Motor Vehicle Driving in High Incidence Psychiatric Disability: Evaluating Risk and Cognitive Predictors of Adverse Driving Outcomes in ADHD and Depression

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Paula A. Aduen, M.A.

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Department of Human Services
Curry School of Education
University of Virginia
Charlottesville, Virginia

APPROVAL OF THE DISERTATION

This dissertation, "Motor Vehicle Driving in High Incidence Psychiatric Disability: Evaluating Risk and Cognitive Predictors of Adverse Driving Outcomes in ADHD and Depression," has been approved by the Graduate Faculty of the Curry School of Education in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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Catherine P. Bradshaw, Ph.D. (Chair of Committee)

_____
Peter Patrick, Ph.D.

_____
Amanda Williford, Ph.D.

_____
Stephanie Bajo, Psy.D.

_____
Michael Kofler, Ph.D.

_____Date

Dedication

To my parents, my steadfast support, mentors, and role models, because without you, this would not have been possible. You inspire me every day.

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Rationale and Conceptual Link across the Three Manuscripts

Paula A. Aduen

University of Virginia

Dissertation Abstract

This dissertation presents a line of research that explores the association between high-incidence psychiatric disorders, specifically Attention-Deficit/Hyperactivity Disorder (ADHD) and depression, and adverse driving outcomes. In addition to examining the magnitude of risk posed by high incidence psychiatric disorders, through evaluation of self-reported as well as criterion-based, objective markers of driving behavior (e.g., number of violations, collisions, at-fault collisions, and collision severity), the role of visual inattention and disinhibition as potential mechanisms of risk is explored. This three paper manuscript style dissertation presents three original empirical manuscripts and a linking document that describes the conceptual and theoretical linkages among the manuscripts. I am the lead author on all of the three manuscripts presented in the dissertation. The first manuscript entitled "Motor Vehicle Driving in High Incidence Psychiatric Disability: A Comparison of Drivers with ADHD, Depression, and No Known Psychopathology" (Aduen, Kofler, Cox, Sarver, & Lunsford, 2015), has been published in the *Journal of Psychiatric Research*. The second manuscript, "Prospective Crash Risk as a Function of ADHD Symptoms and Clinical Status" (Aduen, Kofler, Sarver, Cox, Wells, & Soto), has been submitted to *The Lancet Public Health* and is currently under review. The third manuscript, "The Role of Visual Attention in Predicting Crash Risk in Drivers with ADHD" (Aduen, Kofler, Bradshaw, Sarver, & Cox), will be submitted to the appropriate journal following completion.

Project Overview

Motor vehicle driving is a ubiquitous activity of daily living that cuts across gender, age, and socioeconomic status (SES) (Di Milia et al., 2011). Approximately 33,963 motor vehicle-related deaths occur per year, making injury or fatality due to traffic accidents one of the leading causes of death in the United States (National Highway Traffic Safety Administration, 2014). Converging evidence suggests that drivers with high incidence psychiatric disorders, such as ADHD, disproportionately contribute to motor vehicle accident rates, as well as moving violations and license suspensions/revocations (Cox, Madaan, & Cox, 2011). Drivers with ADHD are estimated to be 1.23 times more at risk for involvement in motor vehicle accidents (Vaa, 2014) and are less likely to sustain attention for longer periods of driving, resulting in greater susceptibility to distraction and less monitoring of changing traffic demands (Biederman et al., 2007; Fuermaier et al., 2015). As such, there is a need for additional research to better understand potential mechanisms, such as visual inattention and disinhibition, that lead to adverse driving outcomes in drivers with ADHD and other high incidence mental health disorders. Exploration of contributing factors and mechanisms that lead to increased crash risk can in turn inform prevention and intervention programs aiming to target the myriad adverse social, financial, health, and legal outcomes associated with functional impairment in driving (Barkley & Cox, 2007; Reimer et al., 2006; Wickens, Smart, & Mann, 2014).

