Lower Cortisol Activity is Associated with First-Time Driving while Impaired

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ABSTRACT: Driving while impaired (DWI) is a grave and persistent high-risk behavior. Previous work demonstrated that DWI recidivists had attenuated cortisol reactivity compared to non-DWI drivers. This suggests that cortisol is a neurobiological marker of high-risk driving. The present study tested the hypothesis that this initial finding would extend to first-time DWI (fDWI) offenders compared to non-DWI drivers. Male fDWI offenders (n = 139) and non-DWI drivers (n = 31) were exposed to a stress task, and their salivary cortisol activity (total output and reactivity) was measured. Participants also completed questionnaires on sensation seeking, impulsivity, substance use, and engagement in risky and criminal behaviors. As hypothesized, fDWI offenders, compared to non-DWI drivers, had lower cortisol reactivity; fDWI offenders also showed lower total output. In addition, cortisol activity was the most important predictor of group membership, after accounting for alcohol misuse patterns and consequences and other personality and problem behavior characteristics. The findings indicate that attenuated cortisol activity is an independent factor associated with DWI offending risk at an earlier stage in the DWI trajectory than previously detected.

KEYWORDS: impaired driving, cortisol, neurobiological marker

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Introduction

Road traffic crashes represent the ninth leading contributor to the global burden of disease and injury.[1] Driving while impaired (DWI) with alcohol accounts for about one-third of crashes in North America.[2] Each successive DWI offense significantly increases the hazard to road safety.[3] Nevertheless, DWI is a persistent behavior with approximately one-third to half of drivers rearrested for DWI within a five-year period.[4,5] Detecting elevated risk for DWI is a strategic prevention priority for most licensing authorities, especially after the first offense. Unfortunately, an incomplete understanding of the underpinnings of DWI behavior significantly complicates this task.[6] While alcohol misuse is a sentinel feature of DWI, several observations make clear that neither alcohol use diagnosis nor intake severity is a sufficient precondition for explaining most DWI events: (a) not all drivers with an alcohol use disorder engage in DWI; (b) most drivers who commit DWI are not suffering from alcohol use disorder; and (c) blood alcohol levels at the time of arrest do not predict future DWI risk.[7–9] Hence, DWI research is increasingly looking to other factors that in combination with alcohol misuse could better explain DWI risk.

The hypothalamic–pituitary–adrenal (HPA) axis is activated following psychological, physical, pharmacological, or neuroendocrinological stress.[10] The hypothalamus releases corticotrophin-releasing hormone (CRH), which in turn triggers the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. ACTH stimulates the secretion of cortisol from the adrenal cortex.[11] Cortisol is, thus, considered a stress hormone and a neurobiological marker of HPA axis activity that can be easily measured in saliva. Salivary cortisol activity shows considerable variation in response magnitude across individuals, situations, or stress tests.[12] Significant sex differences have been also found. While cortisol activity has generally been found not to vary by age, slightly higher levels in older individuals have been observed.[12–14]

Cortisol activity, measured as either total output (ie, assessed by the area under the cortisol output curve with respect to ground; AUCG) or reactivity (ie, change in cortisol levels from baseline in response to stress), has been associated with behaviors relevant to DWI offending. For example, lower AUCG has been associated with increased risk taking.[15] Attenuated cortisol reactivity to stress, on the other hand, has been observed in children with conduct disorder[16] and in individuals who exhibit substance use disorder,[17] resistance to treatment,[18] early onset alcohol misuse,[19] greater sensation seeking,[20] and criminal behavior.[21]

Risk taking, substance misuse, elevated sensation seeking, and intervention refractoriness are characteristics frequently seen in DWI offenders.[22–25] In DWI recidivists, our research group[26] found that cortisol reactivity was inversely and independently correlated to the number of previous DWI convictions after potential confounding demographic and behavioral variables (eg, young age, nicotine intake, and alcohol misuse) were accounted for. In a follow-up study that included a standardized stress protocol and a control group, we[27] confirmed that DWI recidivists show attenuated cortisol reactivity to stress compared to non-DWI controls. In sum, these findings suggest that neurobiological processes that have been linked to other forms of risk-taking behavior are contributing to DWI as well.

Whether attenuated cortisol reactivity is also a feature in first-time DWI (fDWI) offending was not directly addressed in our initial studies. Moreover, other distinct measures of cortisol activity linked to risky behavior, such as AUCG, were not assessed. Testing fDWI offenders and non-DWI drivers using multiple measures of cortisol activity could further elucidate the putative neurobiological underpinnings of DWI behavior at an early stage in the DWI trajectory when accurate risk assessments and effective prevention programs are most critical. Therefore, this study tested the hypothesis that fDWI offenders compared to non-DWI drivers show lower cortisol reactivity and AUCG when exposed to a standardized stress task. Exploratory analyses compared the independent contribution to prediction of group membership between measures of cortisol activity and other common correlates of DWI,[22,23] including frequency of alcohol misuse, family history of alcohol problems, and sensation seeking, impulsivity, and engagement in other risky and criminal behaviors.

Material and Methods

The study was conducted at the Addiction Research Program of the Douglas Hospital Research Centre in Montreal, Canada, and approved by the Research Ethics Boards of the Douglas Mental Health University Institute, McGill University, and the Association of Quebec's Public Addiction Treatment Centres. This research complied with the principles of the Declaration of Helsinki. The data presented in the current manuscript were collected as a part of a larger study into neurobiological markers of the transition from fDWI to DWI recidivist status.

