Erschienen in: Neuroscience Letters ; 619 (2016). - S. 189-195
https://dx.doi.org/10.1016/j.neulet.2016.03.034

Examining cortical thickness in male and female DWI offenders

Katarina Dedovic[a,b,*], Jens Pruessner[a,c], Jacques Tremblay[a,c], Louise Nadeau[d], Marie Claude Ouimet[e], Martin Lepage[a,c], Thomas G. Brown[a,c,f]

[a] *Douglas Hospital Research Centre, Montreal, Canada*
[b] *Department of Psychology, University of California, Los Angeles, USA*
[c] *Department of Psychiatry, McGill University, Montreal, Canada*
[d] *Department of Psychology, Université de Montréal, Montreal, Canada*
[e] *Faculty of Medicine and Health Sciences, University of Sherbrooke, Longueuil, Canada*
[f] *Foster Addiction Rehabilitation Centre, St. Philippe de LaPrairie, Canada*

Keywords:
First-time offenders
Driving while impaired
Alcohol
DWI
DUI
Magnetic resonance imaging
Executive control

A B S T R A C T

Some sex differences have been detected in driving while impaired by alcohol (DWI) offenders. However, understanding of the key factors contributing to DWI among male and female drivers remains elusive, limiting development of targeted interventions. Sex-based neurocognitive analyses could provide the much-needed insight. We examined whether male DWI offenders show cortical thickness anomalies that differ from those in female DWI offenders, when compared to their respective controls. Moderating role of sex and alcohol use on DWI status was also investigated. Sixty-one DWI offenders (29 male; 32 female) and 58 controls (29 male; 29 female) completed an anatomical brain scan and assessments on other relevant characteristics. Only male DWI offenders had reduced cortical thickness in the right dorsal posterior cingulate cortex (PCC), a region involved in cognitive control. Lower cortical thickness was associated with increased odds of DWI status *only* among males who have *not* engaged in very hazardous pattern of alcohol misuse in the previous 12 months. Thus, for these male DWI drivers, interventions that could impact PCC could be most advantageous. Continued multidimensional sex analysis of the neural characteristics of male and female DWI offenders is warranted.

1. Introduction

Driving while impaired by alcohol (i.e., DWI; legally defined by *per se* blood alcohol levels in excess of 0.05–0.08% in most jurisdictions) is involved in approximately 30 – 40% of all fatal traffic related deaths [27]. Marked heterogeneity of the first-time DWI offenders in their psychosocial, personality, and even alcohol use characteristics vexes efforts to develop more effective individualized intervention strategies [6,28]. Given the indications of sex-based selective treatment responsivity [36], driver sex is an obvious basis for selective remedial treatment [20]. However, systematic investigation into sex differences in DWI is in fact infrequent [26] and often yields inconsistent findings.

For example, early psychometric research [18,34] found evidence for a relationship between DWI and sensation seeking in males, who are over-represented among DWI offenders, while neuropsychological studies primarily with male DWI offenders have detected weaknesses in several dimensions of executive control [e.g., [9,14,29]]. Nevertheless, recent systematic sex-based analysis failed to support the specificity of these dimensions to male offenders [10]. Furthermore, greater problem alcohol misuse among female offenders has been reported in some studies [23,24] but not in others [20,23].

Importantly, psychometric personality assessment and neuropsychological task performance are distal to more direct

* Corresponding author. Douglas Hospital Research Centre, 6875 LaSalle Blvd E–4109, Montreal, Quebec H4H 1R3, Canada.
E-mail address: katarina.dedovic@mail.mcgill.ca (K. Dedovic).

assessment of brain health. Poor executive function is a feature linked to maladaptive structure and function in multiple brain regions including anterior insula, dorsal anterior cingulate cortex, and posterior cingulate cortex [e.g., [8,11]]. Magnetic resonance imaging (MRI) studies have detected anomalies in these regions in criminal and other risk-taking populations [2,15]. Neuroimaging may help to identify endophenotypes of a common explanatory pathway to high-risk behaviour that could be viable targets for more tailored interventions [17]. To our knowledge, this is the first study to date to image the brains of DWI male and female offenders.

