The acute effects of low dose of alcohol on simulated driving performance in male and female young drivers with high versus low testosterone levels

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Abstract

Background: According to the World Health Organization, road traffic crashes represent the single leading cause of death for young people. Road traffic crashes are largely preventable, yet the precise mechanisms underlying individual driving risk remain relatively unidentified. Some risky drivers are over-represented among those involved in serious and fatal road traffic crashes, including those who misuse alcohol. Understanding what drives their risk taking is a key to developing evidence-based and effective prevention programs. Research focusing on the causes of risky driving has examined neurobiological markers of risk taking, such as cortisol, serotonin, and adrenaline. The steroid hormone testosterone has received substantial attention in relation to risk taking, but not specifically related to driving behaviour. Testosterone has been associated with sensation seeking and impulsivity, two consistent correlates of risky driving. Furthermore, interactions between testosterone and alcohol in relation to sensation seeking and impulsivity have been observed, potentially making testosterone a specific factor in driving while impaired with alcohol. In this experiment, four hypotheses were tested: H1) Young drivers with higher testosterone level show higher mean speed in simulation than young drivers with lower testosterone level; H2) Alcohol moderates the relationship between testosterone level and mean speed; H3) Sex moderates the relationship between testosterone level and mean speed; H4) Sensation seeking and impulsivity mediate the relationship between testosterone level and mean speed under alcohol.

Methods: This study is part of a larger between-subject, randomized, placebo-controlled experiment. Eleven male and eleven female drivers aged 18-34 years were recruited and their saliva assayed for endogenous testosterone level using radioimmunoassay. Participants also responded to questionnaires assessing sensation seeking and impulsive personality

characteristics, and performed two driving simulation tasks, one at BAC (blood alcohol content) of 0% (i.e., baseline; no-alcohol condition) and another at a positive BAC of 0.02% - 0.05% (i.e., alcohol condition). *Analytic strategy:* A median-split of testosterone level into high and low testosterone levels was done separately for male and female groups. Mean driving speed in simulation was the main dependent measure of risky driving propensity. To test H1, 2, & 3, a mixed-design ANOVA was performed. Testosterone level (high, low) and sex (male, female) were between-subject factors and alcohol condition (no-alcohol, alcohol) was the within-subject factor. The mediation analysis (i.e., H4) was performed using the bootstrapping method with bias-corrected confidence estimates.

Results: H1 was not supported by the findings; young drivers with higher testosterone level did not report higher simulated speed than young drivers with lower testosterone level, $p > .05$. H2 was supported. A significant alcohol X testosterone interaction was detected ($p = .04$; $\eta_p^2 = .20$). Specifically, young drivers with higher testosterone level reported higher mean speed than drivers with lower testosterone level, but only after alcohol consumption. Sex was not a significant moderator of the relationship between testosterone level and simulated speed ($p > .05$). Neither sensation seeking nor impulsivity mediated the relationship between testosterone level and simulated speed under alcohol ($p > .05$).

Conclusion: Interaction between testosterone hormone and alcohol may be one mechanism contributing to risky driving under legal BAC (in Canada < 0.08%). Practically, findings from this study can help future development of educational programs, based on age and sex, to better inform young drivers about neurobiological factors that can affect their ability to drive. A promising avenue for future research would be to test potential mediators between testosterone level and risky driving under alcohol such as reward sensitivity and response inhibition. This

approach could help to verify the findings of this study and could considerably provide potential targets for intervention.

Résumé

Contexte: Selon l'Organisation mondiale de la santé, les collisions routières représentent la principale cause de mortalité chez les jeunes. Les collisions routières sont en grandes partie évitables, mais les mécanismes précis sous-jacents au risque individuel restent encore à identifier. Certains conducteurs à risque sont surreprésentés parmi ceux impliqués dans les collisions routières graves et fatales, incluant ceux faisant un usage abusif de l'alcool. La recherche axée sur les causes de la conduite à risque s'est penchée sur les marqueurs neurobiologiques de la prise de risque, comme le cortisol, la sérotonine et l'adrénaline. La testostérone a reçu beaucoup d'attention en lien avec la prise de risque, mais pas spécifiquement en lien avec les comportements de conduite. Cette hormone a été associée à la recherche de sensations et à l'impulsivité, deux corrélats cohérents de la conduite à risque. En outre, les interactions entre la testostérone et l'alcool mises en relation avec la recherche de sensations et l'impulsivité ont également été observées, faisant de la testostérone un facteur spécifique potentiel de la conduite avec facultés affaiblies par l'alcool. Dans cette expérimentation, quatre hypothèses ont été testées: H1) Lors de simulations de conduite, les jeunes conducteurs ayant un niveau élevé de testostérone conduisent à une vitesse plus élevée que ceux ayant un niveau de testostérone inférieur; H2) L'alcool modère la relation entre le niveau de testostérone et la vitesse en simulation; H3) Le sexe modère la relation entre le niveau de testostérone et la vitesse en simulation; H4) La recherche de sensations et l'impulsivité ont un effet médiateur sur la relation entre le niveau de testostérone et la vitesse en simulation après consommation d'alcool.

Méthodologie: Cette étude fait partie d'une expérimentation inter-sujet, randomisée, contrôlée par placebo plus large. Vingt-deux conducteurs (H=11, F=11) âgés de 18-34 ans ont été recrutés. Leur salive a été analysée pour déterminer leur niveau de testostérone endogène par dosage radio-

immunologique. Les participants ont également répondu à des questionnaires évaluant la recherche de sensations ainsi que des caractéristiques de la personnalité liées à l'impulsivité en plus d'effectuer deux tâches de simulation de conduite, l'une à un taux d'alcoolémie de 0% (ligne de base) et l'autre à un taux d'alcoolémie de 0.02%-0.05% (condition alcool). *Stratégie analytique*: Une séparation en 2 groupes (niveaux haut et bas) divisés autour de la médiane des taux de testostérone a été effectuée pour chaque sexe. La vitesse moyenne lors des simulations de conduite est la mesure dépendante principale de la propension à la conduite à risque. Pour tester H1, 2, & 3, une ANOVA mixte a été réalisée. Le niveau de testostérone (haut, bas) et le sexe (homme, femme) sont les facteurs inter-sujets et le taux d'alcoolémie (ligne de base (0%)) et condition alcool (0.02% - 0.05%) le facteur intra-sujet. L'analyse de la médiation (H4) a été réalisée en utilisant la méthode d'autoamorçage (bootstrap) avec estimateurs de confiance à biais corrigé.

Résultats: H1 n'a pas été corroborée par les conclusions (i.e. lors des simulations, les jeunes conducteurs ayant un niveau élevé de testostérone n'ont pas conduit à une vitesse plus élevée que ceux ayant un niveau inférieur de testostérone, $p > .05$). H2 a été soutenue par les résultats. Une interaction significative entre l'alcool et la testostérone a été détectée ($p = .04$; $\eta_p^2 = .20$). Plus précisément, les jeunes conducteurs ayant un niveau élevé de testostérone ont démontré une vitesse en simulation plus élevée que ceux ayant un niveau plus faible et ce dans la condition alcool, mais pas à la ligne de base. Le sexe n'était pas un modérateur significatif de la relation entre le niveau de testostérone et la vitesse en simulation ($p > .05$). Ni la recherche de sensations, ni l'impulsivité n'avait un effet médiateur sur la relation entre le niveau de testostérone et la vitesse en simulation après consommation d'alcool ($p > .05$).

Conclusion: L’interaction entre la testostérone et l'alcool pourrait être un mécanisme contribuant à la conduite à risque avec un taux d’alcoolémie sous la limite légale (au Canada < 0.08%). En pratique, les résultats de cette étude peuvent aider à élaborer des programmes éducatifs, basés sur l'âge et le sexe, afin de mieux informer les jeunes conducteurs sur les facteurs neurobiologiques qui peuvent affecter leur aptitude à conduire. Une avenue prometteuse pour la recherche future serait de tester des médiateurs potentiels entre le niveau de testostérone et la conduite à risque sous l’influence de l’alcool tels que la sensibilité à la récompense et l'inhibition de la réponse. Cette approche pourrait aider à vérifier les résultats de cette étude et pourrait largement fournir des cibles d'intervention potentielles.

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Preface & Contribution of Authors

All elements of this thesis are considered original scholarship. To the best of my knowledge, the thesis contains no material previously published except where due reference is made. I confirm that I have made a significant contribution to this thesis.

Introduction

The Burden of Road Traffic Crashes

Road traffic crashes (RTC) represent a critical global public health and socio-economic problems. Globally, almost 1.24 million people die as a result of RTCs while 20 to 50 million more people suffer non-fatal injuries, many of which incur significant disability (WHO, 2013). In Canada in 2011, the Transportation Safety Board reported that 2,006 Canadians were killed, and 10,443 were seriously injured due to RTCs (Canada, 2013). RTCs have an enormous annual economic cost of $518 billion worldwide, representing approximately 1-3% of the gross national product of developed countries such as Canada (WHO, 2013).

Risk factors of RTCs

While numerous factors contribute to road traffic fatalities, human factors are implicated to some degree in an estimated 89 % of crashes (NHTSA, 1995). Human factors that impair the ability for safe driving include alcohol intake (driving while impaired by alcohol, or DWI) (Purssell et al., 2010), fatigue and sleep deprivation (Vivoli et al., 2013), distracted driving by cell phones (Adeola & Gibbons, 2013) and passengers' characteristics (Ouimet et al., 2010). Alcohol use, however, represents the primary cause of RTCs (Ogden & Moskowitz, 2004).

Risky driving is an important contributor to RTCs

Different empirical and theoretical approaches have been taken to understand the underpinnings of RTCs. Accumulated research evidence has shown that risky driving is an important contributor to RTCs (Jonah, 1986; Iversen, 2004; Mesken, Lajunen, & Summala, 2002). For instance, Iversen (2004) found that people who had been involved in at least one RTC over the past one year have reported more speeding, reckless driving, and driving while impaired

(DWI) over the same period than those without RTCs over the past year. Risky driving behaviour includes aggressive driving, speeding, and rule violations. Among these, speeding was the most common behaviour and important contributor to RTCs. Young drivers appear to be the most susceptible to speeding (Clarke et al. 2006; Ouimet et al., 2008). For example, in a sample of 276 participants reporting a history of RTCs in the past 12 months in New Zealand, driving at 20 km/h or more over the speed limit was associated with a significantly greater risk of RTCs in younger drivers below the age of 40 (prevalence rate = 3.4) than in older drivers (prevalence rate = 2.0) (Blows et al., 2005). The main objective of this study is to further our understanding of the biological mechanisms underlying individual driver risk taking by addressing two questions: i) what are the individual biological factors contributing to risky driving in young drivers; ii) why do some drivers engage in more driving related risk taking under alcohol - while others do not?

