
4. Income, high vs. low	1.49 (0.82–2.68)	1.60 (0.89–2.89)
5. Excitement seeking	1.01 (0.97–1.05)	1.00 (0.96–1.04)
6. Fast decision-making	1.01 (0.97-1.06)	1.00 (0.95–1.05)
7. Disinhibition	**1.06 (1.01–1.12)**	1.04 (0.99–1.09)
8. Thoughtlessness	**1.05 (1.01–1.10)**	1.03 (0.98–1.07)
9. Frequency of using strong alcoholic beverages	1.22 (0.98–1.52)	1.08 (0.84–1.37)
10. Frequency of using light alcoholic beverages	**1.20 (1.01–1.43)**	1.11 (0.93–1.33)
11. Alcohol-related problems	**1.38 (1.21–1.58)**	**1.24 (1.08–1.43)**
12. Tobacco smoking	**1.38 (1.19–1.59)**	**1.25 (1.07–1.45)**
13. Platelet MAO activity, high vs. low‡	0.90 (0.57–1.43)	0.97 (0.61–1.52)
14. *DAT1* 9R-allele carriers vs. 10R/10R homozygotes	0.96 (0.62–1.51)	1.02 (0.65–1.59)
15. *NPSR1* T-allele carriers vs. A/A homozygotes	**1.76 (1.02–3.03)**	**1.78 (1.03–3.06)**
16. Active traffic accidents, yes vs. no	**1.56 (1.03–2.38)**	1.51 (0.99–2.29)
17. Other traffic violations, yes vs. no	**3.04 (1.65–5.58)**	**2.57 (1.39–4.73)**
18. Drunk drivers vs. controls (2001)	**3.71 (2.29–6.01)**	

MAO, monoamine oxidase; *NPSR1*, neuropeptide S receptor 1.
†Adjusted by drunk driving in 2001; ‡Adjusted for tobacco smoking; Bold indicates significant predictor; hazard ratio (HR) with 95% confidence intervals (CIs).

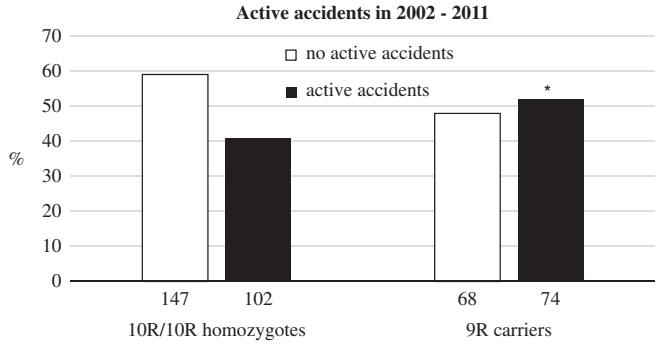

Fig. 2. Dopamine transporter gene (*DAT1*) variable number of tandem repeats (VNTR) distribution in subjects with (n = 102 + 74) and without (n = 147 + 68) active accidents in the years 2002–2011. *$p < 0.05$, statistically significant difference from the 10R/10R homozygotes with active accidents.

behaviour have mostly been cross-sectional. In the current analysis, we could use longitudinal data, including information on traffic violations and accidents.

It has been shown previously that approximately one-third of those arrested for DWI are repeat offenders (52) which is in accordance with our study, where approximately one-third of former drunk drivers had committed DWI within the next 10 years after the original recruitment, which is significantly more compared to controls. Only a few people of the original drunk drivers group were reintroduced into police records as drunk drivers during the second half of the observation period, so the probability of committing DWI again was highest in the 6 years following the initial violation. Although drunk drivers with repeat DWI group had the most subjects whose driver's licence was withdrawn before and during the observation period and also the longest period of time without a valid driver's licence per person, it seems that it was not enough for preventing their new DWI or other traffic violations. Therefore, the temporary withdrawal of drunk drivers' driving licences does not seem to be an efficient enough preventive method, and licences should be withdrawn for a longer period of time and/or the drivers should be introduced to a psychological rehabilitation program.