The present study examined whether neuroimaging can provide new insight into DWI behaviour among male and female drivers and novel directions for intervention development. We hypothesized that male offenders would have cortical thickness abnormalities consistent with weakness in executive control compared to females. If confirmed, additional analyses would be carried out to test the hypothesis that alcohol use and sex moderate the association between cortical thickness and DWI status.

2. Methods

Ethics Boards of the Douglas Hospital Research Centre and Montreal Neurological Institute (MNI), approved the study. All participants provided written informed consent.

2.1. Participant inclusion/exclusion and recruitment

Subjects were recruited from a sample of participants taking part in a large longitudinal study examining neurobiological markers of DWI recidivism risk in first-time DWI offenders. General inclusion criteria were: i) being 18–44 years of age; ii) possessing a valid driver's license, and iii) consenting to access to their official Quebec driving data. For DWI offenders, the inclusion criterion was having a criminal conviction for a first DWI offence within the previous 24 months. Non-DWI drivers had to have a lifetime DWI-free driving record. Exclusion criteria were: i) reading skills of less than 6th grade level; ii) any medical contraindication to study participation; and iii) being under the influence of alcohol and/or drugs during study participation.

2.2. Procedures

At the baseline laboratory session, eligible, consenting participants underwent: i) a Breathalyzer® and drug urinalysis; ii) examination for medical inclusion/exclusion; and iii) assessments of personality characteristics, executive function, sociodemographic information, and alcohol and drug use. Those eligible for and consenting to the MRI session completed an anatomical brain scan on a separate day.

Due to difficulties in scheduling, some participants completed their MRI session closer to a follow-up laboratory visit. Thus, we analyzed initial session data for personality and executive function for all participants. For characteristics that do (e.g. age) or could change over time (e.g. substance use) we analyzed data closest in time to the MRI session. When applicable, the number of days between the laboratory and MRI sessions was used as a covariate. Twenty-nine male first time DWI (MDWI) offenders, 32 female DWI (FDWI) offenders, 29 male non-DWI (MCTRL) and 29 female non-DWI (FCTRL) drivers completed the MRI session.

2.3. Measures

2.3.1. Sociodemographics

Age, marital status, education, and employment data were obtained using subsections of a standardized questionnaire [25].

2.3.2. Personality and executive function

The Barratt Impulsivity Scale version 11 (BIS) measured cognitive, behavioural and planning impulsivity domains [30]. The Sensation Seeking Scale V (SSS-V) [40] measured experience seeking, thrill and adventure seeking, disinhibition, and boredom susceptibility. The D-KEFS Color-Word Interference Test measured executive function regarding the ability to inhibit an overlearned response [22]. We examined scaled scores on Condition 3 (Inhibition: naming the colour of the ink that letters are printed in and not reading the word) *vs* Condition 1 (colour naming) for Inhibition, and Condition 4 (Inhibition/Switching: switching between either naming the colour of the ink that letters are printed in and not reading the word, or reading the word and ignoring the colour of the ink) *vs* Condition 3 for Set-Shifting.

2.3.3. Substance misuse severity and risky behaviours

The Alcohol Use Disorder Identification Test (AUDIT) [4] and the Drug Abuse Screening Test (DAST) [39] screened for alcohol and drug problems in the previous 12 months respectively. The Timeline Followback (TLFB) [33] measured the frequency of risky drinking days during which $\geq$3 or $\geq$5 standard drinks for women and men respectively were consumed over the previous 90 days. The Composite International Diagnostic Interview (CIDI) provided diagnostic DSM-IV classification of lifetime alcohol and drug abuse and dependence [19]. Participants also reported on number of times in the last year that they: i) drove after drinking 1 or 2 drinks; and ii) got into a car driven by a driver who had drunk $\geq$3 drinks in the previous two hours; these were considered indices of propensity to engage in DWI-related risky behaviours.

2.3.4. MRI acquisition and cortical thickness analysis

MRIs were acquired on a 1.5-T Siemens SonataVision (Siemens, Malvern, Pennsylvania), with a high-resolution T1 three-dimensional magnetization-prepared Flair sequence (slice thickness = 1 mm isotropic; repetition time = 22 ms; echo time = 9.2 ms; flip angle = 30°). Cortical thickness analyses were completed using the automated analysis pipeline CIVET 1.1.12 [1] available via the CBRAIN interface [32]. All images were processed according to CIVET guidelines (for details and references see SI).