In the following sections, I begin with a description of risky driving behaviours in young adults. This is followed by consideration of the roles of neurobiological factors, interactions between age and neurobiological factors, and sex.

The 'Young Drivers Problem'

Young drivers are overrepresented in RTCs and their resulting fatalities and injuries. Globally, young drivers below 34 years old were involved in 45% of fatal crashes, 50% of injuries and 49% of property-damage resulting from RTCs in 2001 (NHTSA, 2001). This statistic applies to Canadian young drivers as well. While drivers below 34 years old constitute 20% of licensed drivers in Canada in 2011, they were involved in approximately 40% of road traffic fatalities and 41% of serious injuries (Canada, 2013). Young drivers are also over-involved in alcohol-related RTCs. Among DWI fatalities in the USA in 2013, about 62% involved drivers between 21 and 34 years of age compared to 38% of DWI fatalities involved drivers 35 years of

age and older (NHTSA, 2014). The higher risk for RTC in young drivers is posited to stem from several factors, including: i) lack of experience and driving skills; ii) alcohol use; and iii) the propensity to engage in risk-taking behaviours (Bingham & Shope, 2004).

Inexperience

The association between youthful age and RTCs has been attributed to inexperience. Young drivers are more frequently involved in RTCs and road fatalities than older drivers (Ballesteros & Dischinger, 2000). However, irrespective of age, less experienced drivers are more susceptible to RTCs than more experienced drivers. For example, novice drivers possess 10 times greater crash rates per kilometre travelled than more experienced drivers; moreover, crash risk declines significantly during the first two years of driving experience (Freeman, 2012; Ouimet et al., 2014). Inexperience has been associated with poorer risk and hazard perception (Borowsky & Oron-Gilad, 2013) that have been associated with unintentional driving errors (Waller et al., 2001). Because age and experience are correlated, in general young drivers are the least experienced drivers.

Alcohol

The prevalence rate of alcohol-related RTCs and fatalities is significantly higher in young drivers. Of all road user groups, younger adults (19 to 39 years old) are more likely to have an alcohol-related RTC than older adults (40 to 55 years old) (Norris, Matthews, & Riad, 2000). This could be attributed to higher rates of alcohol-misuse and drink-driving behaviours in young adults. Alternatively, young adults are more vulnerable to the impairing effects of alcohol than older adults.

Alcohol use problems Alcohol misuse is a common risky behaviour pattern in young adults. Alcohol use is a broad term that includes moderate alcohol consumption (i.e., one drink per day for women and up to two drinks per day for men), hazardous alcohol use (i.e., excessive daily consumption in excess of these limits), binge drinking (i.e., heavy single-occasion drinking of ≥ 4 drinks for women and ≥ 5 drinks for men over a few hours), harmful use (i.e., a pattern of drinking that is already causing damage to health and psychosocial functioning), and alcohol use disorder (i.e., a maladaptive pattern of alcohol use that meets clinical diagnostic thresholds for serious impairment) (Dedert et al., 2015). Hazardous and binge alcohol drinking are particularly common in young adults (Miller et al., 2007). For example, in Ireland, hazardous alcohol use has been reported by 65.2% and 67.3% of undergraduate males and females respectively (Davoren et al., 2015). In Canada, in 2004 binge alcohol drinking was reported by 20.6% and 12.5% of undergraduate male and female students respectively (CCSA, 2014).

Drink-driving Drink-driving is one of the most widespread forms of risk taking in young adults. Unlike DWI that is legally defined as operating a motor vehicle with a BAC (blood alcohol content) level above the legal limit (according to jurisdiction), drink-driving is defined as driving after drinking any amount of alcohol (Ministry of Transportation, Ontario). Approximately 24% of college students reported driving after drinking one to four standard alcoholic drinks (Hingson et al., 2003). (A standard drink is defined as a 12-oz bottle or can of beer, a 4-oz glass of wine, a 12-oz bottle of wine cooler or a shot (1.25-oz) of distilled spirits, straight or in a mixed drink (Hingson et al., 2003)). A longitudinal study involving 1253 first-year, 21-year-old students attending a large, mid-Atlantic US university found that 63% of students reported drink-driving, while 25% of students reported engaging in DWI in the past year (Beck, 2010). By comparison, estimates of drink-driving in older drivers indicate that only 2.7%

of them reported a DWI episode within the last month (CDCP, 2011). This underscores the extent of drink-driving problem in young drivers.

One of the most successful policy countermeasures for the drink-driving problem in young drivers is the Graduated Driver Licensing (GDL) program. The GDL program has been adopted in many American and Canadian jurisdictions. For example, in the province of Quebec, drink-driving is prohibited for young drivers under 22 years of age (i.e., zero tolerance) (SAAQ, 2014). Evaluations of the effectiveness of GDL have revealed that the most restrictive programs produce the greatest road safety benefits, particularly for young novice drivers (Masten, Foss, & Marshall, 2011). Nevertheless, young drivers are persistently over-represented in alcohol-related RTCs and fatalities (Miller et al., 2007; Sommers et al., 2013), indicating that younger drivers remain at high risk despite these regulations, and that more effective interventions are still needed.

Vulnerability to alcohol One of the possible causes of over-involvement in alcohol-related RTCs among young drivers is their selective vulnerability to the impairing effects of alcohol. Impairment in this context refers to "a diminished ability to operate a motor vehicle and is based on individuals' abilities comparable to their own performance in an alcohol-free state" (Martin et al., 2013). Overall, the relationship between alcohol dose and involvement in RTCs is incremental. The odd-ratio of RTCs was observed to increase from 1.24 per 10-g of alcohol to 52.0 per 120 g of alcohol, indicating a dose-related risk of alcohol on RTCs (Taylor & Rehm, 2012). However, as compared to older drivers, the risk of alcohol-related RTCs was five times greater in younger drivers at any BAC level (Mayhew et al., 2011; Peck et al., 2008).

Individual variability While young drivers in general are more vulnerable to the impairing effects of alcohol, significant individual variability in driving skills in response to similar alcohol

doses has been observed. Howat (1986) investigated real-road driving skills under alcohol of BAC < 0.1% in a sample of seven males and seven females aged 21 to 32 years. He found that drivers showed substantial variability in speed maintenance under similar doses of alcohol. Indeed, the relationship between BAC and driving risk in young drivers is not consistent, both under illegal BAC of > 0.08% (Jones, 1999) and lower and possibly legal BAC of > .00% - 0.08% (i.e., depending on jurisdiction) (Ferrara, Zancaner, & Giorgetti, 1994). This makes it difficult to establish a "safe" BAC level for young drivers.

Personality

Neglect for the negative consequences of one's actions is a personality feature of great interest to the driving safety community (Parvizi & Hamzehgardeshi, 2014). Two personality features are consistently correlated to risk-taking behaviours in young adults: sensation seeking and impulsivity (Dahl, 2004; Verdejo-Garcia, Lawrence, & Clark, 2008; Zuckerman & Kuhlman, 2000). A meta-analysis of 22 studies conducted by Lauriola et al (2014) investigated the relationship between risk taking measured using the Balloon Analogue Risk Task and sensation seeking and impulsivity among 2820 male and female participants aged between 14 and 27 years old. They found that risk taking is associated with sensation seeking with an effect size in the small-moderate range (r = .14) and with impulsivity with a small effect size (r = .10). These associations were stronger in older adolescents and younger adults (i.e., 18 – 24 years old) compared with other ages. Sensation seeking is considered to be "a biologically based tendency to seek novel, complex, intense sensations and the proclivity to take physical, social, legal, and financial risks in order to achieve such experiences" (Zuckerman, 1994; Zuckerman et al. 1972). Impulsivity, on the other hand, is a multidimensional biologically-based construct (Evenden, 1999) defined as the "inclination of an individual to act on urges rather than thought and with

diminished regard to consequences" (Chamberlain & Sahakian, 2007; Meda et al., 2009). Sensation seeking and impulsivity are conceptually related, leading some researchers to combine them into a single construct (Zuckerman, 1996). Other authorities consider them to be distinct constructs. In support of this perspective, a confirmatory factor analysis using six measures that assess either sensation seeking or impulsivity confirmed that sensation seeking and impulsivity were independent (Magid, MacLean, & Colder, 2007).

Personality and risky driving Sensation seeking has been linked to a range of different risk-taking driving behaviours. For example, speeding, drunk driving, and RTCs have been associated with increased sensation seeking scores (Bachoo, Bhagwanjee, & Govender, 2013; Constantinou et al., 2011; Dahlen et al., 2005; Hatfield & Fernandes, 2009; Hatfield, Fernandes, & Job, 2014; Jonah, Thiessen, & Au-Yeung, 2001; Mirman et al., 2012; Nordfjaern & Rundmo, 2013; Schwebel et al., 2007; Scott-Parker et al., 2012, 2013; Yang et al., 2013). Similarly, impulsivity has been consistently identified as an important factor in risky driving behaviours, including drink-driving (Constantinou et al., 2011; Dahlen et al., 2005; Deffenbacher et al., 2005; Jakubczyk et al., 2013; Paaver et al., 2006; Pearson, Murphy, & Doane, 2013; Ryb et al., 2006; Treloar et al., 2012). Furthermore, impulsivity mediated the association between attention-deficit hyperactivity disorder and risky alcohol-impaired driving (Thompson et al., 2007).

The research aims

RTCs are preventable. As risky driving (e.g., speeding and DWI) are responsible for the majority of road traffic injuries and fatalities in young drivers, understanding the mechanisms pushing individual driver risk in this vulnerable driver group represents a global strategy for reducing RTCs (UN Decade of Action for Road Safety: 2011-2020; WHO, 2011). The present research is predicated upon the over-arching hypothesis that risk taking, including risky driving

and DWI, involves a complex web of psychosocial, neurological, biological and psychological factors and markers, most of which remain incompletely understood (Brown et al., 2010). Therefore, multidisciplinary research that examines risky driving from multiple levels of analysis is needed. At the same time, investigation of risky driving has relied mainly on self-reported subjective measures. Self-reports of behaviour may depart substantially from actual behaviour, particularly if the behaviour is considered to be socially unacceptable or is illegal (e.g., alcohol-related violations) (Chang, Gregory, & Lapham, 2002). Moreover, self-reports are subject to various sources of inaccuracy including convergence with other modes of measurement (i.e., common-method variance) (Podsakoff et al., 2003), recall and under-reporting problems (Chapman, Ismail, & Underwood, 1999), and cultural limitations (Hamamura, Heine, & Paulhus, 2008). There is a need for alternate objective indicators besides self-report measures to advance our understanding of driver risk. Thus, the main objective of this study is to investigate the neurobiological mechanisms influence how alcohol, personality and executive capacities interact to produce risky driving behaviour in young drivers.