Recruitment. The sample of fDWI offenders was recruited through multiple channels, including: (1) newspaper advertisements, (2) posters and invitation letters displayed in public addiction treatment centers designated to conduct DWI relicensing evaluations, (3) posters and invitation letters displayed at three branches of the company certified to install mandated interlock devices, and (4) invitations for study participation in correspondence from Quebec's licensing authority to DWI drivers. The sample of non-DWI drivers was recruited via newspaper advertisements and word of mouth. General study inclusion criteria were: (i) being 18–44 years old and (ii) possessing a minimum of sixth-grade education. The specific inclusion criterion for fDWI offenders was having experienced one DWI conviction within the past 24 months but none in the 10 years preceding that conviction. For non-DWI drivers, the specific inclusion criterion was holding a valid driver's license without history of DWI arrests. General exclusion criteria were: (i) female sex; (ii) medical conditions or medication use precluding safe and unbiased participation; (iii) being under the influence of alcohol or drugs at the time of testing; and (iv) in alcohol withdrawal. Two participants found to have blood alcohol concentration higher than 0.01% on the testing day were rescheduled and successfully tested on another day.

Procedures. Participants were assessed over two sessions on separate days and were asked to stop drinking alcohol the night before each session. The initial session involved obtaining informed consent, assessing vital signs and symptoms of alcohol withdrawal using the Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA[28]), and administrating questionnaires. The second session involved cortisol assessment. In preparation for the cortisol session, participants were asked to stop alcohol use the night before the session and to refrain from drinking coffee on the morning of the cortisol session. The session started at 11:00 with a Breathalyzer® test to confirm abstinence from alcohol, followed by a standard lunch and an opportunity to take a last cigarette break, if needed. A 90-minute rest period ensued during which participants could read from a selection of neutral content magazines and/or watch a documentary film. Then, nine salivary cortisol samples were collected at approximately 15-minute intervals. A 10-minute cognitive stress task, which involved an arithmetic quiz with a time constraint and competitive monetary incentive,[27] was administered between the third and fourth samples.

Measures. *Sociodemographic characteristics.* Sociodemographic information was acquired from responses on the Addiction Severity Index (ASI[29]). Data on age of licensure and number of kilometers driven in the past one and five years were collected via self-report.

Personality traits. Sensation-seeking tendencies were measured with the Sensation Seeking Scale – Form V (SSS-V[30]) that yields four subscale scores: thrill and adventure

seeking, experience seeking, boredom susceptibility, and disinhibition. The SSS-V has shown convergent validity with the ZKPQ_Impulsive Sensation Seeking subscale with correlations of 0.49 for thrill and adventure seeking, 0.61 for experience seeking, 0.43 for boredom susceptibility, and 0.51 for disinhibition. The reported internal consistency coefficients (Cronbach's alpha) were 0.80 for thrill and adventure seeking, 0.75 for experience seeking, 0.76 for boredom susceptibility, and 0.80 for disinhibition.[31] The Barratt Impulsivity Scale version 11 (BIS-11[32]) provides three second-order subscale scores: attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness. BIS-11 showed good convergent validity, with significant correlations with a variety of dimensionally related self-reported questionnaires. Its reliability was supported by the analysis of internal consistency (Cronbach's alpha = 0.83) and test–retest reliability (Spearman's rho = 0.83).[33]

Substance use. The Alcohol Use Disorders Identification Test (AUDIT[34]) and the MacAndrew Alcoholism Scale – Revised (MAC-R[35]) provided information concerning alcohol abuse and dependence consequences and diagnosis, and drinking patterns, as well as personality features (eg, disinhibition) frequently related to substance abuse. Convergent validity of the AUDIT with the Michigan Alcoholism Screening Test was $r = 0.61$ and with the *Diagnostic and Statistical Manual of Mental Disorders* – fourth edition (DSM-IV) criteria was $r = 0.43$.[34] Similarly, the test–retest reliability (0.87–0.95) and the internal consistency (0.75–0.97) are adequate.[36] A meta-analysis estimated the MAC-R sensitivity at 0.70 and the specificity at 0.74.[35] The test–retest reliability was $r = 0.63$, and the internal consistency was 0.56.[37] Alcohol problems in grandparents and parents were determined using the family history section of the ASI.[29] The Timeline Followback (TLFB) assessed days of heavy alcohol use (more than five standard drinks per occasion).[38] This procedure has been found to have good validity and test–retest reliability (typically around $r > 0.85$).[39] The Drug Abuse Screening Test-20 (DAST-20) measured drug abuse-related problems in the previous 12 months.[40] Its internal consistency was estimated at 0.74–0.95 and test–retest reliability at 0.78.[41] The average number of cigarettes smoked per day was measured using the smoking section of the Health Quebec Questionnaire.[42] The Breathalyzer (Alco-Sensor IV; AlcoPro, Inc.) instrument was used to detect and potentially reschedule participants from undergoing cortisol testing if blood alcohol concentration was ≥0.01.