As such, the focus of this dissertation is to examine the link between high incidence psychiatric disorders (e.g., ADHD and depression) and self-reported as well as objective, prospective crash risk, while also exploring the role of visual inattention and

disinhibition as a potential mechanism through which risk is conveyed. The three manuscripts that comprise this dissertation draw upon and review relevant theoretical and empirical literature regarding cognition and driving impairment (Barkley, 2004; Michon, 1985), conceptual models of attention (Posner & Petersen, 1990), and neuropsychological impairment in ADHD (Woods, Lovejoy, & Ball, 2002). The primary aim is to promote further understanding of the prevalence, magnitude, and potential causal pathways of adverse driving outcomes in high incidence psychiatric disorders, specifically ADHD and depression.

All three papers draw upon data from the Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study. Each driver who participated in SHRP-2 consented to having their car outfitted with sophisticated data acquisition systems that continuously captured all aspects of routine driving for up to two consecutive years. This resulted in SHRP-2 collecting approximately 2,000,000 gigabytes of data spanning 5,512,900 individual trips. Through its prospective and longitudinal design, SHRP-2 is uniquely suited to understand the primary research questions examined in this dissertation.

The first manuscript, titled *Motor Vehicle Driving in High Incidence Psychiatric Disability: A Comparison of Drivers with ADHD, Depression, and No Known Psychopathology* (Aduen et al., 2015), is an empirical study that examined the unique association among high incidence psychiatric disorders and adverse driving outcomes through retrospective self-report. Specifically, this study explored violations, collisions, collision-related injuries, and collision fault (over the past 3 years) in a large, nationally representative sample of U.S. drivers with suspected ADHD, Depression, and no known psychopathology participating in SHRP-2. Importantly, because participants completed

diagnostic measures after study enrollment, the extent to which ADHD and Depression were associated with adverse driving outcomes could be examined independent of confounding factors such as self-selection, demand characteristics, and referral bias. Common demographic variables known to be associated with adverse driving outcomes were accounted for including: age, gender, education level, marital status, income, and annual miles driven.

Results revealed differential patterns of risk between ADHD and Depression across driving outcomes. ADHD but not Depression predicted increased risk for multiple violations and multiple collisions. ADHD was also associated with increased risk for collision fault. Conversely, only Depression was uniquely associated with self-reported injury following a collision. Overall, findings from this study suggested that ADHD was uniquely associated with increased risk for multiple violations, multiple collisions, and collision-fault, which is indicative of possible disorder-specific mechanisms that underlie the unique risk associated with the disorder.

The second manuscript, titled *Prospective Crash Risk as a Function of ADHD Symptoms and Clinical Status* (Aduen et al., *Under Review)*, aimed to build upon the initial study by exploring crash risk as a function of ADHD symptomatology using prospective, objective, continuously-monitored, and criterion-based assessment of driving performance. Exploratory analyses were also performed using diagnostic group criteria established in Aduen (2015) to determine if adverse driving outcomes varied by clinical status (ADHD, Depression, No Known Psychopathology). This is the first large-scale study of its kind to examine adverse driving outcomes in high incidence psychopathology using on-road assessment of routine driving. Primary outcomes included objective,

prospective risk of crashes, near-crashes, and crash fault from data acquired from over 5.5 million trips captured.

Findings revealed that greater ADHD symptoms at study entry portended 5%-8% increased crash risk *per symptom* over the following one to two years (IRR=1.05-1.08). This risk corresponds to approximately one annual crash and two annual near-crashes *per driver* for drivers at the sample's maximum ADHD symptom severity. Analyses based on self-reported clinical status indicated similarly elevated rates for ADHD and Depression that were parsimoniously explained by both groups' elevated inattention/concentration symptoms. Risk was not attenuated by ADHD treatment-as-usual, but varied according to antidepressant treatment status. Conclusions drawn from this study suggest that when driving risk is assessed objectively, high incidence psychopathology in general appears to be associated with adverse driving outcomes. Nevertheless, ADHD continues to pose a unique risk per increase in inattention symptoms. Results call for routine clinical monitoring and intervention and are suggestive of possible trans-diagnostic mechanisms of risk.