Neurobiological Correlates of Risky Driving Behaviours

Alcohol's impact on neurobiological functioning related to risky driving

The operation of a motor vehicle requires the integration and evaluation of multiple sources of cognitive and behavioural information (Fastenmeier & Gstalter, 2007) to guide appropriate decision making and driving behaviour (Funahashi, 2001; Hsieh et al., 2009; Ikkai & Curtis, 2011; Li, Adali, & Calhoun, 2012; Provost, Petrides, & Monchi, 2010). Executive and psychomotor functions are inter-related and intimately connected with the intact function of the brain. Executive function is defined as a group of cognitive skills responsible for the implementation of purposeful, goal-directed behaviours such as inhibition, cognitive flexibility,

working memory, and planning (Winter et al., 2014). Psychomotor function is the relationship between executive functions and physical movement such as coordination, manipulation, dexterity, strength, speed, and fine motor skills (R. Kerr, 1982). Alcohol intake significantly affects the frontal cortex, anterior cingulated cortex, insula and cerebellum, which results in impaired executive and psychomotor control performance (Calhoun, Pekar, & Pearlson, 2004; Claus et al., 2011; Dager et al., 2014; Dirksen et al., 2006).

In relation to specific driving skills, alcohol dose has been associated with decreased ability to divide attention (Koelega, 1995; Verster et al., 2009), increased complex reaction time (i.e., the time required to respond to two or more stimuli) (Breitmeier et al., 2007), decreased tracking ability (i.e., ability to maintain position on a roadway) (Evans et al., 1974), and decreased hazard perception (West et al., 1993). Younger drivers have, specifically, been at higher risk of cognitive impairment including memory dysfunction, divided attention and visuospatial deficits after consumption of even small to moderate amounts of alcohol than older drivers (Acheson, Stein, & Swartzwelder, 1998; Freydier et al., 2014). The cognitive and visuospatial deficits have been found to be directly related to driving impairments (Shanmugaratnam, Kass, & Arruda, 2010; Sumer, Ayvasik, & Er, 2005).

Neurobiological correlates of sensation seeking and impulsivity

Sensation seeking and impulsivity characteristics both appear to have a biological basis. For example, high sensation seekers showed stronger fMRI (i.e., functional Magnetic Resonance Imaging) responses to high-arousal stimuli in brain regions (i.e., insula, posterior medial orbito-frontal and prefrontal cortex) associated with arousal and reinforcement compared to low sensation seekers (Cservenka et al., 2012; Joseph et al., 2009). Neuroimaging studies on impulsivity reveal involvement of the prefrontal cortex (Ding et al., 2014), insula (Dambacher et

al., 2014; McHugh et al., 2013), anterior cingulate cortex, and amygdala (Kerr et al., 2014). These areas of the brain, particularly the prefrontal cortex, are involved in executive functioning. Indeed, patients with brain injuries or pathologies affecting the prefrontal cortex have shown a tendency for riskier decision-making and a disregard for the negative consequences of their actions (Knoch & Fehr, 2007).

The relationship between brain and sensation seeking and impulsive behaviour is mediated by hormones and neurotransmitters (Bos, Hermans, et al., 2012; Bos, Panksepp, et al., 2012). For example, the serotonergic and the hypothalamic-pituitary-adrenal (HPA) systems have been found to be correlated with sensation seeking and impulsivity (Couture et al., 2008; Giotakos, 2013; Oreland et al., 2010; Shabani et al., 2011). Another hormone that has received substantial attention in relation to risk taking, sensation seeking, and impulsivity is testosterone. For instance, personality research has shown a positive correlation between the level of circulating testosterone and measures of sensation seeking (Aluja & Torrubia, 2004; Coccaro et al., 2007), and impulsivity in healthy volunteers (Bjork et al., 2001; Fujisawa et al., 2011), antisocial personality (Batrinos, 2012; Rasanen et al., 1999; Yildirim & Derksen, 2012) and bulimia nervosa symptoms (Sundblad, Bergman, & Eriksson, 1994).

Testosterone and risk-taking behaviours

With recent developments in neuroscience and behavioural endocrinology, an emerging body of work is exploring individual variability in risk taking with testosterone. Endogenous testosterone is a steroid hormone from the androgen group that is secreted primarily from the testicles in males and the ovaries in females. In males, testosterone peaks during adolescence and early adulthood, and gradually decline after age 40. Total testosterone declines at a rate of approximately 0.8% per year, whereas free testosterone declines about 2% per year (Feldman et

al., 2002). Individually, testosterone levels vary widely, especially in males (Zitzmann & Nieschlag, 2001). At the same time, about 17% of young females show hyper-androgenic states (Gambineri et al., 2013). Two main measures of testosterone are used: i) the circulating testosterone level, which can be acquired using saliva, hair, or blood samples; and ii) fetal exposure to testosterone which can be acquired using the 2D:4D ratio. The 2D:4D ratio has been used as a marker of fetal exposure to higher testosterone levels (Rivas et al., 2014) and is operationalized as the length of the small bones of the second to the forth fingers measured via radiographs.

Testosterone level has been studied in relation to risk-taking behaviours, with markedly inconsistent results between studies. While some studies have found positive correlations between endogenous testosterone levels and risk taking (Apicella et al., 2008; Peper, Koolschijn, & Crone, 2013; Spielberg et al., 2015; Stanton, Liening, & Schultheiss, 2011), other studies have not (Boksem et al., 2013; Stanton, Mullette-Gillman, et al., 2011; Zethraeus et al., 2009). The discrepancy between study findings may be partly related to the utilization of correlational designs. While a useful and pragmatic first step, a simple directional relationship between testosterone and risk-taking behaviours remains speculative. Evidence suggests that context-related changes in testosterone levels may modulate current or future behaviours (Carré, McCormick, & Hariri, 2011). In fact, acute changes in testosterone levels during competition have predicted subsequent competitive motivation (Carré & McCormick, 2008; Mehta & Josephs, 2006) and aggression (Carré et al., 2014), suggesting a bidirectional relationship between testosterone and behaviour. Concurrent measurement of testosterone level and performance on a risk-taking task may yield misleading levels of circulatory testosterone, as anticipation of the task may affect testosterone level and performance (Apicella, Dreber, &

Mollerstrom, 2014; Casto, James Madison et al., 2012). Therefore, to better understand the relationship between testosterone levels and risk taking behaviour, temporal decoupling between testosterone measurement and a risk taking task may be needed.

Attempts to understand the causal influence of testosterone on risk-taking behaviours have examined the effects of exogenous testosterone administration on risk taking. Neither administration of testosterone to a sample of 200 post-menopausal females for a four-week period nor administration of a single dose of testosterone to a sample of 54 females aged 18-30 has detected any association between exogenous testosterone and risk-taking behaviours (Boksem et al., 2013; Zethraeus et al., 2009). This suggests that testosterone-behaviour effects may be related to chronic exposure to high levels of testosterone. In contrast, a sample of young males did exhibit higher financial risk taking after administration of testosterone dose as compared to placebo (Cueva, 2015), suggesting a different mechanism of action between males and females. An alternative explanation is that endogenous changes in testosterone level may predict subsequent risk taking in males (Apicella et al., 2014). The relationship between fetal testosterone and risk taking has been studied, though the findings are also mixed. Dreber and Hoffman (2007) reported significant inverse associations between fetal testosterone and economic risk taking tasks, while other studies have not (Apicella et al., 2008; Sapienza, Zingales, & Maestripieri, 2009). The inconsistency between the results may be related to the fact that 2D:4D ration is an inherently noisy measure.

Putative mechanisms linking testosterone to behaviour

Testosterone may affect behaviour through neural function, neural connectivity, and brain volume. Animal studies have shown the effects of testosterone on formation and loss of synaptic connections, the neurotransmitter metabolism modulating neuronal activity, or neuron cell

growth, migration, and apoptosis (MacLusky et al., 2006; Matsumoto, 2001, 2005; Zehr et al., 2006). These processes are fundamental for the remodelling of brain structures and function (Blakemore, 2008; Lustig, 1996; Olson et al., 2009). Even if testosterone hormone exposure occurs during the prenatal period, it might affect adult behaviours through neuronal modulation (Cohen-Bendahan, van de Beek, & Berenbaum, 2005).

Mechanisms of testosterone action have also been investigated in humans using neuroimaging. Testosterone was observed to influence neural activity in the amygdala and prefrontal areas, particularly the orbitofrontal cortex (Stanton et al., 2009). The amygdala is part of the emotional circuitry in the brain with reciprocal connections to the orbitofrontal cortex. Higher endogenous testosterone level has been associated with smaller medial orbitofrontal volume and more risk taking in young males (Peper et al., 2013). Moreover, testosterone administration (van Wingen et al., 2010) and high endogenous testosterone levels (Spielberg et al., 2015) have been shown to reduce amygdala-orbitofrontal cortex functional connectivity, suggesting that testosterone reduces regulatory control over amygdala activity. Neural connectivity between the amygdala and the orbitofrontal cortex has been associated with more effective emotional regulation and self-control (Lee et al., 2012), while lesions in this circuitry has disrupted adaptive decision-making (Bechara et al., 1999).

What do we know about the neurobiology of risky driving behaviours?

Researchers are increasingly utilizing the neurobiological approach in an attempt to better understand the underlying mechanisms of risky driving behaviours. The promise of this approach is that it can provide a more objective understanding of risky driving behaviours. For instance, blunted cortisol response to stress, typically observed in alcoholics and in high-risk non-alcoholics, has been associated with an increased number of past DWI convictions (Brown et al.,

2005; Brown et al., 2016; Couture et al., 2008; Couture et al., 2015). Moreover, blunted cortisol response to stress was observed in non-alcohol-related risky driving behaviours in healthy teenage novice drivers (Ouimet et al., 2014) and adult drivers (Brown et al., 2016), indicating that this association is not solely related to alcohol misuse.

Serotoninergic hormonal system has also been studied in relation to alcohol- and non-alcohol-related risky driving. Platelet monoamine-oxidase (MAO) is a robust measure of central serotonergic activity (Oreland, 2004). Platelet MAO activity was found to be lower in a sample of DWI drivers (n = 203) than in a sample of control drivers (n = 201) after accounting for smoking status (Eensoo et al., 2004). Furthermore, platelet MAO activity was a significant predictor of future drinking and driving (Eensoo et al., 2005). In a follow up study, Paaver et al. (2006) investigated MAO activity in subjects caught by the police with different traffic violations, DWI drivers and speed limit exceeders, in comparison to drivers with clean traffic police records. Consistent with previous findings, the study found lower MAO activity in alcohol-related driving violations. Interestingly, the study also found higher MAO activity in association with self-reported non-alcohol related traffic violations (e.g., speed), indicating that dysregulation in central serotonergic activity is associated with risky driving behaviours.