Platelet MAO activity is suggested to reflect the capacity of the central serotonergic system (12) and possibly the developmental differences during the foetal stage, eventually leading to higher risk-taking and impaired decision-making, in particular if intoxicated by alcohol (18). We had previously shown in this sample that platelet MAO activity was lower in drunk drivers as compared to controls and how smoking has a dose-dependent effect on platelet MAO activity (7). It is not surprising that with smoking as a covariate significant differences between the subgroups in platelet MAO activity disappeared, while also the number of non-smokers decreased in these subgroups. It has also been shown before, that both low- and high-platelet MAO activity increases the probability of becoming a smoker, suggesting that smoking is associated with low-platelet MAO activity not only because of the direct inhibitory effect of tobacco constituents on the enzyme but also because subjects with low-platelet MAO activity are more likely to become smokers (53). Indeed, separate consideration of low-intensity smoking, not likely to have any large impact on MAO activity, suggested that higher smoking prevalence in drunk drivers does not explain this association.

We expected to see more DWI in the T-allele carriers of the *NPSR1* rs324981 polymorphism, which has been associated with increased impulsivity, ADHD-related traits (39,42), earlier and higher alcohol use and higher probability of developing alcohol use disorder (41). Being a T-allele carrier did contribute significantly to the risk of repeatedly committing DWI, showing indeed increased impulsivity and more serious alcohol-related problems among T-allele carriers. Recently in a study of bus drivers, *NPSR1* A/A homozygotes had higher incidence of self-reported traffic accidents (44,54). In our study, we did not find any association between *NPSR1* and traffic accidents. Our study is also highly different with regard to the sample formation: bus drivers are highly trained and experienced professionals, and it is unlikely that their involvement in accidents could be largely driven by impulsivity. Indeed, we have demonstrated that impulsivity reduction in traffic schools does diminish the involvement in traffic accidents (55,56). The findings in the bus drivers' study instead suggest that the higher innate anxiety of the A/A homozygotes, that under environmental pressures can develop into maladaptive traits (39), could have contributed to their higher proneness to accidents.

It had been shown that *DAT1* VNTR 9R carriers have higher striatal DAT availability and higher impulsivity than 10R homozygotes (30,31,34), therefore we expected 9R carriers to have more traffic accidents and violations, especially DWI. Significantly more 9R-allele carriers overall had active traffic

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

Table 3. Logistic regression models predicting occurrence of active traffic accidents in 2002–2011

Independent variable	OR (95% CI)	Adjusted OR (95% CI) †
1. Age	**0.98 (0.96–0.99)**	0.98 (0.97–1.00)
2. Education, high vs. low	1.09 (0.70–1.68)	1.18 (0.76–1.85)
3. Relationship status, couple vs. single	0.79 (0.53–1.17)	0.81 (0.54–1.21)
4. Income, high vs. low	**2.27 (1.38–3.73)**	**2.38 (1.44–3.95)**
5. Excitement seeking	**1.06 (1.02–1.10)**	**1.06 (1.02–1.10)**
6. Fast decision-making	**1.07 (1.02–1.12)**	**1.07 (1.02–1.12)**
7. Disinhibition	0.99 (0.95–1.03)	0.98 (0.94–1.03)
8. Thoughtlessness	1.02 (0.98–1.06)	1.01 (0.97–1.05)
9. Frequency of using strong alcoholic beverages	1.24 (1.00–1.53)	1.21 (0.98–1.50)
10. Frequency of using light alcoholic beverages	1.08 (0.92–1.27)	1.06 (0.90–1.25)
11. Alcohol-related problems	1.06 (0.92–1.22)	1.02 (0.88–1.18)
12. Tobacco smoking	0.99 (0.86–1.13)	0.95 (0.82–1.09)
13. Platelet MAO activity, high vs. low‡	0.79 (0.50–1.24)	0.79 (0.50–1.25)
14. *DAT1*, 9R-allele carriers vs. 10R/10R homozygotes	**1.57 (1.04–2.38)**	**1.59 (1.04–2.41)**
15. *NPSR1*, T-allele carriers vs. A/A homozygotes	1.01 (0.65–1.56)	0.95 (0.61–1.48)
16. Other traffic violations, yes vs. no	**1.98 (1.29–3.07)**	**1.85 (1.19–2.88)**
17. Drunk drivers vs. controls (2001)	1.14 (0.77–1.68)	1.01 (0.67–1.51)
18. Drunk driving (2002–2011), yes vs. no	**1.72 (1.07–2.75)**	

MAO, monoamine oxidase; *NPSR1*, neuropeptide S receptor 1.
†Adjusted by drunk driving (2002–2011); ‡Adjusted for tobacco smoking; Bold - significant predictor; Odds ratio (OR) with 95% confidence intervals (CIs).

accidents which reflects impulsive behaviour in traffic. Additionally, *DAT1* VNTR may enhance the effect of socio-economic environment.