Given that the prior two empirical studies demonstrated that ADHD symptoms portend increased risk for adverse driving outcomes when risk is evaluated subjectively, through retrospective self-report, and objectively, through criterion-based, on-road assessment, the third study in this sequence, titled *The Role of Visual Attention in Predicting Crash Risk in Drivers with ADHD* (Aduen et al., *Manuscript in Preparation)*, explored potential cognitive mechanisms that contribute to this heightened risk. Rooted in Posner & Petersen's (1990) well-established multi-component models of attention and models of cognition and driving impairment (Barkley, 2004; Michon, 1985), this study

examined the mediating role of Disinhibition, Endogenous Orienting, Arousal Decrements, and Vigilance Decrements factors, derived from the Conners' Continuous Performance Test, Second Edition (CPT-II; Conners, 2000), in the relation between ADHD symptoms and future crash risk. Additional exploratory models were analyzed examining clinical group (ADHD, Depression, Healthy Control) and medication status as predictors within this mediation framework. All models controlled for age, gender, education, marital status, time in study, and miles driven. Driving outcomes for the third study included objectively, prospectively assessed future crashes, near-crashes, and at-fault crashes/near-crashes.

Primary results revealed that ADHD symptoms exerted an indirect effect on future crash, near-crash, and at-fault crash/near-crash risk through its association with Endogenous Orienting. Additionally, ADHD symptoms at study entry predicted future crash risk (crashes, near-crashes, at-fault crashes/near-crashes) and higher levels of Disinhibition, Endogenous Orienting, and Arousal Decrements. Endogenous Orienting predicted future crashes and at-fault crashes/near-crashes while Vigilance Decrements predicted future near-crashes.

Despite indirect effects not approaching significance in exploratory models examining clinical group and medication status as predictors, clinical group analyses indicated that both drivers with ADHD and Depression experienced more future at-fault crashes/near-crashes. Alternatively, ADHD portended risk for future crashes, whereas Depression predicted future near-crash risk. Both drivers with ADHD and Depression demonstrated worse Endogenous Orienting. Interestingly, drivers with ADHD demonstrated worse Disinhibition and Arousal Decrements while drivers with Depression

demonstrated more Vigilance Decrements. Exploratory medication analyses showed that drivers with ADHD/Depression who were on medication experienced more crashes and at-fault crashes/near-crashes. Differences between medicated and non-medicated drivers with ADHD did not reach significance on any outcomes. However, medicated drivers with Depression demonstrated less Disinhibition compared to non-medicated drivers with Depression.

Overall, present results provide evidence that visual inattention, specifically endogenous orienting attention, mediates relations between ADHD symptoms and future risk for crashes, near-crashes, and crash/near-crash culpability. Importantly, a 14-minute visual-motor attention and inhibition task was found to not only be predictive of adverse driving outcomes 1 to 2 years later following initial assessment, but also highlighted a mechanism through which ADHD symptoms portend future crash risk of low (e.g., near-crash) to high (e.g., crash) severity. This creates a critical opportunity for clinicians to use performance markers of go/no-go tasks to assess, intervene, and monitor ADHD symptoms as it relates to future driving risk.

Summary

Conclusively, evidence corroborates an association between high incidence psychopathology and increased driving risk. The first manuscript in this sequence demonstrated that ADHD was uniquely associated with increased risk for multiple traffic violations, multiple crashes, and being at-fault for crashes, whereas depression was associated with increased likelihood for self-reported injury following a crash. To build upon these results, which were based on each driver's retrospective, self-report of driving performance, the second manuscript explored driving risk through analysis of

prospective, objective, criterion-based driving performance data collected from a 1-2 year on-road driving assessment. Findings from this study revealed that greater ADHD symptoms at study entry portended 5%-8% increased crash risk *per symptom* over the 1-2 year monitoring period. Exploration of driving risk between diagnostic groups indicated that both ADHD and Depression portended an increased risk for multiple collisions. Nevertheless, ADHD was associated with more costly and damaging collisions, whereas Depression predicted successful evasion of impending collisions. The third and final manuscript explored the contributing role of inattention and disinhibition in the relation between ADHD symptoms and future crash risk, with findings revealing that endogenous orienting mediated associations between ADHD symptoms and all markers of future crash risk.