Other hormones that have been investigated in relation to risky driving behaviours include adrenaline, dopamine, and testosterone. Bergomi et al. (2010) found a positive correlation between dopamine levels and frequency of driving violations, while a negative relationship was found between adrenaline levels and frequency of driving errors, indicating that hormonal dysregulation may also distinguish types of risky driving behaviours. To our knowledge, only one study has investigated testosterone in relation to risky driving behaviours. Schwerdtfeger, Heims, and Heer (2010) explored the relationship between fetal testosterone exposure and

penalty driving points during the last five years in a sample of German male drivers (n = 77). According to traffic laws in Germany, four penalty points are given for drivers following a conviction for DWI by alcohol or drug, and one to four points for speeding depending on the driver's speed. The study found a significant association between fetal testosterone exposure and penalty points (r^2 = .13).

Interactions

Interaction between alcohol and testosterone

The pathway between testosterone level and risk-taking behaviours may be moderated by alcohol. Indirect evidence of an alcohol-testosterone interaction showed that alcoholic patients with higher testosterone had elevated risk taking scores than alcoholic patients with lower testosterone (Mattsson et al., 1980; Virkkunen et al., 1994). More direct evidence of alcohol and testosterone interaction was detected by de Water et al., (2013) who found an association between testosterone hormone level and earlier onset of alcohol use in adolescent boys. Additionally, Marten et al (2014) demonstrated that prenatal testosterone exposure in interaction with prenatal alcohol exposure predicted teacher-rated hyperactivity-impulsivity in male children three to six years of age (Martel & Roberts, 2014). The alcohol-testosterone interaction is of particular interest in the traffic safety research. Given the evidence of individual variability on alcohol's impact on the driving performance, it is plausible that alcohol-testosterone interaction could contribute to this variability.

Interaction between alcohol and personality

The conceptual relationship between sensation seeking and impulsivity with alcohol is likely bidirectional. However, the theoretical underpinning of this relationship is different.

Sensation seeking is related to the frequency with which young adults drank alcohol and appears to play an important causal role in problem drinking and the likelihood of developing alcohol-related problems (Cyders et al., 2009; MacPherson et al., 2010; Zakletskaia et al., 2009). Conversely, alcohol intake provokes an increase in sensation seeking behaviours in young adults (Quinn, Stappenbeck, & Fromme, 2011). Furthermore, there is evidence of direct interaction between sensation seeking and alcohol. Elander et al (1993) demonstrated that the interaction between sensation seeking characteristics and transient elements, such as fatigue or drinking, can influence crash risk (Elander, West, & French, 1993).

Impulsivity has predicted greater episodic alcohol intake and alcohol-related negative outcomes (Cyders et al., 2009; de Wit, Crean, & Richards, 2000; Fillmore & Vogel-Sprott, 2000; Miller & Fillmore, 2013). In contrast, alcohol use is associated with sustained impairment of behavioural control and heightened impulsivity (Bates, Bowden, & Barry, 2002; Fillmore, 2003). Furthermore, Fillmore et al (2008) showed that a moderate dose of alcohol (BAC = 0.065%) impaired the ability to inhibit inappropriate actions, thereby decreasing the driving performance (Fillmore, Blackburn, & Harrison, 2008). Not surprisingly, DWI offenders have reported greater impulsivity than healthy controls (Moan, Norstrom, & Storvoll, 2013; Van Dyke & Fillmore, 2014).

Sex-based Differences in RTCs

Although the words sex and gender are often used interchangeably, their meaning is distinct. Sex refers to the biological and physiological characteristics (i.e., male or female), while gender refers to behaviours, roles, expectations, and activities in society (i.e., masculine or feminine) (ASA, 2011). In this section, sex/gender-based differences in relation to three elements

are discussed: prevalence of risky driving behaviours; alcohol impairment; and testosterone-related risk taking.

Gender differences in the prevalence of risky driving behaviours

Gender differences in risky driving and crash involvement are well documented. The literature has shown that males are more likely than females to engage in more risky driving-related behaviours, such as speeding, driving violations, and driving without a seat belt (Liang et al., 1999). Additionally, males are more likely to engage in DWI rather than females (Morrison, Begg, & Langley, 2002). These gender effects may in part be related to the traditionally higher exposure to driving among males (Smart et al., 2004). At the same time, recent trends indicate that risk of alcohol-related crashes in female drivers, particularly young females, are increasing (Robertson et al., 2011). From 1989 to 2011, although the total rate of DWI has decreased by half of what it was before 25 years, the rate of female DWI has increased from 7.8 to 17.6% (Perreault, 2013). In fact, the relative risk for involvement in an alcohol-related crash for young females and young males reached parity in 2007 (Laapotti et al., 2001; Voas et al., 2012). The relative increase in fatalities among female drivers has been related to a parallel increase in female driving exposure (Romano et al., 2008).

Sex differences in alcohol impairment

While females have a lower prevalence rate of alcohol use disorder (Rehm et al., 2009; van Beek et al., 2014), they have been shown to be at higher relative risk of alcohol-related RTCs than males (Zador, 1991). Greater psychomotor impairments following alcohol consumption in specific driving-related competencies (e.g. reaction to visual stimuli, manual dexterity) have been found at lower BAC in females than in males (Elliott et al., 2006; Miller, Weafer, & Fillmore, 2009).

One possible explanation for these observations is sex differences in body composition. Alcohol is dispersed in body water; females have proportionally less body water and more fat than males (Marshall et al., 1983). Therefore, females typically show higher peak BAC than males after consuming similar alcohol doses. Another explanation involves sex-related difference in gastric alcohol metabolism. At low doses of alcohol, gastric alcohol metabolism has been observed to work more efficiently in males compared to females (Frezza et al., 1990). Not surprisingly then, higher peak BAC (Frezza et al., 1990) and more risky driving behaviours (Elliott et al., 2006; Miller et al., 2009; Zador, 1991) are seen in females compared to males after similar, low doses of alcohol.

Sex-based differences related to testosterone and risk-taking

The literature provides ample evidence associating male sex to risk-associated behaviours. Broadly, males have shown significantly higher sensation seeking, impulsivity and risk-taking behaviours than females (Cross, Copping, & Campbell, 2011). Given that males have eight times higher testosterone levels than females, it was generally assumed that sex hormones, mainly testosterone, were the origin of sex-based differences in personality constructs such as impulsivity (Ramirez, 2003). However, studies exploring testosterone level with risk-taking behaviour in males and females have shown inconsistent findings. Some studies have found high testosterone levels associated with more risk-taking tendencies in males and females (Stanton, Liening, et al., 2011). Other studies have produced different findings. Sapienza et al. (2009) reported a positive correlation between testosterone levels and scores on a financial risk-taking task in females, but not in males. In contrast, testosterone levels have been correlated with disadvantageous performance on a gambling risk-taking task in males, but not in females (Schipper, 2012). In sum, the relationship between sex and testosterone in risk-taking behaviours

appears complex. Yet, the higher prevalence of the overall RTCs, regardless of alcohol, is higher in young males than in young females or older males (TIRF, 2004), suggesting the possibility of an interaction between sex and testosterone.

Summary

The young driver problem is a significant public health issue. The rationale for the present study originates from two premises. First, consistent support for the relationship between personality characteristics and RTC risk naturally leads to consideration of the neurobiological underpinnings of risky driving. Second, young drivers are particularly susceptible to risky driving behaviour under alcohol, even at low doses. Testosterone may represent a biomarker of risky behaviours in young adults. High testosterone has been correlated with increased measures of impulsivity and sensation seeking, which may heighten risky driving behaviour. From a developmental perspective, testosterone levels are higher in males under the age of 40, which is consistent with age related prevalence of driving risk. Thus, high testosterone might be a specific risk factor in this vulnerable group. Despite these suggestive findings, to the author's knowledge, no studies have focused specifically on the relationship between endogenous testosterone levels and risky driving. Moreover, there is a substantial overlap and interplay between testosterone, alcohol, sensation seeking, and impulsivity. Both alcohol and high testosterone levels have been associated with risk-taking characteristics. Finally, given the apparent sex differences in psychomotor impairment of driving specific competencies and testosterone-behaviour relationships, it is plausible that sex may moderate the relationship between testosterone and risk-taking driving behaviours.

This study seeks to understand the mechanisms underlying young drivers' involvement in risky driving under alcohol. We use a randomized-controlled, within-subject design experiment to examine the role of testosterone level on simulated risky driving behaviours in young male and female drivers through the mediating roles of sensation seeking and impulsivity and the moderating roles of alcohol and sex (see Figure 1 for our conceptual model).

Objectives and Hypotheses

Objective 1*:* Investigate whether young drivers with higher testosterone level have heightened risky driving behaviour.

Hypothesis 1: Drivers with higher testosterone levels have higher mean speed in driving simulation than drivers with lower testosterone levels.

Objective 2*:* Investigate whether alcohol interacts with testosterone in relation to risky driving behaviour.

Hypothesis 2: Alcohol moderates the relationship between testosterone level and mean speed in driving simulation.

Objective 3: Investigate whether sex interacts with testosterone in relation to risky driving behaviour.

Hypothesis 3: Sex moderates the relationship between testosterone level and mean speed in driving simulation.

Objective 4: Investigate the roles of sensation seeking and impulsivity as mediators between testosterone level and alcohol-related risky driving behaviours.

Hypothesis 4a: Sensation seeking mediates the relationship between testosterone levels and mean speed in driving simulation under alcohol.

Hypothesis 4b: Impulsivity mediates the relationship between testosterone levels and mean speed in driving simulation under alcohol.

Methods

Site and Ethics

This study was conducted at the Addiction Research Program of the McGill University-affiliated Douglas Mental Health University Institute, located in Montreal, Quebec, Canada. The Research Ethics Board of the Douglas Mental Health University Institute approved the protocol (Research Ethics Board certificate #14/08).

Participants

1) Recruitment strategy

The current study was aligned with a larger project (Brown et al., Canadian Institutes of Health Research MOP # 123346; Research Ethics Board certificate # 12/18) that examines the effects of sleep deprivation (SD) and legal BAC (0.02 - 0.05 %) on executive functions and simulated driving in young drivers. In that protocol (see Appendix 1), equal numbers of males and females were randomized into 5 groups stratified by age: i) [alcohol 0.02% + rested]; ii) [no-alcohol + SD]; iii) [alcohol + SD]; iv) [no-alcohol + rested]; and v) [alcohol 0.05% + rested].

For the present study, male and female participants assigned to the [alcohol 0.02% + rested] and [alcohol 0.05% + rested] groups were given the consent forms for participation in this study following the 3rd session of the main study, which included a brief description of the protocol. Interested individuals were asked for permission to be contacted within a few days by phone. If they agreed to take part in this study, they were scheduled to return to the lab on a separate day (within two weeks of the main study).