In addition to their DWI violation, repeat offenders had more other traffic violations than subjects in all the other groups. There were also significantly more other traffic violations among controls with DWI and drunk drivers without further DWI, compared to controls without DWI. Therefore, by their other traffic violations, subjects who had committed DWI at least once were more hazardous drivers in traffic than controls without DWI, and subjects with repeat DWI were more hazardous than those who did not repeat drunk driving in the 10-year period.

DWI has previously mostly been associated with maladaptive impulsivity (thoughtlessness and disinhibition; 7,8) and all groups with DWI differed in their maladaptive impulsivity from controls without DWI. Interestingly drunk drivers without further DWI and drunk drivers with repeat DWI had no difference in thoughtlessness and disinhibition, so maladaptive impulsivity is consistently associated with DWI but does not differentiate subjects with repetitive DWI from one-time offenders.

Finally, consistent with former studies (5,9,57), all groups with DWI had significantly more alcohol-related problems, and subjects in those groups were more frequent alcohol users than controls without DWI. Further, repeat offenders reported more alcohol-related problems than drunk drivers without further DWI, which reflects their more serious substance use problems. Nevertheless, previous DWI was a better indicator of future DWI than self-reported alcohol-related problems. All in all, the results show a clear need for preventive programs of alcohol abuse and dependence, and the need for more thorough examination of driver licence applicants' fitness to drive.

In conclusion, drunk driving is a serious violation that some people repeat. Drunk driving can be predicted by higher alcohol use and more frequent occurrence of alcohol-related problems and aspects of impulsivity. Biological markers of impulsivity can be reliably associated with everyday traffic behaviour and help in contributing to the understanding of the need for more personalized prevention activities.

Acknowledgements. We are grateful to the EPSTB participants and the whole study team. This work was supported by Estonian Ministry of Education and Research Project IUT20-40, the European Commission Seventh Framework Programme (FP7 2007-2013) Project Aggressotype (n°602805), Horizon 2020 Programme Projects CoCA (n°667302) and Eat2beNICE (n° 728018) and Estonian Road Administration.

Authors' Contribution. JH and DE contributed to the design of the study and data collection. TT and DE contributed equally to the literature searches, undertook the statistical analysis and wrote the first draft of the manuscript. JH and MV helped with the writing of the manuscript. MV, KL and AR helped with genotyping. All authors critically reviewed the content and approved the final version for publication.

Financial Support. This work was supported by Estonian Ministry of Education and Research Project IUT20-40, the European Commission Seventh Framework Programme (FP7 2007-2013) Project Aggressotype (n° 602805), Horizon 2020 Programme Projects CoCA (n°667302) and Eat2beNICE (n°728018) and Estonian Road Administration.

Conflicts of Interest. None.

Ethical Standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

References

1. **World Health Organization** (2015) *Global status report on road safety 2015*. Geneva: World Health Organization.
2. **Evans L** (1993) Comments on driver behavior and its role in traffic crashes. *Alcohol Drugs Driving* **9**, 185–195.
3. **Hels T, Lyckegaard A, Simonsen KW, Steentoft A and Bernhoft IM** (2013) Risk of severe driver injury by driving with psychoactive substances. *Accid Anal Prev* **59**, 346–356.
4. **Stacy AW, Newcomb MD and Bentler PM** (1991) Personality, problem drinking, and drunk driving: Mediating, moderating, and direct-effect models. *J Pers Soc Psychol* **60**, 795–811.
5. **Lapham SC, Smith E, C'de Baca J, Chang I, Skipper BJ, Baum G and Hunt WC** (2001) Prevalence of psychiatric disorders among persons convicted of driving while impaired. *Arch Gen Psychiatry* **58**, 943–949.
6. **Dickman SJ** (1990) Functional and dysfunctional impulsivity: Personality and cognitive correlates. *J Pers Soc Psychol* **58**, 95–102.
7. **Eensoo D, Paaver M, Pulver A, Harro M and Harro J** (2004) Low platelet MAO activity associated with high dysfunctional impulsivity and