Other risky and criminal behaviors. Frequency of engagement in 19 risky driving maneuvers (eg, overtaking other vehicles) was measured in the last year of driving using the ACR questionnaire (Analyse des Comportements Routiers/Driving Behaviour Analysis). The ACR was found to possess internal consistency ranging from 0.88 to 0.92 and concurrent validity with documented driving infractions.[43] The number of non-DWI major driving convictions and criminal arrests since age 18 years was obtained from the legal section of the ASI. The ASI questionnaire has established convergent, predictive, and discriminant validity and test–retest reliability.[29]

Salivary cortisol. Participants' salivary cortisol was collected using cotton swabs that were centrifuged and assayed with an Amerlex radioimmunoassay kit (Catalogue number 8758401; Ortho-Clinical Diagnostics, Inc., Rochester, New York). Sensitivity of assay is 0.1 µg/100 mL, and intra-assay and inter-assay coefficients of variation were 4.3 and 7.7%. Cortisol activity was assessed via two measures. The total cortisol output was operationalized by the AUCG[44] using all nine cortisol samples. In addition, as cortisol reactivity to stress typically peaks 15 minutes after stress task exposure and in line with our previous work,[27] we also calculated a single cortisol reactivity score for each participant as follows: cortisol level at 15 minutes post-stress task (sample 5) – pre-task cortisol level (sample 3).

Analysis. *Missing data.* Participants who provided four or more samples with inadequate saliva (for cortisol extraction) were excluded from the analysis (nine fDWI, one non-DWI). A total of 15 fDWI offenders and 1 non-DWI driver included in analyses had missing data points for saliva samples (4 fDWI offenders had two or three missing samples, and the rest had one missing sample). Replacement values for missing data points were estimated using individual growth curve analyses.[45] One missing data point for kilometers driven during past five years and one for age of licensure were not replaced.

Group comparisons. Characteristics of fDWI offenders and non-DWI drivers were compared using independent samples *t*-tests, Mann–Whitney *U* test, and Pearson's chi-squared test. Separate ANOVAs compared fDWI offenders and non-DWI drivers on cortisol reactivity and cortisol AUCG. ANCOVA was also used for controlling factors such as age, alcohol, and nicotine consumption that have previously been shown to have an acute impact on cortisol.[17] To verify the influence of unequal sample sizes, separate ANCOVAs using either Type II or III sum of squares were conducted. Both methods produced equivalent results. Nevertheless, since Type II sum of squares is generally considered preferable for ANCOVA with unbalanced sample sizes (eg, Ref. [46]), the results from these analyses are presented. Finally, we used stepwise logistic regression to parsimoniously model independent characteristics (ie, sociodemographics, personality, substance use, risky and criminal behaviors, and cortisol) distinguishing between fDWI offender and non-DWI driver groups.

Alpha for inferences. To minimize Type I error in testing our main hypothesis (ie, for associations between group membership and two different cortisol measures), Bonferroni-corrected alpha for inferences was set at ≤0.025 for each analysis. In order to avoid Type II error in preparatory correlational analyses or exploratory logistic regression, no corrections to alpha were made. Effect sizes of significant analyses were presented as partial η^2 or r^2. Statistical Package for the

Social Sciences (SPSS®) version 20.0 software was used for all analyses.

Results

Sample characteristics and group comparisons. Table 1 summarizes the characteristics of fDWI offenders (n = 139) and non-DWI drivers (n = 31). fDWI offenders were younger than the non-DWI drivers ($t(168) = -4.32$, $P < 0.001$), younger at licensure (U = 1574.50, P = 0.018), drove more kilometers during the past five years (U = 1547.00, P = 0.016), scored higher on thrill and adventure seeking ($t(168) = 2.84$, $P = 0.005$), and experience seeking ($t(168)$ = 2.29, P = 0.023) and disinhibition ($t(168)$ = 2.34, P = 0.021). Moreover, compared to non-DWI drivers, fDWI offenders were higher on the AUDIT (U = 1085.50, $P < 0.001$), MAC-R ($t(168)$ = 2.88, $P = 0.005$), days of heavy alcohol use ($U = 1047.00$, $P < 0.001$), number of cigarettes consumed per day ($U = 1558.00$, $P = 0.004$), and past major non-DWI driving convictions ($U = 1606.00$, $P = 0.025$).

Figure 1 depicts the individual cortisol sampling episodes of fDWI offenders and non-DWI drivers, as well as average cortisol reactivity and cortisol AUCG. Analysis indicated that, in comparison to the non-DWI drivers, fDWI offenders have lower cortisol reactivity to stress (M = 0.47, SD = 0.86 vs. M = 0.14, SD = 0.33; $F(1, 168) = 12.39$, $P = 0.001$, partial $\eta^2 = 0.07$) as well as lower cortisol AUCG (M = 169.03, SD = 128.36 vs. M = 66.89, SD = 83.84; $F(1, 168) = 30.34$, $P < 0.001$, partial $\eta^2 = 0.15$).

We experimentally controlled for the number of potential acute confounds to cortisol, namely, by screening for recent alcohol consumption with a Breathalyzer instrument and alcohol withdrawal via the CIWA at the time of testing, and by restricting smoking and coffee consumption at least 90 minutes before cortisol sampling. Nevertheless, in order to detect and statistically adjust for other potential confounders in our analysis of cortisol, we conducted Spearman rho correlational analyses between

Table 1. Sociodemographic characteristics, personality traits, substance use, risky and criminal behaviors of first-time driving while impaired offenders (fDWI; n = 139) and non-driving while impaired drivers (non-DWI; n = 31).