Taken together, this body of literature highlights the importance of understanding the prevalence, magnitude, and implications of driving risk associated with high incidence psychiatric disorders. Given that individuals with ADHD disproportionately contribute to the rising number of motor vehicle collisions and fatalities per year (National Highway Traffic Safety Administration, 2014; Vaa, 2014), understanding the mechanisms associated with this increased risk has significant public health and clinical implications. Current findings are consistent with past studies that have identified inattention as a primary contributor to crash risk (Dingus et al., 2016; Fuermaier et al., 2015), thus creating an important opportunity for treatment and prevention initiatives to focus on this area of impairment.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD)

Attention-Deficit/Hyperactivity Disorder (ADHD) is a chronic, heterogeneous, and potentially impairing neurodevelopmental disorder. Affecting approximately 5% of children (Polanczyk et al., 2007), ADHD is primarily characterized by a pervasive behavioral pattern of inattention, impulsivity, and hyperactivity (Faraone et al., 2003). Results from prospective and longitudinal studies have shown that ADHD shows continuity into adulthood with recent estimates stating that between 46-70% of children may continue to meet diagnostic criteria for ADHD into adolescence and adulthood (Biederman et al., 2011; Sibley et al., 2012). Current ADHD persistence estimates are consistent with prevalence rates reporting that approximately 4.4-5.2% of adults in the Unites States are affected by ADHD (Wilens, Faraone, & Biederman, 2004). The persistent behavioral and cognitive impairments associated with ADHD carry broad implications for various domains of functioning throughout the lifespan (Biederman et al., 2011; Wilens, Faraone, & Biederman, 2004). In adulthood, impairments in social, academic, and familial functioning are known to persist alongside other functional impairments that are unique to this developmental period. One such impairment is increased risk for adverse driving outcomes, which has been associated with known features of ADHD, including attentional and executive dysfunction (Barkley & Cox, 2007; Barkley & Fischer, 2011; Jerome, Habinski, & Segal, 2006).

Neurocognitive Deficits in ADHD. Inattention is a core symptom of ADHD, with large magnitude impairments documented throughout the lifespan (Barkley et al., 2002; Biederman et al., 2007; Kofler, Rapport, & Alderson, 2008). The implementation

of standardized, controlled neuropsychological assessment measures has allowed for broader cognitive skills, such as attention, to be dissected into their component parts. In doing so, ADHD has morphed from a disorder of 'inattention' more generally, to having distinct neurocognitive endophenotypes with unique patterns of impairments that further elucidate under what circumstances attentional vulnerabilities emerge. Three components of attention are frequently identified: *alerting*, *orienting*, and *executive attention*, each associated with distinct neural areas and functional processes (Figure 1; Posner & Petersen, 1990; Petersen & Posner, 2012).

Alerting refers to the concept of arousal and is responsible for enhancing physiological activation to maintain a state of high awareness to incoming stimuli (Posner & Petersen, 1990; Strum et al., 1999). Alerting is conceptualized as a foundational aspect of attentional capacity and a prerequisite to more complex attentional processes (Cohen, 2014; Sturm et al., 1999). Its function has been associated with lateralized, right-hemisphere frontal and posterior parietal cortices, the locus coeruleus, and brain stem, and is primarily reliant on noradrenergic systems (Petersen & Posner, 2012; Posner, 2008; Samuels & Szabadi, 2008; Strum & Willmes, 2000). Posner & Petersen (1990) further dichotomized arousal into *tonic alertness* and *phasic alertness* to differentiate between: *a)* resting state of physiological arousal and *b)* sustained state of readiness or increases in alertness following an external cue or warning, respectively. The term phasic alertness is often used interchangeably with sustained attention/vigilance to describe decrements in attention over time, while tonic alertness characterizes the basic orienting response (Oken, Salinsky, & Elsas, 2006).