2. Inclusion and exclusion criteria

Inclusion criteria were: i) experience with alcohol, involving consumption at least 2 to 4 times per month for the last six months as indicated by response to the first question of the Alcohol Use Disorder Identification Test (AUDIT); ii) possession of a provisional or a restriction-free driver's license; iii) having driven in the past 3 months and at least once per week; iv) be medication-free. Exclusion criteria included: i) a health problem that contraindicated participation (i.e., unresolved depressive disorder, attention-deficit hyperactivity disorder diagnosis; substance use disorder as screened by an AUDIT, and a Drug Use Disorder Identification Test (DUDIT); ii) being pregnant or breastfeeding; iii) dental work within 24 hours of saliva sampling; iv) being under the influence of alcohol or drugs upon arrival to the lab.

Measures

Data for the present study were derived from two sets of variables: a) those measured exclusively for the present study; and b) those measured in the main study and used in the present study.

a) Variables measured for the present study

Eligibility measures

Alcohol Consumption The Breathalyzer® is a device used for estimating BAC from a breath sample. The device used in this study was the Alco-Sensor IV from AlcoPro. The mouthpieces are complemented with disposable straws for hygienic screening of the subjects. Participants were asked to blow into the Breathalyzer® mouthpiece for approximately 5 seconds. Research has confirmed that BAC levels recorded by the Breathalyzer® are reliable. The correlation between the Breathalyzer® alcohol measures and serum alcohol levels was equal to

.96, and the accuracy of the Breathalyzer® has been reported to be within ± 0.01 (Gibb et al., 1984).

Drug Consumption The DrugWipe® is a device used to investigate traces of drugs such as cocaine, amphetamine, benzodiazepine, cannabis, heroin and morphine via saliva. The DrugWipe® demonstrated a sensitivity of 100% to amphetamine, 90% to cocaine (Wille et al., 2010), 47% to cannabis (Strano-Rossi et al., 2012). It is also able to detect benzodiazepine at relatively low levels (Blencowe, Vimpari, & Lillsunde, 2011). The DrugWipe® specificities were 99.2%, 97.4%, 99.6%, and 99.6% for amphetamine, cocaine, opiates, and cannabinoids respectively (Crouch et al., 2008).

Pregnancy Innovacon hCG® works by detecting the presence of the hormone human chorionic gonadotropin in a woman's urine (Wilcox, Baird, & Weinberg, 1999). Midstream sample of urine was used for analysis. Innovacon hCG® has shown a diagnostic specificity of 86-100%, and sensitivity of 85-100% (Daviaud et al., 1993).

Personality measures

Impulsivity The Barratt Impulsiveness Scale (BIS-11) is the second version of the BIS released in 1995. It is a 30-item questionnaire that yield six first-order factors (attention, motor, self-control, cognitive complexity, perseverance, and cognitive instability impulsiveness) and three second-order factors (attentional, motor, and non-planning impulsiveness) (Patton, Stanford, & Barratt, 1995). The BIS-11 has been found to provide a reliable and valid assessment of impulsivity in adult and adolescent population (Fossati et al., 2002). Test-retest reliability over one month shows statistically significant correlation coefficients. The correlation (*r*) between BIS-11 Total score and the Wender Utah Rating scale of impulsivity is reported at .43, and with the Aggression Questionnaire Subscales at .33 for physical aggression; .32 for verbal aggression;

.46 for anger; and at .14 for hostility. The internal consistency (Cronbach alpha) is reported at .78 (Fossati et al., 2001).

Sensation seeking The Sensation Seeking Scale Version V (SSS-V) (Zuckerman et al., 1972; Zuckerman, Eysenck, & Eysenck, 1978) is a revision of the original measure (Zuckerman et al., 1964). The SSS-V is a self-report 40-item questionnaire which provides a global score and four subscales: thrill and adventure seeking, disinhibition, experience seeking, and susceptibility to boredom. Each subscale consists of 10 questions each with a binary choice. A psychometric investigation yielded sufficient support for the validity of SSS-V in measuring the sensation seeking characteristics (Beauducel et al., 1999; Wang et al., 2000). The internal consistency alpha ranges from .55 for boredom susceptibility and .80 for the global score (Zuckerman, 1994).

Saliva Testosterone Level

Saliva testosterone level was assessed using direct radioimmunoassay. It offers a simple cheap alternative to serum free testosterone measurement, with the additional advantage of being relatively stress-free and non-invasive (Johnson, Joplin, & Burrin, 1987). Levels of free and total testosterone are highly correlated in both females (r = .64) (Longcope, Hui, & Johnston, 1987) and males (r = .97) (Winters, Kelley, & Goodpaster, 1998). Levels of testosterone show high stability within two weeks interval in males (r = .65) and females (r = .78) (Liening et al., 2010). Menstrual cycle has no significant effect on testosterone level (Dabbs, 1990; Liening et al., 2010).

b) Variables measured in the main study and used in the present study

Alcohol use The AUDIT was developed by the World Health Organization to identify individuals with hazardous and harmful patterns of alcohol consumption (Saunders et al., 1993).

It consists of 10 questions about recent alcohol use and is a validated screening measure of alcohol-use problems (Hendricks, 2001; Saunders et al., 1993) and has been shown to be valid across gender, age, and cultures (Allen et al., 1997). AUDIT scores of ≥ 8 in males or ≥ 6 in females indicate a probable alcohol-use problem. A cut-off value of 8 yielded sensitivities in the mid .90's for various indices of problematic drinking and specificities across countries and across criteria averaged in the .80's (Saunders et al., 1993). The internal consistency (Cronbach's alpha) of the AUDIT is .73 (Fonte & Mota-Cardoso, 2013) and test-retest reliability is .86 in a sample consisting of non-hazardous drinkers, cocaine abusers, and alcoholics (Babor et al., 2001).

Drug use The DUDIT is used to identify individuals with current drug-related problems, those who are at risk, and those who do not have any current problems (Berman et al., 2005). DUDIT scores of ≥ 6 for males or ≥ 2 for females indicate probable drug use problems (Berman et al., 2005). The DUDIT predicted drug dependence in a sample of drug user with a sensitivity of 90%, specificity of 78% and reliability of .80 (Berman et al., 2005; Matuszka et al., 2014).

Mean speed in driving simulation Driving simulation allows evaluation of driving performance under reproducible conditions in a safe, experimentally controlled setting. Evidence indicates adequate external validity with respect to real-world driving (Bedard et al., 2010; de Winter et al., 2009; Ouimet et al., 2011; Shechtman et al., 2009; Wang et al., 2010). The driving simulator at the Addiction Research Program at Douglas Hospital consists of a graphics-enhanced CPU that powers three computer displays, a steering wheel, an accelerator, and brake pedals that provide drivers with a realistic interactive visual, audio and physical driving experience. Figure 2 depicts the simulator from the perspective of the driver.

According to the condition of participants, validity studies support the use of the simulator to measure driving performance for research purposes, either when subjects are sober (Mayhew

et al., 2011) and after alcohol intake (Helland et al., 2013). When comparing self-reported driving behaviours from a written questionnaire to assess the measurement validity of risky driving data derived from a driving simulator, a significant relationship was found across measures of risky driving: crashes (r = .32), speeding (r = .52), risky passing manoeuvres (r = - .34), weaving between traffic (r = .36), and behaviour at stop signs (r = .29) (Reimer et al., 2006).

Procedures

The full protocol of this study consisted of three sessions, one week a part from each other. The first and second sessions were part of the main protocol (see Appendix 1 for detailed description of the protocol). All participants performed the driving simulation tasks twice: i) a baseline session with no alcohol; and ii) a second session with alcohol.

Alcohol condition

For alcohol condition, ethanol was mixed with a carbonated beverage depending on the participants' height and weight according to standard formulas. The mixture was divided into two equal drinks of approximately 125ml each. A glass was given to the participant every five minutes. Given that the groups in the main study included both alcohol and placebo conditions, both the participants and the research assistants were blinded to the alcohol condition. Experimentation started 60-75 minutes after the start of drinking. Alcohol Breathalyzer® tests were conducted and reported every 30 minutes until protocol termination. Participants performed the driving simulation tasks at BAC level between 0.02 - 0.05 %. Participants were informed of their alcohol condition after termination of the experiment and they were followed until their BAC fell to 0%.

Driving simulation tasks

Driving simulation tasks were performed both under no-alcohol (baseline session) and under alcohol (experimental session). The length of each task was about one hour divided into two tasks, 30 minutes each; the order of the tasks was randomly selected in the baseline and experimental session. To avoid any possible learning effect, the simulation tasks varied between the baseline and experimental sessions. However, the level of difficulty was similar between the two sessions. Subjects sit in a car seat and were provided with noise-cancelling headphones, which emit the sound of driving but cancel ambient noise. When participants accelerate, brake, turn, decelerate, etc., the vehicle reacts on the accelerated road as it would on an actual road. **Task 1:** This involved driving on a rural road that ends in a built-up area and on motorways. Pedestrian crossings and traffic lights were encountered during the two-lane rural road and urban road sections. Stop signs and pedestrians were encountered in the built-up areas. On motorways, there were leading vehicles at specific km locations, including trucks moving at 65km/hr. Participants may accelerate and cross a lane to pass these vehicles. **Task 2:** Participants drive down a curved road with one lane in each direction and have the opportunity to pass slow-moving vehicles ahead of them in their lane, by overtaking them, at the risk of crashing into oncoming vehicles in the other lane. Because the road was curved and the other vehicles in their lane were large, the driver's view of the oncoming lane was obstructed. Oncoming vehicles pass in the opposite direction at both random and fixed intervals. The following simulated driving behaviours were sampled several times per second by the simulator: mean speed (km/h), following distance (meters between participants' vehicle and leading vehicle), acceleration and deceleration (time in milliseconds), and lane keeping (deviation in the movement of the steering wheel). **Scoring:** The mean speed was the main outcome measure in this study. The mean speed is the average speed of the driving simulation tasks. Two mean speeds were reported: under no-

alcohol condition and under alcohol condition. Speed was measured digitally by the simulator and reported by an experienced simulation technician who was blinded to the participant as well as to the alcohol condition.

Procedures of the third session

On the day of the third session, subjects arrived at the lab at 10:00 AM. They were asked to present picture identification. Subjects read the Informed Consent Form and questions pertaining to their rights, confidentiality, and procedures of the study were answered. Subjects then undergo the Breathalyzer® and the DrugWipe® tests, and the pregnancy test was performed for female subjects. Eligible participants were asked to fill the BIS-11 and the SSS-V questionnaires. Participants were then asked to rinse their mouth with water. After around 10 minutes, collection of saliva was done by direct spitting into the test tube (Fiers et al., 2014). To avoid diurnal variations in testosterone levels, saliva samples were collected in the morning time (between 10 am and 11 am), as recommended by the Endocrine Society in its clinical practice guidelines (Bhasin et al., 2010). The samples were stored frozen at ≤ -20°C within 24 hours of collection (Toone et al., 2013). On the day samples were to be assayed, samples were brought to room temperature, centrifuged and assayed. Previous procedures took about one hour to complete; participants were paid 40$ as compensation for participating in the present study.