	FDWI OFFENDERS		NON-DWI DRIVERS		
	M (%)	*SD*	*M* (%)	*SD*	*P*
Sociodemographics					
Age	28.32	7.02	34.26	6.43	0.001
Income less than $20 000 CDN	(41.7)		(35.5)		
Kilometres driven past 12 months	10,483.42	13,173.53	11,856.65	16,220.91	
Kilometres driven past five years	95,010.29[a]	87,823.35	73,256.00	100,330.84	0.016
Age at licensure	17.93[a]	2.56	19.52	3.71	0.018
Personality					
SSS-V Thrill and adventure seeking	7.45	2.28	6.06	3.10	0.024
SSS-V Experience seeking	6.40	2.00	5.45	2.45	0.023
SSS-V Boredom susceptibility	2.61	1.89	3.23	2.43	
SSS-V Disinhibition	5.28	2.51	4.13	2.35	0.021
BIS-11 Attentional impulsiveness	17.45	3.40	16.81	3.30	
BIS-11 Motor impulsiveness	22.18	4.02	21.90	6.23	
BIS-11 Non-planning impulsiveness	24.73	4.41	23.52	4.61	
Substance use					
AUDIT	9.08	7.03	4.42	5.24	0.001
MAC-R	23.81	4.20	21.42	4.15	0.005
Positive family history of alcohol	(44.6)		(48.4)		
Heavy alcohol use in past 90 days	10.27	14.25	2.45	6.78	0.001
DAST-20	2.44	3.06	1.68	2.99	
Cigarettes/day	5.78	9.38	1.48	5.65	0.004
Risky and criminal behaviors					
High-risk driving behaviors	61.29	15.77	57.55	15.66	
Past non-DWI major driving convictions	3.35	4.37	1.74	2.34	0.025
Past non-DWI criminal arrests	1.74	8.19	0.68	1.80	

Note: [a]n = 138.
Abbreviations: AUDIT, *Alcohol Use Disorders Identification Test*; BIS-11, *Barratt Impulsivity Scale version 11*; DAST-20, *Drug Abuse Screening Test-20*; DWI, driving while impaired; fDWI, first-time driving while impaired; MAC-R, *MacAndrew Alcoholism Scale Revised*; SSS-V, *Sensation Seeking Scale form V.*

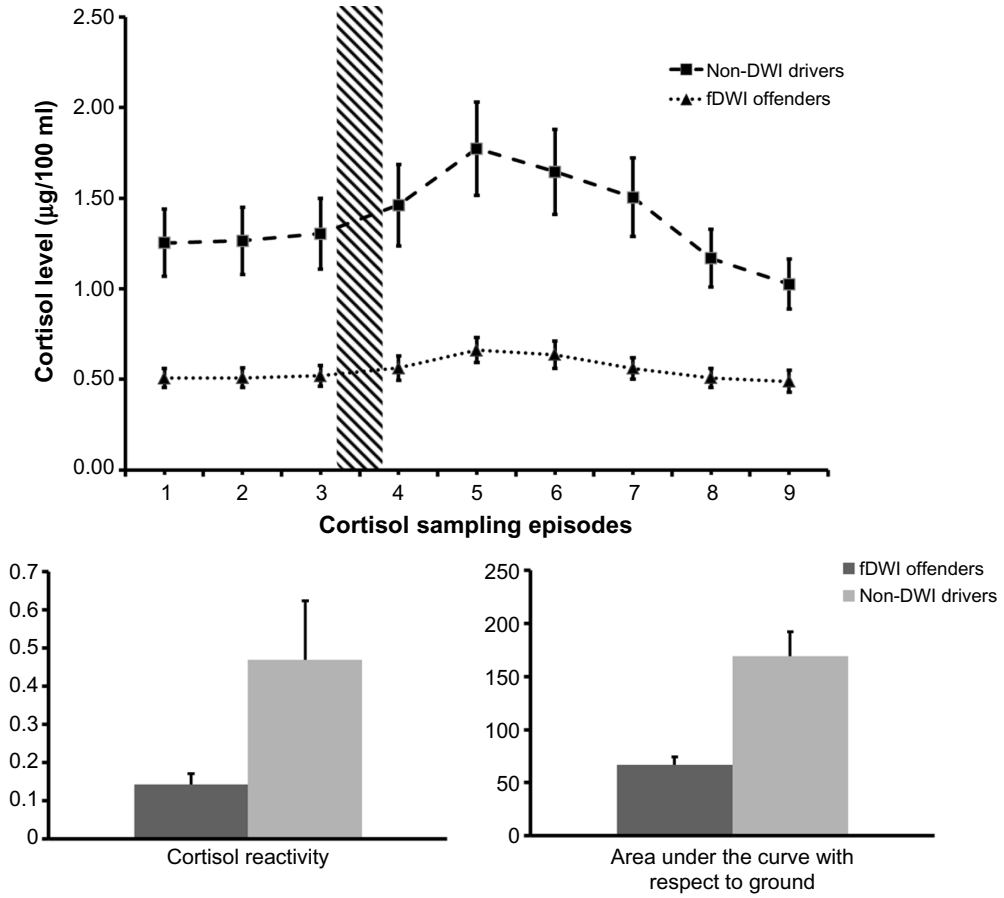

Figure 1. Mean salivary cortisol level (µg/100 ml) before and after the stress task, cortisol reactivity and total cortisol output of first-time driving while impaired offenders (fDWI; $n = 139$) and non-driving while impaired drivers (non-DWI; $n = 31$).
Note: Error bars represent standard errors. The diagonal stripe bar indicate the stress task.

cortisol reactivity, cortisol AUCG, age, age at licensure, AUDIT score, frequency of heavy drinking days in the past 90 days, DAST-20 score, and average number of cigarettes consumed per day.[17,47] With respect to cortisol reactivity, significant correlations were found with age ($r_s = 0.19$, $P = 0.016$), heavy drinking days ($r_s = -0.20$, $P = 0.009$), DAST-20 ($r_s = -0.17$, $P = 0.027$), and number of cigarettes consumed per day ($r_s = -0.21$, $P = 0.007$). After controlling for these covariates, ANCOVA revealed that cortisol reactivity remained significantly lower in fDWI offenders compared to non-DWI drivers ($F(1, 164) = 6.25$, $P = 0.013$, partial $\eta^2 = 0.04$). A trend was observed between cortisol AUCG and age ($r_s = 0.15$, $P = 0.051$). Controlling for age in an ANCOVA revealed that cortisol AUCG remained significantly lower in fDWI offenders compared to non-DWI drivers ($F(1, 167) = 24.86$, $P < 0.001$, partial $\eta^2 = 0.13$). (All correlations between these variables are provided in Supplementary Table A in the Supplementary File).