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

antisocial behavior: evidence from drunk drivers. *Psychopharmacol* **172**, 356–358.
8. **Paaver M, Eensoo D, Pulver A and Harro J** (2006) Adaptive and maladaptive impulsivity, platelet monoamine oxidase (MAO) activity and risk-admitting in different types of risky drivers. *Psychopharmacol* **186**, 32–40.
9. **Eensoo D, Paaver M, Harro M and Harro J** (2005) Predicting drunk driving: contribution of alcohol use and related problems, traffic behaviour, personality and platelet monoamine oxidase (MAO) activity. *Alcohol Alcohol* **40**, 140–146.
10. **von Knorring L, Oreland L and Winblad B** (1984) Personality traits related to monoamine oxidase activity in platelets. *Psychiatry Res* **12**, 11–26.
11. **Oreland L** (1993) Monoamine oxidase in neuro-psychiatric disorders. In: Yasuhar H, Parves SH, Oguchi K, Sandler M and Nagatsu T, editors. Monoamine Oxidase: Basic and Clinical Aspects. Utrecht: VSP; p. 219–247.
12. **Oreland L** (2004) Platelet monoamine oxidase, personality and alcoholism: the rise, fall and resurrection. *Neurotoxicol* **25**, 79–89.
13. **von Knorring L and Oreland L** (1996) Platelet MAO activity in type 1/ type 2 alcoholics. *Alcohol Clin Exp Res* **20**, 224a–230a.
14. **Sabre L, Harro J, Eensoo D, Vaht M, Kabel V, Pakkanen M, Asser T and Kõrv J** (2016) A new risk factor for traumatic spinal cord injury. *J Neurotrauma* **33**, 1946–1949.
15. **Stalenheim EG** (2004) Long-term validity of biological markers of psychopathy and criminal recidivism: follow-up 6–8 years after forensic psychiatric investigation. *Psychiatry Res* **121**, 281–291.
16. **Oreland L, Nilsson K, Damberg M and Hallman J** (2007) Monoamine oxidases—activities, genotypes and the shaping of behaviour. *J Neural Transm* **114**, 817–822.
17. **Jokinen J, Königsson J, Moberg T, Jönsson EG, Tiihonen J, Nordström P, Oreland L and Åsberg M** (2018) Platelet monoamine oxidase activity and interpersonal violence in male suicide attempters. *Psychiatry Res* **260**, 173–176.
18. **Harro J and Oreland L** (2016) The role of MAO in personality and drug use. *Prog Neuropsychopharmacol Biol Psychiatry* **69**, 101–111.
19. **Ikemoto S and Panksepp J** (1999) The role of nucleus accumbens dopamine in motivated behavior: a unifying interpretation with special reference to reward-seeking. *Brain Res Rev* **31**, 6–41.
20. **Bergh C, Eklund T, Södersten P and Nordin C** (1997) Altered dopamine function in pathological gambling. *Psychol Med* **27**, 473–475.
21. **Thapar A, O'donovan M and Owen MJ** (2005) The genetics of attention deficit hyperactivity disorder. *Hum Mol Genet* **14**, R275–R282.
22. **Barkley RA, Murphy KR, Dupaul GJ and Bush T** (2002) Driving in young adults with attention deficit hyperactivity disorder: knowledge, performance, adverse outcomes, and the role of executive functioning. *J Int Neuropsychol Soc* **8**, 655–672.
23. **Fried R, Petty C, Surman C, Reimer B, Aleardi M, Martin J, Coughlin J and Biederman J** (2006) Characterizing impaired driving in adults with ADHD: a controlled study. *J Clin Psychiatry* **67**, 567–574.
24. **Puumala T and Sirviö J** (1998) Changes in activities of dopamine and serotonin systems in the frontal cortex underlie poor choice accuracy and impulsivity of rats in an attention task. *Neuroscience* **83**, 489–499.
25. **Winstanley CA, Theobald DE, Dalley JW, Cardinal RN and Robbins TW** (2005) Double dissociation between serotonergic and dopaminergic modulation of medial prefrontal and orbitofrontal cortex during a test of impulsive choice. *Cereb Cortex* **16**, 106–114.
26. **De Wit H, Enggasser JL and Richards JB** (2002) Acute administration of d-amphetamine decreases impulsivity in healthy volunteers. *Neuropsychopharmacol* **27**, 813–825.
27. **Friedel RO** (2004) Dopamine dysfunction in borderline personality disorder: a hypothesis. *Neuropsychopharmacol* **29**, 1029–1039.
28. **Chen N and Reith ME** (2000) Structure and function of the dopamine transporter. *Eur J Pharmacol* **405**, 329–339.
29. **Costa A, Riedel M, Müller U, Möller HJ and Ettinger U** (2011) Relationship between SLC6A3 genotype and striatal dopamine transporter availability: a meta-analysis of human single photon emission computed tomography studies. *Synapse* **65**, 998–1005.