Data storage and coding

Only data required to meet the scientific goals of this study project are described here. In order to protect participant identity and the confidentiality of the information they provided, a code number was used to identify participants in data files. The file linking their code to their name was kept by the project coordinator. These data will be destroyed seven years after data

collection is completed. Data without personal identifying information will be conserved for an additional three years after this period.

Analysis and sample size

Analytic strategy

Statistical analyses were conducted using SPSS version 20 (SPSS Inc., Chicago, IL). Normality tests were performed using the Shapiro-Wilk test. If the data were not normally distributed in one or more groups per variable (p-value < .05), the following transformation procedures were followed: i) outliers were identified using the standard z-score values (smaller than -3.3 or larger than +3.3) and truncated to the next nearest high or low variable. Shapiro-Wilk test was then repeated. If the p-value was less than .05, log-transformation or square-root transformation was performed. Log transformation was performed when the standard deviation was proportional to the mean and square root transformation was used when the variance was proportional to the mean. If normality was achieved after transformation, parametric tests were performed. If normality was not achieved after transformation, non-parametric tests of the original data were used. Transformations were reported if applicable. To detect differences between groups, independent sample t-test was performed for continuous data showing normal distribution, and independent sample Mann-Whitney U-test was performed for continuous data showing violation of normality. For categorical variables, test of independence (Chi-square test) was utilized. Descriptive statistics were presented as means (M) and standard deviations (SD) for continuous variables and percentages (%) for categorical variables. Effect sizes were reported as Cohen's d for t-test and correlation (r) for Mann Whitney test. Because of the preliminary nature of this study, the alpha level was kept at $p \leq .05$ for all analyses to increase the sensitivity of analyses to detect effects that could contribute to hypothesis generation for future research.

Hypotheses 1, 2, & 3 were analyzed using a mixed-design repeated measure analysis of variance (ANOVA) with alcohol condition (no-alcohol, alcohol) being a within-subject factor, and sex (male, female) and testosterone group (high testosterone, low testosterone) the between-subject factors. Testosterone groups were identified by the median split of testosterone levels, separately for male and female groups (Stanton, Mullette-Gillman, et al., 2011). The mean speed was the dependent variable. Control for exposure to driving during the last 12 months was performed because it was significantly different between the testosterone groups ($p < .01$), and because of a significant correlation with the mean speed in males, $r(11) = .50$, $p = .05$. If a significant interaction was detected, *post-hoc* tests were performed by decomposing the simple main effects and running *Bonferroni* tests to detect differences between groups. Effect sizes for ANOVA were reported as partial eta-squared (η_p^2).

The mediation analyses in H4a & H4b were tested using PROCESS, a computational procedure for SPSS software. It is an alternative method of the *Sobel test* to test the mediation hypothesis, and is recommended for small sample sizes (Hayes, 2010, 2012) and utilizes a bootstrapping method with bias-corrected confidence estimates. The 95% confidence intervals (*CI*) of the indirect effects are reported (Hayes, 2012; Preacher & Hayes, 2004). PROCESS can also test for indirect effects even in the absence of direct effects (Hayes, 2009). In H4a & H4b, the dependent variable was the mean speed under alcohol, testosterone level was the independent variable, and the mediating variables were SSS-V Total score in H4a and BIS-11 Total score in H4b. Because it is not appropriate to examine testosterone level in male and female groups together, we analyzed H4a and H4b separately by sex (Peters et al., 2015). Effect sizes were reported as 95% *CI* for the indirect effects.

Sample size

G*Power 3.1 was used to estimate sample size needed for statistical significance. For H1, we based our sample size calculation on previous work (Schwerdtfeger et al., 2010). In that study, the effect size (r^2) was equal to .13 for the association between the fetal exposure to testosterone level and the self-reported driving penalty points. To detect significant effects using a mixed-design ANOVA with three main measures, $\alpha = .05$, power = .8, total sample size of 14 divided into two groups was estimated to detect significant effects. For H4a and H4b, we based our sample size calculation on a similar study (Coccaro et al., 2007), which investigated the relationship between testosterone level in the cerebrospinal fluid and risk-taking characteristics. Based on this study, the effect size for the relationship between testosterone level and sensation seeking was estimated at $r = .42$. With critical alpha level of .05 and power of .8, total sample size needed to detect significant differences was estimated to require 9 subjects. We also over sampled by 20% to account for no-shows or missing data to arrive at the final sample.

Results

Sample Characteristics

Twenty-two subjects participated in this study. Females comprised 50% (N = 11) of the sample. The mean age of the whole sample was 23.7 years old. Sixty-three percent of the young drivers were European-American, 10% were African American, 8.2% were multiracial, 8.1% were Hispanic/Latino, 6% were Asian, and 4.7% were other races.

Table 1 displays sample characteristics of the study sample. Mann-Whitney U test for age did not indicate a statistically significant difference between male (Mdn = 24) and female (Mdn = 21) groups, U = 47.0, p = .42, r = .13. With regard to the number of years of education, an independent sample t-test was used to identify group differences. Results did not indicate significant differences between males (M = 16.2, SD = 2.14) and females (M = 15.5, SD = 2.77) on the years of education, $t(20) = 0.2$, p = .5, d = 0.28. For ethnicity, a chi-square test revealed no significant differences in ethnic distribution between males and females, X^2 (2, N = 22) = 2.32, p = .22. With regard to age at licensure, a t-test revealed a significant difference between males and females, $t(20) = -2.3$, p = .03, d = 1.03. Males had significantly lower age at licensure (M = 17.6, SD = 1.36) than females (M = 19.2, SD = 1.72).

Personality Characteristics

In males, Pearson correlation revealed a correlational trend [$r(11) = .45$, p = .084] between testosterone level (M = 105.3, SD = 32.9) and SSS-V Total score (M = 22.7, SD = 3.82). Results did not detect a significant correlation [$r(11) = .33$, p = .16] between testosterone level and BIS-11 Total score (M = 58.5, SD = 7.13). With respect to association of SSS-V Total score with the mean speed, results did not reveal significant correlations between SSS-V Total score

and mean speed under no-alcohol condition (M = 97.7, SD = 26.4) nor under alcohol condition (M = 105.9, SD = 34.7) [no-alcohol: $r(11) = .05$, $p = .43$; alcohol: $r(11) = .05$, $p = .4$]. With respect to association of BIS-11 Total score with the mean speed, results did not reveal significant correlations between BIS-11 Total score and mean speed under no-alcohol condition nor under alcohol condition [no-alcohol: $r(11) = -.03$, $p = .45$; alcohol: $r(11) = -.11$, $p = .37$].

In females, Pearson correlation revealed a trend for a correlation [$r(11) = .51$, $p = .051$] between testosterone level (M = 35.8, SD = 12.0) and SSS-V Total score (M = 20.4, SD = 3.51). Results did not detect a significant correlation [$r(11) = .064$, $p = .43$] between testosterone level and BIS-11 Total score (M = 59.3, SD = 11.3). With respect to association of SSS-V Total score with the mean speed, results did not reveal significant correlations between SSS-V Total score and mean speed under no-alcohol condition (M = 87.9, SD = 28.9) nor under alcohol condition (M = 93.4, SD = 36.7) [no-alcohol: $r(11) = -.13$, $p = .35$; alcohol: $r(11) = -.10$, $p = .39$]. With respect to association of BIS-11 Total score with the mean speed, results did not reveal significant correlations between BIS-11 Total score and mean speed under no-alcohol condition nor under alcohol condition [no-alcohol: $r(11) = -.15$, $p = .33$; alcohol: $r(11) = -.14$, $p = .34$].

Results of Hypotheses 1, 2, & 3

Hypothesis 1 was not supported by the findings. Results did not indicate a significant main effect of testosterone, $F(1,19) = 1.23$, $p = .31$. Drivers with higher testosterone level did not report higher mean speed (M = 95.7, SD = 25.31) than drivers with lower testosterone level (M = 89.3, SD = 30.92). Further, within-sex analyses did not reveal any significant differences in mean speed between high testosterone [males: M = 93.9, SD = 27.4; females: M = 97.4, SD = 25.4] and low testosterone [males: M = 102.1, SD = 27.6; females: M = 76.5, SD = 31.3] groups, neither in

males nor in females [males: $t(11) = -0.49$, $p = .63$, $d = .17$; female: $t(11) = 1.22$, $p = .25$, $d = .28$].

Hypothesis 2 was supported by the findings. ANOVA revealed a statistically significant alcohol X testosterone interaction, $F(1, 19) = 4.84$, $p = .04$, $\eta_p^2 = .20$. *Post-hoc* tests revealed that young drivers with higher testosterone level reported significantly higher mean speed than young drivers with lower testosterone levels under alcohol condition ($M = 108.4$, $SD = 10.6$) than under no-alcohol condition ($M = 96.6$, $SD = 8.47$) (see Figure 3).

Hypothesis 3 was not supported by the findings. ANOVA did not reveal a significant sex X testosterone interaction in relation to the simulated mean speed, $F(1, 19) = 1.11$, $p = .33$.

Results of Hypotheses 4a & 4b

In males, results did not reveal significant mediation by SSS-V Total score, 95% *CI* [-1.0, 0.71] of the relationship between testosterone level and mean speed under alcohol. Furthermore, results did not reveal significant mediation by BIS-11 Total score, 95% *CI* [-0.62, 0.23] in the relationship between testosterone level and mean speed under alcohol. In females, results did not reveal significant mediation by SSS-V Total score, 95% *CI* [-2.30, 2.22] of the relationship between testosterone level and mean speed under alcohol. Furthermore, results did not reveal significant mediation by BIS-11 Total score, 95% *CI* [-0.42, 1.61] of the relationship between testosterone level and mean speed under alcohol.

Discussion

To our knowledge, this preliminary study is the first to investigate endogenous testosterone levels in relation to risky driving behaviours in young male and female drivers. The first hypothesis posited that higher testosterone levels are associated with more simulated risky driving behaviours. This was not supported by our findings. Young drivers with higher salivary testosterone levels did not report higher simulated speed than young drivers with lower testosterone levels. Our null finding in the first hypothesis goes against the results of Schwerdtfeger et al. (2010) study, which found a significant association between fetal testosterone exposure and penalty driving points. One potential explanation for this discrepancy is the differences in tasks and/or measures used in both studies. The main dependent variable in the present study was mean speed that was measured objectively using the simulator. Further, this study used a randomized-controlled within-subject design, with mean speed assessed under two conditions: no alcohol and alcohol on two different days. In contrast, Schwerdtfeger et al. (2010) study utilized a cross-sectional correlational design and the dependent variable was the self-reported number of penalty driving points. Penalty driving points included both alcohol and non-alcohol-related driving violations as one variable, making it difficult to compare between the studies. Of note, in our first hypothesis, the outcome measure was the mean speed under the no-alcohol condition. Therefore, the significant results in Schwerdtfeger et al. (2010) study may relate to the inclusion of alcohol-related driving violations.