2.4. Main analytic strategy

2.4.1. Sociodemographic, psychological trait and executive function data

Planned comparisons within a sex by group (i.e., CTRL, DWI) analysis of variance (ANOVA) framework [31] tested for differences between male and female DWI offenders and their respective controls, and for differences between male and female DWI offenders while accounting for baseline sex differences. When data deviated from assumptions for ANOVA or were categorical, group comparisons used Mann-Whitney *U* statistics and tests of independence (i.e., χ^2 statistic or Fisher's exact test). Alpha for all inferences was $p < 0.05$, corrected for multiple comparisons.

2.4.2. Cortical thickness

For comparisons of cortical thickness at every vertex of the whole brain, the general linear model was used via Surfstat (http://www.math.mcgill.ca/keith/surfstat/). The model included age at the time of the MRI and handedness as covariates of no interest, sex and group as the between-group factors, and sex $\times$ group interaction term. The sex $\times$ group interaction term resulted in four columns (FDWI, FCTRL, MDWI, MCTRL). The main contrast of interest was (MCTRL-MDWI) > (FCTRL-FDWI) to establish whether the effect of having DWI-offender status among males is different from the effect of having this status among females. Correction for multi-

Table 1
Measures of sociodemographic characteristics, substance use, risky behaviour, personality and executive function in the study sample.

	Male				Females			
	Non-DWI (n = 29)		DWI (n = 29)		Non-DWI (n = 29)		DWI (n = 32)	
	M (%)	SD	M (%)	SD	M (%)	SD	M (%)	SD
Age	30.3	8.5	29.7	6.9	31.3	7.9	33	8.2
Education (years)	12.8	5.8	11.9	5.7	9.6	6.8	9.7	7.7
Marital Status								
Married or cohabitating	(44.8)		(27.6)		(34.5)		(25)	
Right handedness	(79.3)		(79.3)		(93.1)		(90.6)	
Substance Use								
AUDIT	6.0	6.1	6.9	4.1	3.2	3.2	**7.4***	5.5
DAST	1.2	1.6	1.5	2.9	0.6	1.3	**1.0***	1.1
Risky Drinking days (last 90 days)	4.4	7.2	**8.4***	8.7	4.3	6.7	**13.1***	17.7
Alcohol Dependence Dx	(27.6)		(31.0)		(10.3)		**(46.9)***	
Alcohol Abuse Dx	(27.6)		**(62.1)***		(34.5)		**(53.1)***	
Risky behaviour (number of times) in the last year								
Driving after 1 or 2 drinks	2.8	1.7	2.9	1.4	2.3	1.4	2.8	1.7
Got into a car with a driver who consumed ≥ 3 drinks in last 2 hrs	2.1	1.3	2.4	1.3	1.7	1.0	**2.5***	1.4
BIS								
Planning	23.8	5.9	23.9	3.7	23.8	4.0	25.2	3.7
Motor	23.6	6.6	21.4	3.6	20.4	3.2	22.0	3.9
Cognitive	17.8	4.1	17.1	2.9	16.5	2.8	16.8	2.7
SSS								
Thrill	7.1	2.9	6.7	2.8	6.0	2.5	6.2	2.8
Experience	6.7	2.0	5.8	1.8	6.6	2.1	6.8	1.9
Disinhibition	5.1	2.7	4.9	2.5	3.7	2.2	4.4	2.4
Boredom	3.4	2.3	2.6	2.4	2.6	2.1	2.6	1.8
Executive function								
Inhibition	11.4	1.9	11.6	2.1	11.1	1.9	11.1	1.9
Set-Shifting	9.4	3.3	9.3	2.5	10.4	1.9	9.6	2.3

DWI: driving while impaired by alcohol, AUDIT: Alcohol Use Disorder identification Test; DAST: Drug Abuse Screening test; Dx: Diagnosis; BIS: Barratt Impulsivity Scale; SSS: Sensation Seeking Scale.
* $p < .05$, corrected for multiple comparisons, for contrasts with groups' respective non-offender controls.

ple comparisons was conducted via random field theory for clusters at a level of $p < 0.05$, corrected.