30. **van de Giessen EM, de Win MM, Tanck MW, van den Brink W, Baas F and Booij J** (2009) Striatal dopamine transporter availability associated with polymorphisms in the dopamine transporter gene SLC6A3. *J Nucl Med* **50**, 45–52.
31. **Faraone SV, Spencer TJ, Madras BK, Zhang-James Y and Biederman J** (2014) Functional effects of dopamine transporter gene genotypes on in vivo dopamine transporter functioning: a meta-analysis. *Mol Psychiatry,* **19**, 880–889.
32. **Ma Y, Fan R and Li MD** (2016) Meta-Analysis Reveals Significant Association of the 3′-UTR VNTR in SLC 6A3 with Alcohol Dependence. *Alcohol Clin Exp Res* **40**, 1443–1453.
33. **Franke B, Vasquez AA, Johansson S, Hoogman M, Romanos J, Boreatti-Hümmer A, Heine M, Jacob CP, Lesch KP, Casas M and Ribasés M** (2010) Multicenter analysis of the SLC6A3/DAT1 VNTR haplotype in persistent ADHD suggests differential involvement of the gene in childhood and persistent ADHD. *Neuropsychopharmacol* **35**, 656–664.
34. **Forbes EE, Brown SM, Kimak M, Ferrell RE, Manuck SB and Hariri AR** (2009) Genetic variation in components of dopamine neurotransmission impacts ventral striatal reactivity associated with impulsivity. *Mol Psychiatry* **14**, 60–70.
35. **Pearson MR, Murphy EM and Doane AN** (2013) Impulsivity-like traits and risky driving behaviors among college students. *Accid Anal Prev* **53**, 142–148.
36. **Ghazal P** (2016) The physio-pharmacological role of the NPS/NPSR system in psychiatric disorders: a translational overview. *Curr Protein Pept Sci* **17**, 380–397.
37. **Si W, Aluisio L, Okamura N, Clark SD, Fraser I, Sutton SW, Bonaventure P and Reinscheid RK** (2010) Neuropeptide S stimulates dopaminergic neurotransmission in the medial prefrontal cortex. *J Neurochem* **115**, 475–482.
38. **Dannlowski U, Kugel H, Franke F, Stuhrmann A, Hohoff C, Zwanzger P, Lenzen T, Grotegerd D, Suslow T, Arolt V and Heindel W** (2011) Neuropeptide-S (NPS) receptor genotype modulates basolateral amygdala responsiveness to aversive stimuli. *Neuropsychopharmacol* **36**, 1879–1885.
39. **Laas K, Reif A, Kiive E, Domschke K, Lesch KP, Veidebaum T and Harro J** (2014) A functional NPSR1 gene variant and environment shape personality and impulsive action: a longitudinal study. *J Psychopharmacol* **28**, 227–236.
40. **Laas K, Reif A, Akkermann K, Kiive E, Domschke K, Lesch KP, Veidebaum T and Harro J** (2014) Interaction of the neuropeptide S receptor gene Asn107Ile variant and environment: contribution to affective and anxiety disorders, and suicidal behaviour. *Int J Neuropsychopharmacol* **17**, 541–552.
41. **Laas K, Reif A, Akkermann K, Kiive E, Domschke K, Lesch KP, Veidebaum T and Harro J** (2015) Neuropeptide S receptor gene variant and environment: contribution to alcohol use disorders and alcohol consumption. *Addict Biol* **20**, 605–616.
42. **Laas K, Eensoo D, Paaver M, Lesch KP, Reif A and Harro J** (2015) Further evidence for the association of the NPSR1 gene A/T polymorphism (Asn107Ile) with impulsivity and hyperactivity. *J Psychopharmacol* **29**, 878–883.
43. **Reinscheid RK, Xu YL, Okamura N, Zeng J, Chung S, Pai R, Wang Z and Civelli O** (2005) Pharmacological characterization of human and murine neuropeptide s receptor variants. *J Pharmacol Exp Ther* **315**, 1338–1345.
44. **Taranov AO, Puchkova AN, Slominsky PA, Tupitsyna TV, Dementiyenko VV and Dorokhov VB** (2017) Associations between chronotype, road accidents and polymorphisms in genes linked with biological clock and dopaminergic system. *ZH NEVROL PSIKHIATR* **117**, 28–33.
45. **Laas K, Reif A, Herterich S, Eensoo D, Lesch KP and Harro J** (2010) The effect of a functional NOS1 promoter polymorphism on impulsivity is moderated by platelet MAO activity. *Psychopharmacol* **209**, 255–261.
46. **Hallman J, Oreland L, Edman G and Schalling D** (1987) Thrombocyte monoamine oxidase activity and personality traits in women with severe premenstrual syndrome. *Acta Psychiatr Scand* **76**, 225–234.
47. **Harro M, Eensoo D, Kiive E, Merenäkk L, Alep J, Oreland L and Harro J** (2001) Platelet monoamine oxidase in healthy 9-and 15-years old children: the effect of gender, smoking and puberty. *Prog Neuropsychopharmacol Biol Psychiatry* **25**, 1497–1511.