Another difference between studies was that we measured endogenous testosterone levels using saliva samples, while the Schwerdtfeger et al. (2010) study used the fetal exposure to testosterone. Recent investigations into the mechanisms of action of testosterone throughout the stages of development found that testosterone affects behaviours through the combination of

organizational (i.e., fetal testosterone) and activational effects (i.e., circulatory testosterone) (Celec, Ostatníková, & Hodosy, 2015; Welker, Gruber, & Mehta, 2015). In other words, exposure to testosterone during the developmental fetal stages, influences behaviour and affects the way in which individuals respond to higher testosterone level over the lifespan, indicating that the combined measures of both fetal and circulatory levels may reflect two distinct neurobiological mechanisms of behaviours. Relatedly, future studies on testosterone-related behaviour may consider assessment of both fetal and circulatory testosterone levels.

The second hypothesis proposed that an interaction between alcohol and testosterone would be associated with an increase in risky driving. This hypothesis was supported by our findings. Specifically, young drivers with higher testosterone levels had higher mean speed than young drivers with lower testosterone levels, but only after alcohol consumption. Our results are consistent with the findings of other studies regarding testosterone-alcohol interactions in other domains of risk taking behaviours (de Water et al., 2013; Martel & Roberts, 2014; Virkkunen et al., 1994). For instance, de Water et al (2013) found an association between testosterone hormone levels and earlier onset of alcohol use in adolescent boys. Moreover, Martel et al (2014) showed that fetal testosterone exposure in combination with prenatal alcohol exposure predicted teacher-rated impulsivity and disruptive behaviours in children. In our study, findings of a non-significant main effect of testosterone but a significant alcohol X testosterone interaction are coherent with the hypothesis of individual variation in response to alcohol in young drivers.

The putative neural mechanisms of the alcohol X testosterone interaction may be related to frontal volume and amygdala-orbitofrontal cortex connectivity. The influences of testosterone and alcohol on the neural systems that underlie risk taking overlap to some extent. Neuroimaging studies have shown that testosterone is associated with reduced amygdala-orbitofrontal cortex

functional connectivity (Peters et al., 2015), suggesting that testosterone levels may reduce regulatory control of amygdala activity. Furthermore, higher endogenous testosterone levels have been associated with smaller medial orbitofrontal cortex volume and more risk taking in young males (Peper et al., 2013). Importantly, acute alcohol administration has been also associated with reduced amygdala-orbitofrontal connectivity (Gorka et al., 2013). Neural connectivity between the amygdala and the orbitofrontal cortex is associated with more effective emotional regulation, decreased reward sensitivity, and better self-control (Lee et al., 2012), while lesions in this circuitry have been associated with the disruption of adaptive decision-making (Bechara et al., 1999) and risk-taking behaviours (Crone & Dahl, 2012; Peper & Dahl, 2013; Peper et al., 2013). The recent evidence of the mediation by amygdala-orbitofrontal neural connectivity in the relationship between testosterone levels and alcohol use in a sample of adolescent males (Peters et al., 2015) suggests that that neural connectivity is the most plausible neural mechanism of the alcohol X testosterone interaction. A promising avenue for future research is to explore the interplay between testosterone, alcohol, and risky driving behaviours in young drivers via imaging analyses of the amygdala-orbitofrontal cortex neural connectivity.

The third hypothesis, namely that an interaction between sex and testosterone is related to increases in risky driving, was not supported by our findings. The absence of an interaction between testosterone group and sex shows that while the main effect of testosterone is not significant when tested in males and females separately, the difference in magnitude of the testosterone effect is also not significant between both sexes. Our findings are in line with Stanton, Liening, et al. (2011) study which failed to detect a significant testosterone X sex interaction on risk taking measured by the Iowa Gambling Task. Our finding, however, goes against Sapienza et al. (2009) study which used a mixed sample of males and females. They

found a significant negative association between testosterone level and risk aversion in females, but not in males. A possible explanation of this discrepancy is the different sampling between studies. While our study recruited volunteers from the community, the sample in the Sapienza et al. (2009) study was entirely made up of graduate students in a business school program; this may have biased their risk assessment in some way. A significant note on the studies investigating the testosterone-risk taking relationship is that only one sex was tested within a single study (Batrinos, 2012; Blanco et al., 2001; Campbell et al., 2010; Coccaro et al., 2007), which left open questions regarding different methodologies and the ability to generalize the findings to the other sex.

The fourth hypothesis posited mediating roles for sensation seeking and impulsivity in the relationship between testosterone levels and simulated risky driving behaviours. First, our study did not detect significant mediating roles of sensation seeking between testosterone level and simulated speed irrespective of sex. Nevertheless, our study confirmed previous findings regarding the association between testosterone level and sensation seeking in males (r^2 = .20) and females (r^2 = .26). Furthermore, our study did not find a significant relationship between sensation seeking and speed. This finding is inconsistent with other studies that found associations between sensation seeking with risky driving and drunk-driving (Bachoo et al., 2013; Constantinou et al., 2011; Dahlen et al., 2005; Hatfield et al., 2014). One significant limitation of these studies is that they used self-report questionnaires of involvement in risky driving or alcohol violations, which are vulnerable to bias from common-method variance (Podsakoff et al., 2003) and social desirability, particularly in alcohol-related risky driving (Chang et al., 2002). A particularity of the present methodology, on the other hand, was that we used only variable, speeding in simulation, as an indicator of risky driving. Overall, risk-taking is

not only contextual and affected by internal and external factors (Bechara, 2003), as well as methodological factors, but there might also be unique relationships between personality and risk taking within each driving context.

Hypothesis 4b posited that impulsivity mediates the relationship between testosterone level and mean speed. Our findings did not support this contention. Furthermore, we did not find significant correlations between testosterone level and BIS-11 total score irrespective of sex. The lack of significant associations between testosterone level and BIS-11, though indirectly hypothesized here, is in line with other studies using self-reported measures of impulsivity as measured by the Eysenck Personality questionnaire (Blanco et al., 2001), the Impulsiveness-Venturesomeness-Empathy Inventory (Dolan, Anderson, & Deakin, 2001), or the Minnesota Multiphasic Personality Inventory (Blanco et al., 2001). In contrast, testosterone levels were associated with the Iowa Gambling Task in a sample of males and females (Stanton, Liening, et al., 2011). The disadvantageous decision making in the Iowa Gambling Task has been associated with deliberate risk-taking, not impulsive decision making (Steinberg et al., 2008; Upton et al., 2011). It is possible then that impulsivity-related risk-taking behaviours may manifest in behavioural tasks of impulsivity (i.e., deliberate decision making), but not with self-reported measures of impulsivity. In support of this possibility, a sample of non-alcohol related risky drivers, documented by police records, exhibited significant differences from the control group (i.e., no past driving violation) on behavioural measures of risk taking, including mean simulator speed, Stop Light Task, Iowa Gambling Task, and the Continuous Performance Task (Brown et al., 2016). The same sample, however, did not report any significant differences from controls on the Big-five Personality measures, impulsivity measured by the UPPS-P subscales of lack of premeditation, urgency, and lack of perseverance, or the Sensitivity to Punishment, Sensitivity to

Reward Questionnaire. Therefore, the failure to detect a significant indirect effect of impulsivity between testosterone level and the simulated speed may be related to the use of psychometric measures of impulsivity, and not behavioural measures of behavioural inhibition and decision making. Future research could investigate the indirect effect of impulsivity between testosterone level and risky driving using a behavioural task of impulsivity such as the Iowa Gambling Task and the Stop Light Task.

The null findings in Hypothesis 4 may also suggest that other potential mediators are involved in the association between testosterone and simulated speed, for example reward sensitivity, approach behaviours, and punishment sensitivity. Indeed, testosterone has been associated with enhanced risk taking to obtain rewards (Stanton, Liening, et al., 2011; van Honk et al., 2004), and with substance abuse (Reynolds et al., 2007), consistent correlates of high reward sensitivity and low punishment sensitivity (Genovese & Wallace, 2007).

Implications and Future Research

This study extends our understanding of risky driving from a multidimensional perspective. In addition to self-reported measures of psychological and psychosocial factors in risky driving, use of objective biological measures can improve our understanding of the individual variability in risky driving. Consequently, more individualized interventions for mitigating these mechanisms in specific subgroups of young adults may emerge. These efforts have the potential to save the lives of young drivers.

Findings of this study require replication, preferably in varied contexts that may affect testosterone's relationship with risky driving, for example in the presence of peer influence. Further, concurrent investigations of testosterone with other hormones, such as cortisol and MAO, may help to clarify the potential interactions in relation to risky driving behaviours. Baseline cortisol activity and phasic cortisol reactivity to stressors have an important hormonal modulator of the testosterone-behaviour relationship (Glenn et al., 2011; Terburg, Morgan, & van Honk, 2009). Moreover, the interaction between the serotonin and testosterone predicted impulsivity more accurately than either factor alone (Kuepper et al., 2010), suggesting that hormonal factors may modulate the testosterone-risky driving behaviour pathway.

Strengths and Limitations

The study has several strengths and limitations. The study's main strengths lie in its robust experimental design and analyses, which were based upon data gathered mostly using objective measures (i.e., saliva testosterone level, simulated driving behaviour). In addition, use of a within-subject design has allowed the manipulation of alcohol condition in the same subjects to more precisely explore alcohol effects without the need to control for confounding factors such as inter-individual variation in alcohol metabolism.

The study has also several limitations to note. The sample size of this study was small limiting our ability to detect lesser effects. Moreover, the study is limited by the use of only a single measure, the mean speed, and thus, we do not have the ability to discuss testosterone's association with other parameters of risky driving. Noteworthy, however, is that other valid parameters of risky driving were collected by the simulator such as the acceleration, deceleration, and brake time. Given the time consideration to completing a Master's dissertation, we purposefully chose the mean speed as our outcome measure because of its documented validity as well as its accessibility in the digital recorded simulation data. We are still recruiting and testing participants for this study and we will further test our hypotheses using other measures of risky driving (e.g., mean acceleration, deceleration, etc.) prior to publication.

Another important limitation is that our study examined the association of risky driving with only one sex hormone. It is possible that estradiol is also associated with risk taking, specifically in females. Testosterone binds to androgen receptors in the brain that regulate gene expression and modulate neural excitability (Do Rego et al., 2009). However, testosterone has an additional indirect effect in the brain through its conversion to estradiol by aromatase (Rahman & Christian, 2007). Estradiol levels have previously been associated with risk taking behaviours

(Bröder & Hohmann, 2003). Investigation of testosterone level as well as estradiol level is warranted in future research.