Studies have assessed the broad construct of alertness through lengthy, monotonous sustained vigilance tasks (Posner, 2008). Varying the presentation rate of sensory stimuli, that is the interstimulus interval (ISI), during these sustained vigilance tasks has been found to reliability assess alertness level in both children and adults (Kuntsi et al., 2005; van der Meere, 2005; Wiersema et al., 2006). Separate subdomains of alertness are measured through manipulations of these paradigms, with *tonic alertness* assessed through reaction time to sensory (visual, auditory) stimuli and *phasic alertness* assessed through changes in reaction time as a function of an external change in the task or sensory warning stimulus.

Males with ADHD appear to generally have increased variability in response time irrespective of stimulus presentation rate (e.g., faster, slower), suggestive of broader deficits in arousal (Cohen, 2014; Wiersema et al., 2006). Meta-analyses examining alertness in ADHD have concluded that ADHD is not consistently characterized by dysfunction in tonic alertness (Huang-Pollock & Nigg, 2003). However, adults with ADHD have been shown to have slower response times with longer ISIs, providing evidence for phasic arousal decrements as a function of increased task duration (Wiersema et al., 2006). Conclusively, there is some evidence to suggest arousal deficits in ADHD, which may be more apparent during monotonous, sustained tasks. These deficits may contribute to broader impairment in sustained attention and other attention subsystems (Epstein et al., 1997; Posner & Petersen, 1990; Tucha et al., 2015; Woods, Lovejoy, & Ball, 2002).

Orienting refers to the detection of external sensory input and the ability to give priority to salient stimuli (Posner & Petersen, 1990). Orienting has been further

characterized as either *exogenous* or *endogenous* to differentiate between reflexive/automatic orientation (e.g., bottom-up processing) to a salient sensory cue in the environment and controlled/voluntary (e.g., top-down processing) orientation toward an object, respectively (Berger, Henik, & Rafal, 2005; Jonides, 1981; Posner, 1980). Studies have linked orienting of attention to the frontal eye fields, superior parietal lobe, temporal parietal junction, superior colliculus, and the thalamic reticular nucleus (Petersen & Posner, 2012; Posner & Petersen, 1990), and have found cholinergic systems to underlie these processes (Petersen & Posner, 2012; Voytko et al., 1994). Anatomically distinct neural networks have been distinguished that align with *exogenous* and *endogenous* orienting of attention. Specifically, the locus coeruleus, superior parietal cortex, pulvinar, and superior colliculus, have been associated with exogenous, automatic orienting while the anterior cingulate gyrus, supplementary motor cortex, and mid-prefrontal cortex have been linked to endogenous, voluntary orienting (Berger & Posner, 2000; Posner & Raichle, 1994).

Tasks assessing orienting processes include simple detection designs or predictive designs that involve presenting a cue in the location where a target stimulus will appear (Huang-Pollock & Nigg, 2003). Primary outcomes of interest in these tasks are reaction time as well as omissions and anticipatory responses for exogenous and endogenous orienting, respectively (Fan et al., 2005; Novak, Solanto, & Abikoff, 1995). Studies examining orienting of attention have provided the most evidence for dysfunction in endogenous orienting in samples of children and adults with ADHD (d= 0.30-1.32) (Nigg, Swanson, & Hinshaw, 1997; Novak, Solanto, & Abikoff, 1995). Nevertheless, in their review of the literature, Huang-Pollock and Nigg (2003) reported that evidence is

inconsistent for deficits in endogenous, voluntary orienting in ADHD. Conversely, findings have been more conclusive regarding intact exogenous, automatic orienting in ADHD (Aman et al., 1998; Epstein et al., 1997; Perchet et al., 2001).