Modeling of characteristics of fDWI offenders vs. non-DWI drivers. We conducted additional analyses to parsimoniously model group membership using forward stepwise logistic regression with all variables in Table 1 and the two cortisol activity measures separately. When using cortisol reactivity, a significant six-variable model emerged ($\chi^2(6) = 58.57$; $P < 0.001$; Nagelkerke $r^2 = 0.48$). At the final step, fDWI status was associated with younger age, younger age at licensure, less boredom susceptibility on the SSS-V, greater alcohol use and severity of consequences, more nicotine intake, and attenuated cortisol reactivity. A one unit decrease in cortisol reactivity was associated with a 28% increase in odds of being an fDWI offender. When using cortisol AUCG, a five-variable model emerged ($\chi^2(5) = 60.72$; $P < 0.001$; Nagelkerke $r^2 = 0.49$). At the final step, fDWI status was associated with younger age, less boredom susceptibility on the SSS-V, greater alcohol use and severity of consequences, more nicotine intake, and attenuated cortisol AUCG. Table 2 summarizes the regression coefficients, Wald statistics, and P values in the first and final steps for both cortisol reactivity and cortisol AUCG models.

Conclusions and Discussion

Understanding the trajectory from non-DWI to fDWI status and the nature of DWI risk are ongoing challenges for the traffic safety research field. Our previous work revealed that levels of cortisol, a neurobiological marker of HPA axis activity, inversely track increased DWI risk among recidivists.[26]

Table 2. Significant predictors of first-time driving while impaired (fDWI) group membership: results of logistic regression analysis with fDWI vs. non-driving while impaired drivers (n = 168).

VARIABLES	B (SE)	ODDS RATIO	LOWER 95% CI	UPPER 95% CI	*P*
A. The model with cortisol reactivity					
Step 1					
Constant	5.11 (1.00)				
Age	−0.12 (0.03)	0.89	0.84	0.94	<0.001
Step 6					
Constant	9.28 (2.40)				
Age	−0.13 (0.04)	0.88	0.82	0.95	0.002
Age at licensure	−0.20 (0.08)	0.82	0.70	0.97	0.020
SSS-V Boredom susceptibility	−0.47 (0.14)	0.62	0.47	0.82	0.001
AUDIT	0.17 (0.06)	1.19	1.05	1.34	0.007
Cigarettes/day	0.14 (0.06)	1.15	1.03	1.28	0.010
Cortisol reactivity	−1.29 (0.48)	0.28	0.11	0.70	0.007
B. The model with cortisol AUCG					
Step 1					
Constant	2.35 (0.31)				
Cortisol AUCG	−0.01 (0.00)	0.99	0.99	1.00	<0.001
Step 5					
Constant	6.50 (1.57)				
Age	−0.14 (0.04)	0.87	0.81	0.94	<0.001
SSS-V Boredom susceptibility	−0.34 (0.13)	0.72	0.55	0.92	0.010
AUDIT	0.12 (0.06)	1.13	1.01	1.26	0.036
Cigarettes/day	0.15 (0.05)	1.16	1.05	1.28	0.005
Cortisol AUCG	−0.01 (0.00)	0.99	0.99	1.00	<0.001

Notes: (**A**) Cortisol reactivity model: Nagelkerke $r^2 = 0.16$ for Step 1, nagelkerke $\Delta r^2 = 0.32$ for Step 5 ($P < 0.001$). (**B**) AUCG model: Nagelkerke $r^2 = 0.19$ for Step 1, nagelkerke $\Delta r^2 = 0.30$ for Step 5 ($P < 0.001$).
Abbreviations: AUDIT, Alcohol Use Disorders Identification Test; SSS-V, Sensation Seeking Scale form V; AUCG, area under the curve with respect to ground.

The present study sought to assess whether lower cortisol levels were a feature of fDWI offenders as well. In support of our primary hypothesis, and consistent with our previous study with recidivists,[27] fDWI offenders showed attenuated cortisol reactivity to stress compared to non-DWI drivers – even after controlling for variables that can acutely influence cortisol activity experimentally by screening for alcohol withdrawal symptoms and recent alcohol intake using a Breathalyzer; restricting smoking and coffee intake; and statistically, by covarying age, average daily nicotine intake, and alcohol misuse patterns and severity of consequences. Importantly, exploratory logistic regression, which forced personality, substance use, and risky and criminal behavior measures as covariates, revealed a final model in which cortisol reactivity to stress was the most important predictor of fDWI status. As an indicator of increased DWI risk, a one unit decrease in cortisol reactivity was associated with a 28% increase in odds of being an fDWI offender.