2.4.3. Additional analyses

We used PROCESS [16] to model multiplicative moderation effects of sex and alcohol misuse on association between cortical thickness and DWI status in male and female drivers. Heteroscedasticity-consistent standard error estimator, HC3, was used to ensure the validity of inferences. Statistical significance of indirect effects was determined by using bias-corrected bootstrapping method with 1000 samples.

3. Results

Table 1 summarizes the sample's sociodemographic, substance use, personality characteristics and executive function.

3.1. Sample sociodemographics

Planned comparisons yielded no significant effects for marital status, age, and years of education.

3.2. Impulsive personality and executive function

Planned comparisons regarding SSS-V and BIS subscales, and indices of executive function did not reveal any significant effects.

3.3. Substance use and risky behaviour

Compared to FCTL, FDWI reported greater alcohol-related problems in the last 12 months via the AUDIT ($U = 210$, $p < 0.001$) and endorsed more risky drinking days on TLFB ($U = 260.5$, $p = 0.003$). Furthermore, FDWI compared to FCTL showed more lifetime alcohol dependency ($\chi^2(1) = 9.76$, $p = 0.002$), alcohol abuse (Fisher's exact test, $p < 0.001$), and drug problem severity ($U = 306.5$, $p = 0.01$), and were more frequently driven by a driver who had consumed ≥3 drinks in the last hour during the preceding year ($U = 290$, $p = 0.007$). Finally, MDWI compared to MCTL showed greater incidence of alcohol abuse ($\chi^2(1) = 11.90$, $p = 0.001$). No other differences were observed.

3.4. MRI

Data from 10 participants (4 MCTRL; 3 MDWI; 2 FCTRL; 1 FDWI) were identified by quality control analysis as compromised due to high number of surface-surface intersections between white and gray matter surfaces, and were excluded from analyses. Whole-brain analyses of the specific sex × group interaction contrast revealed a significant 60-vertex cluster in the right dorsal posterior cingulate cortex (PCC) with the peak voxel located at the MNI coordinates, $X = 3$, $Y = -12$, $Z = 32$, with $t = 3.59$, while controlling for age and handedness (Fig. 1A). We decomposed this effect at the whole brain level by conducting separate comparisons between male and female DWI offender groups and between these groups and their controls. Comparison of MDWI and MCTRL groups revealed a significant cluster of 132 voxels in the right dorsal PCC (peak at $X = 4$, $Y = -7$, $Z = 31$, $t = 3.78$) showing that male DWI offenders have reduced cortical thickness compared to their controls (Fig. 1B). No differences were found between female DWI and their controls. Comparing male and female DWI offenders did not reveal any significant differences within the PCC, but we did