Executive attention describes attentional mechanisms responsible for resolving conflict between opposing responses, thus involving monitoring and response selection processes (Posner & Petersen, 1990). These executive control processes of attention are responsible for voluntary control and processing of attention in space (Jonides, 1981; Posner & Raichle, 1994). Several processes commonly attributed to broader executive functions, such as interference control, are subsumed within this sub-component of attention (Posner & DiGirolamo, 1998). Executive attention mechanisms are associated with the prefrontal and lateral ventral cortices, anterior cingulate, supplementary motor cortex, and basal ganglia (Botvinick et al., 2001; Fan et al., 2005) and have been linked to dopaminergic systems. Executive attention has historically been assessed through measures involving competing response selection, such as Stroop and Color-Word Inhibition tasks. Consistent findings have implicated impairment in executive attention in ADHD throughout the lifespan (Berger & Posner, 2000; Durston & Konrad, 2007; Mullane et al., 2009),

Executive Functioning. Executive functioning (EF) is an umbrella construct used to describe a set of 'top-down' neurocognitive processes necessary for goal-directed behavior (Welsh & Pennington, 1988). Typically, EF is discussed to include processes such as planning, initiation and discontinuation of action, problem solving, inhibition, monitoring, set switching, working memory, and regulation of attention (Castellanos et al., 2006; Miyake et al., 2000; Stuss & Alexander, 2000).

In their meta-analytic review, Pennington and Ozonoff (1996) systematically examined the association between ADHD and EF impairments and found that ADHD was associated with weaknesses across all assessed EF domains, with effect sizes ranging from *d*=0.40-0.70. Other meta-analyses have revealed that executive dysfunction is common, though not pervasive, in ADHD with the most pronounced deficits existing in the domains of inhibitory control, verbal and spatial working memory, vigilance, and planning (Boonstra et al., 2005; Hervey, Epstein, & Curry, 2004; Nigg et al., 2005; Willcutt et al., 2005).

Inhibitory control refers to a set of interrelated cognitive processes that underlie the ability to withhold (action restraint) or stop (action cancellation) an on-going behavioral response (Alderson et al., 2007; Schachar et al., 2000). These processes have been linked to the septo-hippocampal system with associated projections to the inferior frontal cortex (Quay, 1997), and to fronto-basal-ganglia circuitry (Aron et al., 2007). Inhibitory control has been classically assessed by go/no-go or stop-signal tasks. Go/no-go tasks differ from stop-signal tasks in that they require a continuous response pattern that is only interrupted when a stimulus signals to inhibit responding. Adults with ADHD have demonstrated poorer performance on response inhibition tasks compared to adults with no known psychopathology and adults with anxiety (Epstein et al., 2001). Nevertheless, studies examining differences in inhibition between ADHD, other clinical groups, and healthy control groups have failed to consistently replicate these findings (Lijffijt et al., 2005; Nigg, 2001), with recent meta-analyses concluding that inhibition processes are generally intact in ADHD (Alderson et al., 2007).

Neurocognitive Impairment in Mood Disorders

There has been a recent upsurge in literature focusing on the characterization of neuropsychological impairment in Major Depressive Disorder (MDD), given its high prevalence (6.7%-13.2%) in adults and known impact on functional outcomes (Hasin et al., 2005; World Health Organization [WHO], 2017). According to recent estimates, neurocognitive impairment occurs in approximately two-thirds of individuals with depression and is known to persist even after symptom remission, particularly in the areas of attention and executive functioning (Abas, Sahakian, & Levy, 1990; Afridi et al., 2011; Paradiso et al., 1997; Reppermund et al., 2009). Studies have been consistent in finding that individuals reporting severe depressive symptoms experience more profound attentional and executive dysfunction (Austin, Mitchell & Goodwin, 2001; Grant, Thase, & Sweeney, 2001; McDermott & Ebmeier, 2009). Furthermore, neurocognitive impairment has been found to be more pronounced in adult compared to young adult or adolescent populations, a finding that may be related to age of onset and frequency of depressive episodes throughout the lifespan (Baune et al., 2014; Gollan et al., 2005; Naismith et al., 2003).