We also observed that fDWI offenders showed attenuated cortisol AUCG as a measure of total cortisol output. Like cortisol reactivity, AUCG was a significant predictor of fDWI status, being one of the variables retained in the final exploratory logistic regression model. However, compared to cortisol reactivity, its relative contribution to predicting fDWI offender status was more modest. This might be because AUCG aggregates different HPA axis-related processes (ie, resting, in response to stress, and downregulation of stress response), with each exhibiting potentially distinct relationships to DWI. Overall, these results suggest that attenuated cortisol reactivity in response to stress is an important distinguishing feature of fDWI offenders, an offender group whose other risky attributes, such as alcohol misuse and sensation seeking, are more heterogeneous than in the recidivist samples frequently studied.[48] As self-report data are also vulnerable to error and distortion,[49,50] cortisol reactivity shows promise for (i) gaining more unbiased understanding of the underpinnings of DWI behavior, (ii) developing more accurate markers of DWI risk, and (iii) suggesting innovative prevention approaches.

For the moment, the precise role of dysregulation of the HPA axis in promoting DWI and other problem behaviors remains speculative.[51,52] For some drivers, attenuated cortisol reactivity may be a marker of poor regulatory capacity over alcohol use.[17,53,54] Support for this possibility in fDWI

emerged by a significant inverse relationship detected here between cortisol reactivity and risky drinking days in the prior 90 days (see Supplementary Table A). Alternatively, a strong cortisol response to stressful events may be involved in emotional memory encoding and retention, which are both self-regulatory processes linked to more adaptive behavioral inhibition and risk avoidance.[20,55,56] This latter possibility is supported by a preliminary longitudinal study with healthy newly licensed teen drivers.[57] It found that attenuated cortisol response to stress was associated with more sustained rates of risky driving behavior over an 18-month period. In light of this latter finding, the present results suggest that DWI is a specific manifestation of a general inability to inhibit and/or avoid risky behavior. In sum, cortisol is a neurobiological marker that may be sensitive to multiple plausible mechanisms of DWI risk. Further research is required to discern the predominant DWI pathways that cortisol activity reflects, and that could possibly be targeted for intervention.

Limitations. This study possesses a number of methodological strengths. DWI investigations frequently recruit offenders attending remedial programs, though their representativeness to the DWI population is suspect.[58] One strength, therefore, was its recruitment of a naturalistic sample of offenders drawn from both the general DWI population and drivers involved in Quebec's DWI relicensing program. Another strength was the exercise of experimental and statistical control over factors that could confound cortisol measurement, namely, age, alcohol intake, smoking, and food intake, among others.

The study also possesses several limitations. The study's cross-sectional design cautions against causal inferences about cortisol activity's role in the transition from non-offender to DWI offender status. Research to more unequivocally determine whether cortisol activity predicts the transition from non-DWI to fDWI status is challenging, however, as DWI is an uncommon enough behavior to require very large sample sizes. Nevertheless, future longitudinal research could more pragmatically appraise cortisol activity's explanatory potential, and hence infer the causal role of HPA axis dysregulation in DWI behavior, by investigating its relationship in the transition from fDWI to higher-risk recidivist status. Also, female DWI offenders were not included in this study, despite being a group garnering mounting concern among traffic safety authorities.[59,60] Sex effects in the link between HPA axis and high-risk characteristics have been found.[14] Thus, future studies are needed to confirm whether the present findings generalize to female fDWI offenders. Moreover, experimental rather than statistical control over group characteristics (eg, age) via matching may have strengthened certain conclusions. Finally, the risk of an arrest and subsequent conviction for DWI is influenced by several individuals (eg, socioeconomic status) and jurisdictional circumstances (eg, DWI laws and enforcement practices, availability of alternate transportation options). Hence, generalization of the findings to (a) the population of all drivers who engage in DWI behavior and (b) other jurisdictions with significantly different circumstances than the one where this study was conducted should be undertaken cautiously.

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Author Contributions

Conceived and designed the experiments: SC, MCO, CG, JT, NMK NYK, TGB. Analyzed the data: SC, CG, NMK NYK, TGB. Wrote the first draft of the manuscript: SC, MCO, TGB. Contributed to the writing of the manuscript: SC, MCO, KD, SB, TGB. Agree with manuscript results and conclusions: SC, MCO, CG, JT, NMK NYK, SB, JP, KD, TGB. Jointly developed the structure and arguments for the paper: SC, MCO, TGB. Made critical revisions and approved final version: SC, MCO, CG, JT, NMK NYK, SB, JP, KD, TGB. All authors reviewed and approved of the final manuscript.

Supplementary Data

Supplementary table A. Spearman rho correlation matrix of cortisol activity covariates ($n = 170$).