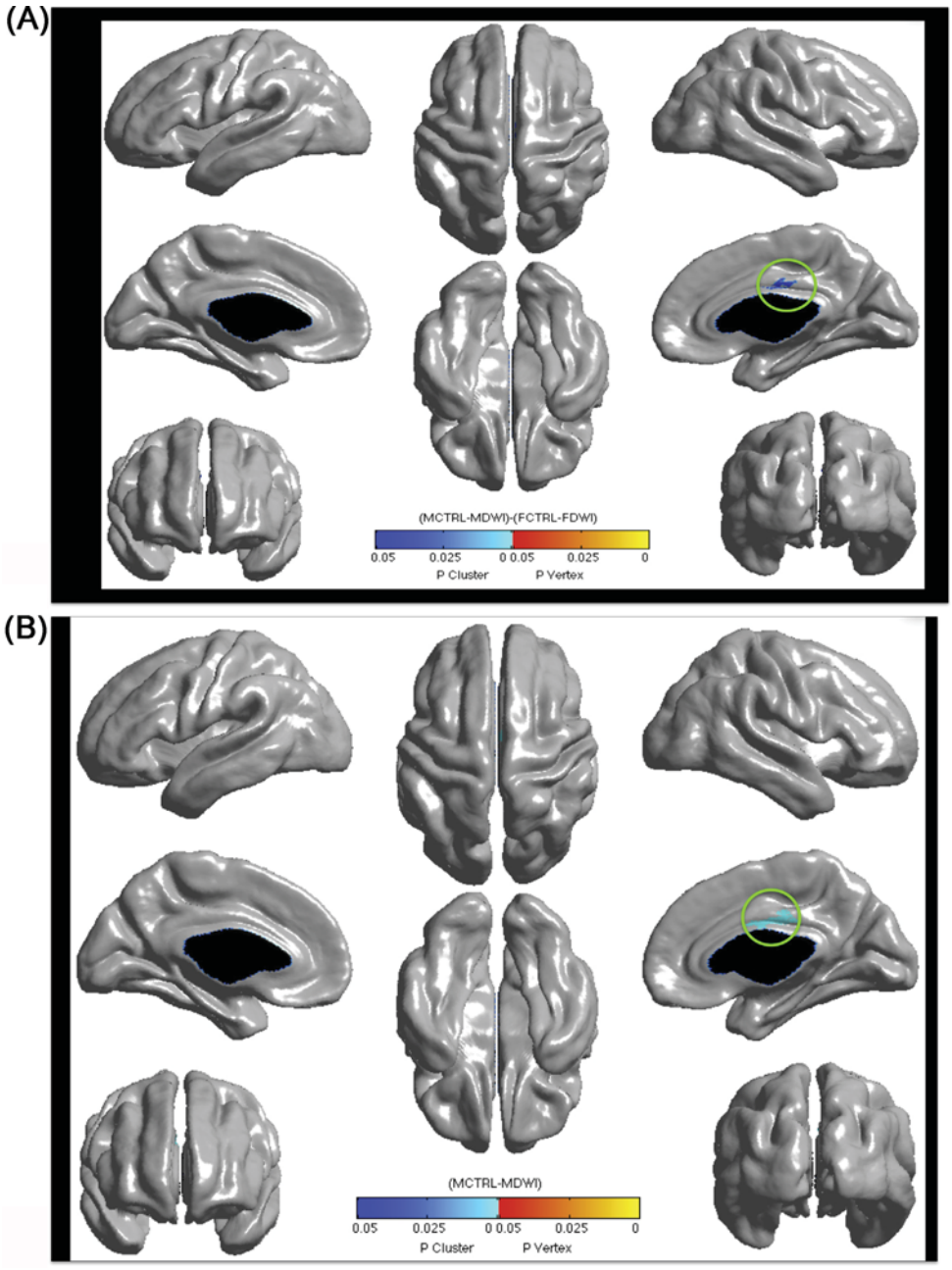

Fig 1. Results of the main interaction contrast for cortical thickness analysis (A) (MCTRL-MDWI)-(FCTRL-FDWI) Interaction contrast revealing a significant cluster in the right posterior cingulate cortex (green circle). (B) Decomposing of the effect reveals a reduced cortical thickness in the right posterior cingulate cortex (green circle) in MDWI group compared to MCTRL. MCTRL: male controls; MDWI: male first time driving while impaired by alcohol (DWI) offenders; FCTRL: female controls; FDWI: female first time DWI offenders. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

observe a significant cluster in the left fusiform gyrus (329 vertices, peak at X = −13, Y = −40, Z = 2, t = 3.65).

3.5. Moderation of the relationship between cortical thickness and DWI status by alcohol and sex

In the whole group, we ran a multiplicative moderation analysis, including the mean cortical thickness from the right dorsal PCC cluster that showed the significant interaction contrast effect as a predictor (X), alcohol misuse measures as a moderator (M), sex as an additional moderator (W), and DWI status as the outcome (Y) (Fig. 2A); the time period between the testing sessions was a covariate. Only with AUDIT as a primary moderator, the PCC × alcohol_misuse × Sex interaction term was significant (Z = −2.35, p = 0.02). This indicated that only in males, with very low to high levels of alcohol problems in the previous 12 months (10–75th percentile inclusive), lower cortical thickness in the PCC was associated with heightened risk of possessing DWI status; in those falling within the 90th percentile of alcohol misuse levels, the association was not significant (Fig. 2B, C).

Explorative investigation of the association between cortical thickness in the right dorsal PCC and psychometric measures yielded no significant effects for the key contrasts of interest (see SI).