Paelecke-Habermann and colleagues (2005) found that adults with depression had marked deficits across all components of attention including visual orienting, sustained attention, and executive attention. Additionally, converging evidence suggests that impairment in sustained attention may be the most prominent, with effect sizes as large as 0.86 found in individuals with depression compared to non-depressed individuals. Within the domain of executive functioning, set-shifting impairments in patients with depression are well documented (Lee et al., 2012; Meiran et al., 2011), with effect sizes ranging

from medium to large (Klimkeit et al., 2011; Smith, Muir, & Blackwood, 2006). Impairments in working memory have also been implicated in MDD (Austin, Mitchell & Goodwin, 2001; Paradiso et al., 1997), particularly deficits in the "strategic aspects of working memory." Within this population, however, it appears that inhibitory control is largely spared (Austin, Mitchell & Goodwin, 2001).

Conclusively, there is evidence that suggests deficits in sustained attention in addition to set-shifting and working memory in depression. This suggests that both attention processes and executive functions are vulnerable to mood or stress-related factors (Austin, Mitchell & Goodwin, 2001) and may be especially sensitive to symptom severity. The identification of vulnerabilities in neurocognitive functioning in depression is critical given known associations between cognitive deficits and adverse driving outcomes (Brunnauer et al., 2008; Bulmash et al., 2006; Wingen, Ramaekers, & Schmitt, 2006).

Cognition and Driving: A Model of Impairment

Being that some of the processes critical to driving performance, such as basic and complex attention in addition to executive functioning, are often compromised in ADHD and depression, it is unsurprising that converging evidence suggests that drivers with high incidence psychopathology disproportionately contribute to high automobile collision rates (Barkley & Cox, 2007; Cox, Madaan & Cox, 2011; Vaa, 2014). With motor vehicle accidents being prevalent among drivers with ADHD, conceptual models have emerged with the aims of disentangling the multidimensional task of driving and understanding the mechanisms by which ADHD symptoms interfere (Barkley, 2004; Ranney, 1994).

Adapted from Michon's (1985) model of driving and cognitive control, Barkley (2004) proposed a conceptual framework to depict the possible influence of ADHD symptomatology on *operational*, *tactical*, and *strategic* levels of driving (Barkley & Cox, 2007; Figure 3). According to Michon's original model (1985), the activity of driving is comprised of three, hierarchically organized levels (operational, tactical, and strategic) that require specific cognitive skills. The *operational* level, describes immediate vehicle control (e.g., steering, braking, shifting gears) and is thought to require attention, concentration, reaction time, visual scanning, spatial perception and orientation, visual-motor integration, processing speed, and motor coordination. The *tactical* level involves negotiating traffic and pedestrian demands (e.g., obstacle avoidance, entering traffic stream), and involves the following cognitive processes: self-monitoring, visual tracking, and set-shifting/flexibility (Ranney, 1994). Lastly, the *strategic* level involves more complex aspects of driving including trip planning and selecting optimal routes, thus involving planning abilities and working memory. This model postulates that successful execution of higher, more complex levels of driving performance depends on intact basic attention, orienting, and visual-motor integration processes (Barkley, 2004).

Motor Vehicle Driving in High Incidence Psychopathology

Motor vehicle driving is a complex activity of daily living that involves negotiating traffic, passenger, and technology demands simultaneously. The skillful execution of this task requires the interplay and synchrony of perceptive, motor, and cognitive abilities (Cox, Madaan, & Cox, 2011; Fuermaier et al., 2015). Estimates from the National Highway Traffic Safety Administration indicate approximately 33,963 deaths related to motor vehicle accidents in 2009 with an additional 2,317,000 annual,

non-fatal motor vehicle accidents reported (Blincoe et al., 2010). Drivers with ADHD have more citations and collisions, more expensive collisions, and are more likely to be at-fault for collisions, with relative risk ranging from 1.23 to 1.88 (Cox, Madaan, & Cox, 2011; Vaa, 2014). Specifically, drivers with ADHD are more likely to exceed the speed limit, have less vehicle control, and increased levels of distractibility, all which are risk factors for adverse driving outcomes (Fischer et al., 2007; Reimer et al., 2006).