REFERENCES

1. Peden M, Scurfield R, Sleet D, et al. *World Report on Road Traffic Injury Prevention: Summary*. Geneva: World Health Organization; 2004:52.
2. National Highway Traffic Safety Administration. Traffic Safety Facts 2010: A Compilation of Motor Vehicle Crash Data from the Fatality Analysis Reporting System and the General Estimates System. Washington, DC: U.S. Department of Transportation; 2010:217.
3. Ahlin EM, Zador PL, Rauch WJ, Howard JM, Duncan GD. First-time DWI offenders are at risk of recidivating regardless of sanctions imposed. *J Crim Justice*. 2011;39:137–42.
4. Blows S, Ameratunga S, Ivers RQ, Lo SK, Norton R. Risky driving habits and motor vehicle driver injury. *Accid Anal Prev*. 2005;37:619–24.
5. Lapham SC, Skipper BJ, Hunt WC, Chang I. Do risk factors for re-arrest differ for female and male drunk-driving offenders? *Alcohol Clin Exp Res*. 2000;24:1647–1655.
6. Nochajski TH, Stasiewicz PR. Relapse to driving under the influence (DUI): a review. *Clin Psychol Rev*. 2006;26:179–95.
7. Dugosh KL, Festinger DS, Marlowe DB. Moving beyond BAC in DUI. *Criminol Public Policy*. 2013;12:181–93.
8. Flowers NT, Naimi TS, Brewer RD, Elder RW, Shults RA, Jiles R. Patterns of alcohol consumption and alcohol-impaired driving in the United States. *Alcohol Clin Exp Res*. 2008;32:639–44.
9. Moan IS, Norstrom T, Storvoll EE. Alcohol use and drunk driving: the modifying effect of impulsivity. *J Stud Alcohol Drugs*. 2013;74:114–9.
10. Adinoff B, Junghanns K, Kiefer F, Krishnan-Sarin S. Suppression of the HPA axis stress-response: implications for relapse. *Alcohol Clin Exp Res*. 2005;29:1351–5.
11. Lupien SJ, Ouellet-Morin I, Hupbach A, et al. Beyond the stress concept: allostatic load-a developmental biological and cognitive perspective. In: Cicchetti D, Cohen DJ, eds. *Developmental Psychopathology: Developmental Neuroscience*. 2nd ed. Hoboken, NJ: John Wiley & Sons, Inc; 2006:578–628.
12. Kudielka BM, Hellhammer DH, Wüst S. Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. *Psychoneuroendocrinology*. 2009;34:2–18.