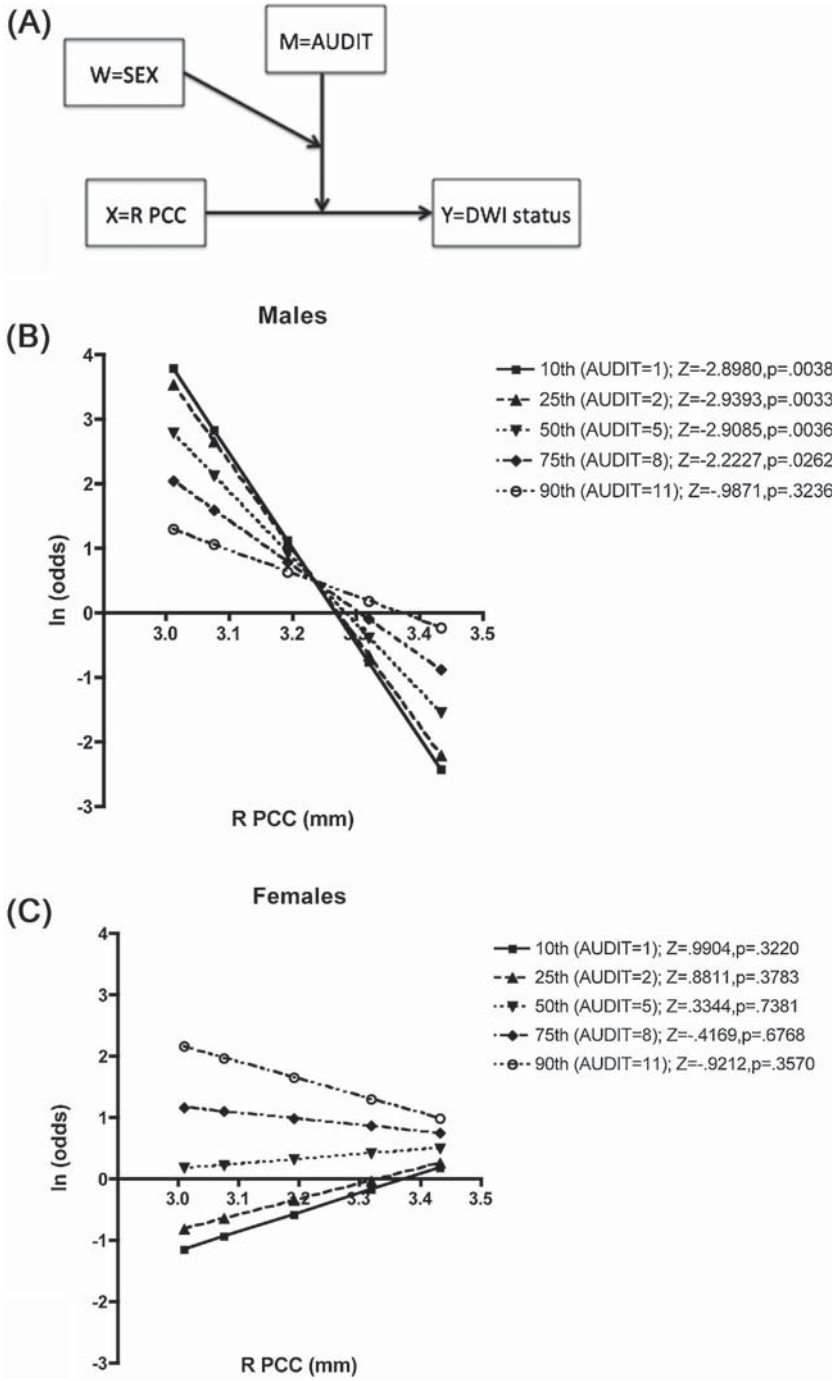

Fig. 2. Results of the multiplicative moderation of AUDIT x SEX x cortical thickness in the right posterior cingulate cortex (R PCC) on the odds of having a driving while impaired (DWI) status (A) Conceptual model of the multiplicative moderation tested. (B) Moderating effect shown among male drivers. (C) Moderating effect shown among female drivers. AUDIT: Alcohol Use Disorder Identification Test.

4. Discussion

Only male DWI offenders compared to their controls showed detectable brain anomalies – lower cortical thickness in the right dorsal PCC. Furthermore, only in males *not* engaging in the most hazardous patterns of alcohol consumption in the last 12 months, lower cortical thickness was associated with increased risk of DWI status. Overall, the findings suggest that sexual dimorphism at the cortical thickness level is associated with DWI status.