Conclusion

This is the first study on the interplay between alcohol and testosterone in risky driving behaviours. Although preliminary, findings provide an important insight into the neurobiological mechanisms behind risky driving under small doses of alcohol and may eventually contribute to the development of prevention strategies aimed at reducing the risk associated with deep-level individual mechanisms of risk-taking.

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Table 1. Sociodemographic characteristics, alcohol misuse, personality characteristics, testosterone levels, and mean speed in males and females

Variable	Males (n = 11)		Females (n = 11)	
	M (%)	*SD*	*M (%)*	*SD*
Age	**24.5**	**4.69**	**23.0**	**4.31**
Education (number of years)	**16.2**	**2.14**	**15.5**	**2.77**
Race				
White	**(55)**		**(62)**	
Non-white[a]	**(45)**		**(38)**	
Yearly income				
≤$20 000	**(73)**		**(91)**	
>$20 000	**(27)**		**(9)**	
Age at first alcohol drink	**14.7**	**1.85**	**14.8**	**1.66**
AUDIT	**6.36**	**3.41**	**7.45**	**5.18**
Personality				
SSS-V	**22.7**	**3.82**	**20.4**	**3.15**
BIS-11	**58.5**	**7.13**	**59.3**	**11.3**
Testosterone level (pg/ml)	**105.3****	**32.9**	**35.8**	**12.0**
Age at licensure	**17.6***	**1.36**	**19.2**	**1.72**
Driving simulation				
Mean speed (no-alcohol condition)	**97.7**	**26.4**	**87.9**	**28.9**
Mean speed (alcohol condition)	**105.9**	**34.7**	**93.4**	**36.7**

Notes: [a]Non-white = Black/Indian/Native/Asian/Hispanic/others; Group differences were detected by t-test or Mann-Whitney test for continuous variables and χ^2 for categorical data;* < 0.05; ** < 0.01; **Abbreviations:** AUDIT: Alcohol Use Disorder Identification Test; SSS-V: Sensation Seeking Score version V; BIS-11: Barratt Impulsiveness Score.

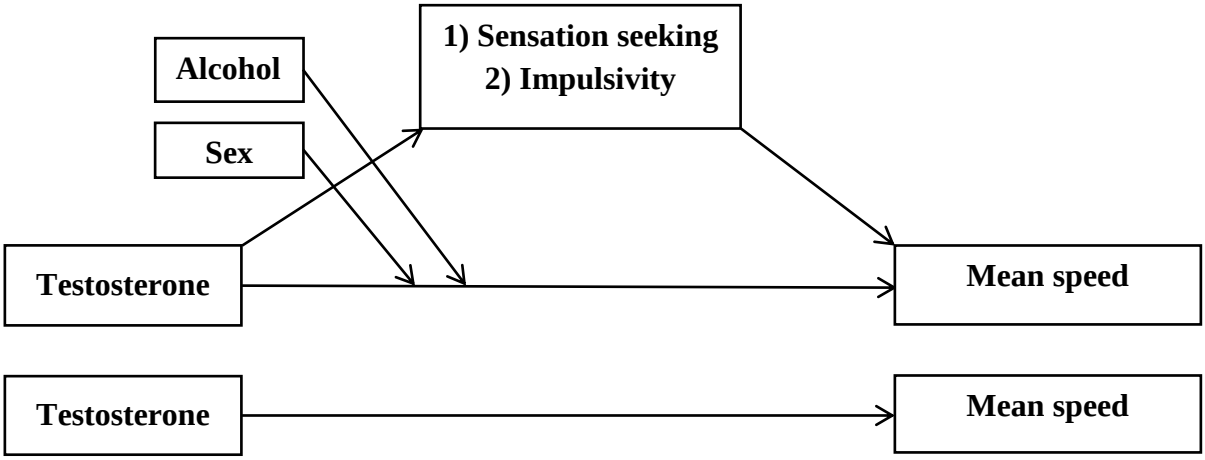

Figure 1. Conceptual model for the hypothesized relationship between testosterone and simulated mean speed in young drivers with high versus low testosterone levels through the mediating roles of sensation seeking and impulsivity and the moderating roles of sex and alcohol

Figure 2. Driving simulation hardware and projected computerized scenarios

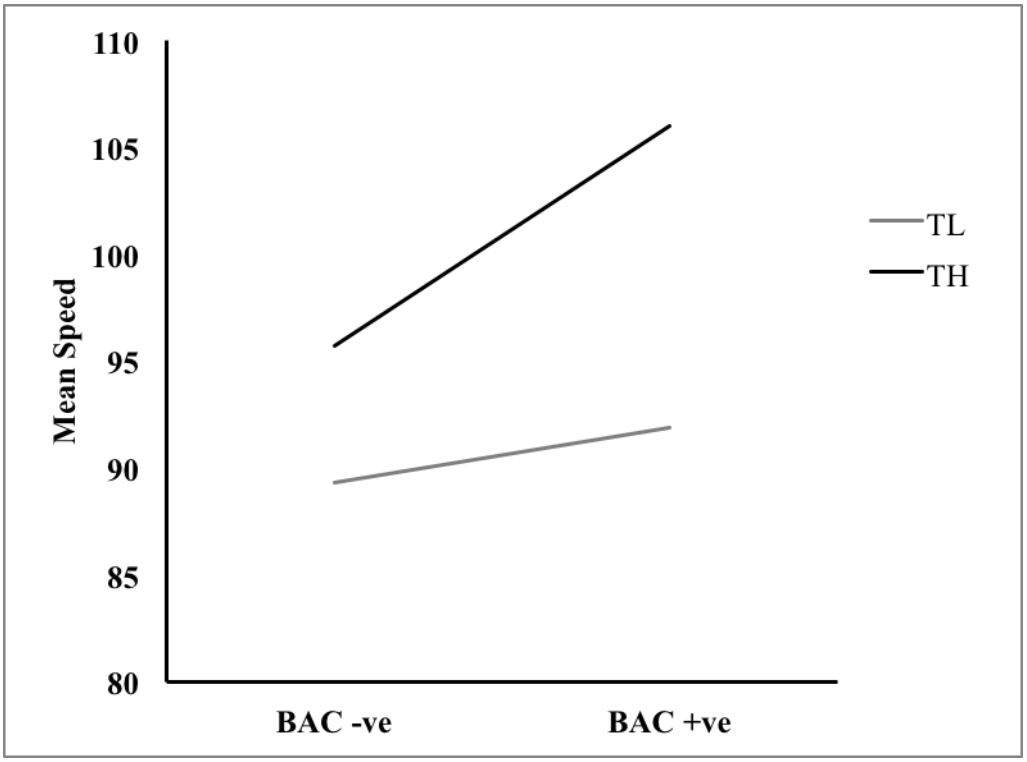

Figure 3. Mean speed of drivers with high (TH) versus low testosterone (LT) and under BAC +ve (BAC = 0.02 – 0.05%) and BAC –ve (BAC = 0%).

Appendix 1

Description of the Protocol of the Main Study

This study will take place at the Addiction Research Program (ARP) at the Douglas Mental Health University Institute. The entire protocol consists of three visits. Study candidates are first telephone screened for eligibility. To determine study eligibility, prospective subjects responding to advertisements are questioned about age, driving license status, kilometers driven in the past three months, pregnancy and breastfeeding status. The **health condition screening protocol** queries on past experience of seizure, reported head trauma or other central nervous system injury, self-reported psychiatric disorder, blood pressure ≥ 150/90, alcohol-induced discomfort, sleep disorder (e.g. self-reported snoring or difficulty sleeping), repeated motion sickness, and any other source of physical and/or psychological distress. Administration of the following objective screeners ensues: **Pittsburgh Sleep Quality Index (PSQI)** (12 items) used to detect sleep disturbances, the **Alcohol Use Disorder Identification Test (AUDIT)** (10 items) for alcohol problems**,** the **Drug Use Diagnosis Identification Test (DUDIT)** (10 items) for drug problems. Eligible candidates are scheduled to come to the lab for three sessions. The initial and the test visits should take approximately 5 hours.

<u>Initial recruitment visit</u>

- Participants will arrive at 11:00 AM, they will be asked to present picture identification, as well as proof of their driver's license status. They will be offered snacks or juices on their arrival.
- They will be asked to provide proof of their driving record.
- Demographic questions (ethnicity, education), driving history.
- A research assistant will accompany the participant to the Centre d' Avancement de la Recherche Clinique (CARC) where they will be asked to undergo a Breathalyzer test. A research nurse will complete a drug screening test. Subjects under the influence of alcohol or drugs at the time of the visit will not be allowed to continue the session. Female participants will undergo pregnancy test.

- It is possible that participants will be asked questions regarding their health status and have their blood pressure and pulse measured by a nursing staff.
- Participants will be asked to fill out several questionnaires related to substance use, attitudes and driving behaviours.
- Participants will be asked to drive on a driving simulator for about 10 minutes to assess whether they have a simulator sickness.
- The above tasks will take slightly less than 2 hours. Participants will have a 20-minute break at 13:00 PM.
- After break, they will be asked to complete several skills including two 30-minute driving simulation.
- Participants will be given Actiwatches. These watch like instruments are used to assess their sleep habits.
- The recruitment visit will end around 3:30 PM.

<u>Between the initial and test visit</u>

- On day 6, participants are requested to come to Douglas Hospital with wrist watches. These watches are required to assess their normal sleep.
- During the visit, participants will be told whether they have to reduce their sleep or continue their normal sleep habits during six nights proceeding test day. This process may take 60 minutes and they will be paid 50$ as compensation.
- Alternatively, research assistance can come to their home to collect sleep watches on day 6 and they will receive a phone call on day 7, explaining their allocation to sleep condition. In this case, they will not be paid.

<u>Test visit</u>

- Participants will be asked to provide picture identification. Snacks will be offered upon request.
- A research assistant will accompany the participant to the Centre d'Avancement de la Recherche Clinique (CARC) where they will be asked to undergo a Breathalyzer test. A research nurse will complete a drug screening test. Pregnancy test for female participants.
- Participants will practice driving simulation for 10 minutes.

- They will be given drinks around 12:00PM. They will have to drink three glasses of juices over 15 minutes. Breath alcohol will be verified every 20-30 minutes.
- During 12:15 PM to 12:55 PM, they will be allowed to watch videos, the snacks will be provided at 12:55.
- Psychological testing will start around 1:15PM followed by two driving simulations of approximately 25-30 min each.
- At the end of the session, participants will be asked questions regarding their driving performance.
- Participants will be informed about the drink (alcohol or not) that they have consumed.
- In case they have received alcohol, they will be requested to stay till the end of experiment till the BAC level drops to zero.
- In case they have received alcohol, they are requested to take public transport and they can ask for taxi as well. This will be arranged by the research staff.