13. Kudielka BM, Buske-Kirschbaum A, Hellhammer DH, Kirschbaum C. HPA axis responses to laboratory psychosocial stress in healthy elderly adults, younger adults, and children: impact of age and gender. *Psychoneuroendocrinology*. 2004;29:83–98.
14. Rosenblitt JC, Soler H, Johnson SE, Quadagno DM. Sensation seeking and hormones in men and women: exploring the link. *Horm Behav*. 2001;40:396–402.
15. Daughters SB, Gorka SM, Matusiewicz A, Anderson K. Gender specific effect of psychological stress and cortisol reactivity on adolescent risk taking. *J Abnorm Child Psychol*. 2013;41:749–58.
16. van Goozen SHM, Matthys W, Cohen-Kettenis PT, Buitelaar JK, van Engeland H. Hypothalamic–pituitary–adrenal axis and autonomic nervous system activity in disruptive children and matched controls. *J Am Acad Child Adolesc Psychiatry*. 2000;39:1438–45.
17. Gianoulakis C, Dai X, Brown TG. Effect of chronic alcohol consumption on the activity of the hypothalamic–pituitary–adrenal axis and pituitary beta-endorphin as a function of alcohol intake, age, and gender. *Alcohol Clin Exp Res*. 2003;27:410–23.
18. van de Wiel N, van Goozen SHM, Matthys W, Snoek H, van Engelend H. Cortisol and treatment effect in children with disruptive behavior disorders: a preliminary study. *J Am Acad Child Adolesc Psychiatry*. 2004;43:1011–8.
19. Evans BE, Greaves-Lord K, Euser AS, Franken IHA, Huizink AC. The relation between hypothalamic–pituitary–adrenal (HPA) axis activity and age of onset of alcohol use. *Addiction*. 2012;107:312–22.
20. Freeman HD, Beer JS. Frontal lobe activation mediates the relation between sensation seeking and cortisol increases. *J Pers*. 2010;78:1–32.
21. Cima M, Smeets T, Jelicic M. Self-reported trauma, cortisol levels, and aggression in psychopathic and non-psychopathic prison inmates. *Biol Psychol*. 2008;78:75–86.
22. C'de Baca J, Miller WR, Lapham S. A multiple risk factor approach for predicting DWI recidivism. *J Subst Abuse Treat*. 2001;21:207–15.
23. Dahlen ER, Martin RC, Ragan K, Kuhlman MM. Driving anger, sensation seeking, impulsiveness, and boredom proneness in the prediction of unsafe driving. *Accid Anal Prev*. 2005;37:341–8.
24. Impinen A, Rahkonen O, Karjalainen K, Lintonen T, Lillsunde P, Ostamo A. Substance use as a predictor of driving under the influence (DUI) rearrests. A 15-year retrospective study. *Traffic Inj Prev*. 2009;10:220–6.
25. Schell TL, Chanb KS, Morral AR. Predicting DUI recidivism: personality, attitudinal, and behavioral risk factors. *Drug Alcohol Depend*. 2006;82:33–40.
26. Brown TG, Gianoulakis C, Tremblay J, et al. Salivary cortisol: a predictor of convictions for driving under the influence of alcohol? *Alcohol Alcohol*. 2005;40:474–81.
27. Couture S, Brown TG, Ouimet MC, Gianoulakis C, Tremblay J, Carbonneau R. Hypothalamic–pituitary–adrenal axis response to stress in male DUI recidivists. *Accid Anal Prev*. 2008;40:246–53.
28. Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar). *Br J Addict*. 1989;84:1353–7.
29. McLellan AT, Cacciola JS, Alterman AI, Rikoon SH, Carise D. The addiction severity index at 25: origins, contributions and transitions. *Am J Addict*. 2006;15:113–24.
30. Zuckerman M. *Behavioral Expressions and Biosocial Bases of Sensation Seeking*. New York, NY: The Cambridge University Press; 1994.
31. Roberti JW, Storch EA, Bravata E. Further psychometric support for the Sensation Seeking Scale – form V. *J Pers Assess*. 2003;81:291–2.
32. Barratt E, Stanford MS, Kent TA, Alan F. Neuropsychological and cognitive psychophysiological substrates of impulsive aggression. *Biol Psychiatry*. 1997;41:1045–61.
33. Stanford MS, Mathias CW, Dougherty DM, Lake SL, Anderson NE, Patton JH. Fifty years of the Barratt Impulsiveness Scale: an update and review. *Pers Individ Dif*. 2009;47:385–95.
34. Conley TB. Construct validity of the MAST and AUDIT with multiple offender drunk drivers. *J Subst Abuse Treat*. 2001;20:287–95.
35. Craig RJ. Assessing contemporary substance abusers with the MMPI MacAndrews Alcoholism Scale: a review. *Subst Use Misuse*. 2005;40:427–50.
36. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. *Alcohol Clin Exp Res*. 2007;31:185–99.
37. Butcher JN, Graham JR, Ben-Porath YS, Tellegen A, Grant Dahlstrom W, Kaemmer B. *MMPI-2 (Minnesota Multiphasic Personality Inventory-2) Manual for Administration, Scoring, and Interpretation*. Revised ed. Minneapolis, MN: NCS Pearson; 2001.
38. Sobell LC, Brown J, Leo GI, Sobell MB. The reliability of the alcohol timeline followback when administered by telephone and by computer. *Drug Alcohol Depend*. 1996;42:49–54.
39. Sobell LC, Sobell MB. *Timeline Followback: User's Guide*. Toronto, ON: Addiction Research Foundation; 1996.
40. Skinner HA. The drug abuse screening test. *Addict Behav*. 1982;7:363–71.
41. Yudko E, Lozhkina O, Fouts A. A comprehensive review of the psychometric properties of the drug abuse screening test. *J Subst Abuse Treat*. 2007;32:189–98.
42. Health Quebec Questionnaire. *Lifestyle and Health Questionnaire*. Centre for Health and Social Surveys of Quebec. Montréal.1998:61.
43. Bergeron J, Joly P. *Questionnaire ACR (Version E)*. Montréal, QC: Département de Psychologie, Université de Montréal; 1997.
44. Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology*. 2003;28:916–31.
45. McKnight PE, McKnight KM, Sidani S, Figueredo AJ. Patrick E. McKnight, Katherine M. McKnight, Souraya Sidani, Aurelio José Figueredo, eds. Individual growth curve analysis. Missing Data: *A Gentle Introduction*. New York, NY: The Guilford Press; 2007:152–6.
46. Langsrud Ø. ANOVA for unbalanced data: use type II instead of type III sums of squares. *Stat Comput*. 2003;13:163–7.
47. Childs E, de Wit H. Hormonal, cardiovascular, and subjective responses to acute stress in smokers. *Psychopharmacology (Berl)*. 2009;203:1–12.
48. Traffic Injury Research Foundation of Canada. *Understanding Drunk Driving*. Ottawa, ON: 2010:15. Publisher: Traffic Injury Research Foundation. ISBN: 978-1-926857-03-9.
49. Lapham SC, C'de Baca J, Chang I, Hunt WC, Berger LR. Are drunk-driving offenders referred for screening accurately reporting their drug use? *Drug Alcohol Depend*. 2002;66:243–53.
50. Lapham SC, C'de Baca J, McMillan G, Hunt WC. Accuracy of alcohol diagnosis among DWI offenders referred for screening. *Drug Alcohol Depend*. 2004;76:135–41.
51. Marsman R, Swinkels SHN, Rosmalen JGM, Oldehinkel AJ, Ormel J, Buitelaar JK. HPA-axis activity and externalizing behavior problems in early adolescents from the general population: the role of comorbidity and gender: the TRAILS study. *Psychoneuroendocrinology*. 2008;33:789–98.
52. Sondeijker FE, Ferdinand RF, Oldehinkel AJ, et al. Disruptive behaviors and HPA-axis activity in young adolescent boys and girls from the general population. *J Psychiatr Res*. 2007;41:570–8.
53. Junghanns K, Backhaus J, Tietz U, et al. Impaired serum cortisol stress response is a predictor of early relapse. *Alcohol Alcohol*. 2003;38:189–93.
54. Lovallo WR, Dickensheets SL, Myers DA, Thomas TL, Nixon SJ. Blunted stress cortisol response in abstinent alcoholic and polysubstance-abusing men. *Alcohol Clin Exp Res*. 2000;24:651–8.
55. Quas JA, Yim IS, Rush E, Sumaroka M. Hypothalamic pituitary adrenal axis and sympathetic activation: joint predictors of memory in children, adolescents, and adults. *Biol Psychol*. 2012;89:335–41.
56. Tops M, Boksem MAS. Cortisol involvement in mechanisms of behavioural inhibition. *Psychophysiology*. 2011;48:723–32.
57. Ouimet MC, Brown TG, Guo F, et al. Higher crash and near-crash rates in teenaged drivers with lower cortisol response: an 18-month longitudinal, naturalistic study. *JAMA Pediatr*. 2014;168:517–22.
58. Brown TG, Ouimet MC, Nadeau L, et al. DUI offenders who delay relicensing: a quantitative and qualitative investigation. *Traffic Inj Prev*. 2008;9:109–18.
59. Romano E, Kelley-Baker T, Voas RB. Female involvement in fatal crashes: increasingly riskier or increasingly exposed? *Accid Anal Prev*. 2008;40:1781–8.
60. Traffic Injury Research Foundation of Canada. Alcohol-Crash Problem in Canada: 2008, Publisher: Canadian Council of Motor Transport Administrators Road Safety Report Series. Ottawa, ON: 2010:225.