Dorsal PCC is involved in cognitive control and in "detecting and responding to environmental events that may require a change in behaviour and that are not part of the current cognitive set" [p. [24,21]]. For male DWI offenders, reduced dorsal PCC might compromise the ability to change typical behaviour (e.g., driving their car versus taking a taxi or public transport) in response to a change in circumstances (e.g., when going to a venue where heavy drinking is likely to occur). For example, reduced thickness in dorsal PCC has been associated with difficulties in judging long-term consequences of illegal social actions (e.g., being involved in hit-and-run, or underage drinking) in a study on adolescents [12]. On the other hand, we did not observe direct associations between PCC cortical thickness and neuropsychological indices related to risk taking (e.g. inhibition, set-shifting,) or self-reported risky driving, a null finding consistent with a previous report in a larger sample of DWI

offenders [10]. As risk taking can be context specific [e.g., [5,7]], neuropsychological measures may not possess adequate ecological validity to discern such relationships. Future neuroimaging studies could include experimental assessment of participants' behaviour in a driving simulation environment to test this possibility.

Alcohol misuse, a signal characteristic of DWI, has been consistently related to structural brain anomalies [e.g.,11]. Our findings reveal that the linkage between alcohol, brain anomalies, and DWI status is complex. Notably, the strongest negative association between PCC cortical thickness and odds of having a DWI status was actually observed among males reporting minimal alcohol usage in the last 12 months; this association steadily flattened to non-significance with each increase in alcohol misuse. This suggests that at low levels of alcohol misuse commonly observed in the general population, a structural anomaly within a localized brain region may selectively proffer higher risk for DWI in male drivers. On the other hand, as alcohol misuse increases to hazardous levels, the risk to engage in DWI might be related to more complex brain and behavioural effects [38]. Indeed, consistent with social-push theory, greater social, psychological and environmental dysfunction accompanying more severe alcohol misuse is likely to weaken direct relationships between biological risk factors and asocial behaviour [37].

Overall, cortical thickness anomalies in the male DWI group reveal a maladaptive neuroanatomical profile that on its own and in combination with alcohol misuse could contribute to some of the neuropsychological deficits previously observed in samples of predominantly male DWI offenders. For females, in contrast, sociodemographic, substance use and personality descriptors seem more prominent in DWI risk. These sex differences are in line with proposition that psychosocial dysfunction characterizes female DWI more than male DWI [35].

4.1. Implications for future research

These preliminary findings suggest that DWI among male drivers is associated with a structural brain deficit. If they are replicated, intervention strategies that target these neural substrates could be explored. For example, client change talk, a targeted strategy of Motivational Interviewing, may in males have a selectively positive impact on emotional learning/memory circuits, which encompass the PCC [13]. Overall, the results reinforce the need for more multidimensional studies to prospectively test the relative advantage of specific intervention by DWI driver sex.

4.2. Limitations

While this study is the first to assess cortical thickness in male and female DWI offenders, it possesses some noteworthy limitations. Sample sizes were moderate, thereby potentially limiting statistical sensitivity to detect subtler group differences. Using a DWI conviction as an index for group membership is potentially biased by individual as well as environmental factors [3]. These circumstances may limit the representativeness of this sample and hence the generalizability of findings to jurisdictions where conditions significantly differ from those of the study site. The cross-sectional study design cannot clarify the origins of potential brain abnormalities in DWI offenders. Nevertheless, we applied statistical models to test the over-arching hypotheses that DWI is a complex behaviour not uniquely or directly a consequence of alcohol misuse. Replication of these associations in another study is warranted. Finally, the non-DWI driver group showed a higher than expected rate of alcohol use disorder. While this does not necessarily confound the main findings with respect to the association between cortical thickness and group membership, it may have attenuated some between-group distinctions that could stem from alcohol use patterns.

Acknowledgements

The authors acknowledge Ms. Lucie Legault, Ms. Laurence Fecteau-Fortin and Ms. Lysiane Robidoux-Leonard for their assiduous coordination of this study, our research assistants for their dedication in collecting the data, and study participants for their precious time. The study was funded by a grant from the Canadian Institutes of Health Research (MOP-86451) awarded to the senior author, Dr. Brown. Dr. Ouimet was supported through a career grant from the Quebec Health Research Fund (*Fonds de recherche du Québec – Santé*).

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