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press

48. **Maksimov M, Vaht M, Murd C, Harro J and Bachmann T** (2015) Brain dopaminergic system related genetic variability interacts with target/mask timing in metacontrast masking. *Neuropsychol* **71**, 112–118.
49. **Bannon MJ, Michelhaugh SK, Wang J and Sacchetti P** (2001) The human dopamine transporter gene: gene organization, transcriptional regulation, and potential involvement in neuropsychiatric disorders. *Eur Neuropsychopharmacol* **11**, 449–455.
50. **Domschke K, Reif A, Weber H, Richter J, Hohoff C, Ohrmann P, Pedersen A, Bauer J, Suslow T, Kugel H and Heindel W** (2011) Neuropeptide S receptor gene—converging evidence for a role in panic disorder. *Mol Psychiatry* **16**, 938–948.
51. **Fowler JS, Logan J, Wang GJ and Volkow ND** (2003) Monoamine oxidase and cigarette smoking. *Neurotoxicol* **24**, 75–82.
52. **Warren-Kigenyi N and Coleman H**. DWI Recidivism in the United States: An Examination of State-Level Driver Data and the Effect of Look-Back Periods on Recidivism Prevalence. Traffic Safety Facts Research Note 2014; DOT HS 811 991. NHTSA.
53. **Harro J, Fischer K, Vansteelandt S and Harro M** (2004) Both low and high activities of platelet monoamine oxidase increase the probability of becoming a smoker. *Eur Neuropsychopharmacol* **14**, 65–69.
54. **Dorokhov VB, Puchkova AN, Taranov AO, Ermolayev VV, Tupitsyna TV, Slominsky PA and Dementiyenko VV** (2017) Polymorphisms in sleep and cognitive function related genes are associated with vehicle crash history in shift working bus drivers. *ZH VYSSH NERV DEYAT* + **67**, 49–54.
55. **Paaver M, Eensoo D, Kaasik K, Vaht M, Mäestu J and Harro J** (2013) Preventing risky driving: A novel and efficient brief intervention focusing on acknowledgement of personal risk factors. *Accid Anal Prev* **50**, 430–437.
56. **Eensoo D, Paaver M, Vaht M, Loit HM and Harro J** (2018) Risky driving and the persistent effect of a randomized intervention focusing on impulsivity: the role of the serotonin transporter promoter polymorphism. *Accid Anal Prev* **113**, 19–24.
57. **Sloan FA, Eldred LM and Davis DV** (2014) Addiction, drinking behavior, and driving under the influence. *Subst Use Misuse* **49**, 661–676.

https://doi.org/10.1017/neu.2018.30 Published online by Cambridge University Press