Depression has been associated with a relative risk for increased collision rates ranging from 1.10 to 2.55 (Vaa, 2014). Although few studies have examined the impact of depressive symptoms on driving performance, results suggest that drivers with depression are more likely to experience collisions in a simulated driving environment. Specifically, drivers with depression are more likely to have lapses in attention and slower reaction time in high-risk driving scenarios that result in collisions or near-misses (Brunnauer et al., 2008; Bulmash et al., 2006; Wingen, Ramaekers, & Schmitt, 2006).

Given the consistent association between high incidence psychiatric diagnoses and adverse driving outcomes, several studies have focused on the assessment of driving performance, using varied methodological approaches. Methodologies have primarily included examination of self and informant reports of driving behavior, review of official driving records, driving simulator studies, and to a lesser extent assessment of on-road driving. Studies that have examined driving performance in ADHD through retrospective self-report have found that drivers with ADHD report more frequent and severe collisions compared to healthy control drivers (Barkley et al., 1993, 2004; Jerome, Habinski, & Segal, 2006). Additionally, these drivers report a higher number of traffic citations and are more likely to have a history of license suspensions and revocations (Fischer et al.,

2007; Fried et al., 2006). The primary advantage of the self-report methodology is its ability to capture drivers' perception of how their clinical disorder impacts their driving performance. However, these studies are limited by expectancy effects, positive illusory biases, and can be significantly influenced by individuals underreporting the frequency or severity of these events (Cox, Madaan, & Cox, 2012; Knouse et al., 2005).

Retrospective insurance database studies have found that ADHD is a significant predictor of filing a motor vehicle claim with overall costs that are significantly higher when compared to individuals without the disorder (Swensen et al., 2004). Additionally, review of official driving records reveals that the mean number of road accidents appears to increase as a function of ADHD status (Chang et al., 2014). Although examination of official driving records provides an objective report of driving performance, it is limited by collisions defined by increased severity (i.e., emergency hospital visits, mortality) and omits less severe accidents or indicators of unsafe driving.

With the aim of more directly assessing driving performance, driving simulator studies have emerged as an additional methodological approach to analyze driving behavior. Results from driving simulator studies have suggested that individuals with ADHD are more likely to have increased collision and violation rates (Biederman et al., 2007; Cox et al., 2004; Groom et al., 2015; Michaelis, McConnell & Smither, 2012). Drivers with ADHD are more likely to speed, travel a greater distance over the speed limit, and have less vehicle control. Although driving simulators have strong face validity and provide a safe way to assess driving behavior, they are limited to the evaluation of short-term driving skills that may not capture routine driving habits and responses to critical, real-time road events (Barkley & Cox, 2007; Knouse et al., 2005).

On-road assessment of driving performance addresses several methodological limitations and provides a unique opportunity to directly examine driving risk and how it varies as a function of several factors. A small number of studies have adopted this approach during which drivers were continuously recorded for a period of time using vehicle mounted accelerometers and digital video cameras (Aduen et al., 2016; Dingus et al., 2016; Sobanski et al., 2013; Verster et al., 2008). Converging findings from on-road studies show that drivers with ADHD experience significantly more collisions (Cox et al., 2012; Merkel et al., 2016). Additionally, drivers with ADHD are more likely to commit a greater number of driving errors (e.g., sudden decelerations, swerving, and braking), with lapses in inattention frequently preceding these errors.

Drawing from the existing literature, conclusions strongly indicate that both ADHD and depression pose increased risk for adverse driving outcomes. Although varied methodologies have been implemented to examine this relationship, there is a paucity of studies that have used criterion-based, on-road assessments of driving performance, which would allow for increased generalizability of conclusions. Additionally, there is a need for studies to compare driving outcomes in drivers with ADHD and depression directly in order to better understand whether this is a transdiagnostic or disorder-specific risk. Understanding whether this is a shared or unique risk will delineate potential mechanisms of risk and specify targets for intervention.

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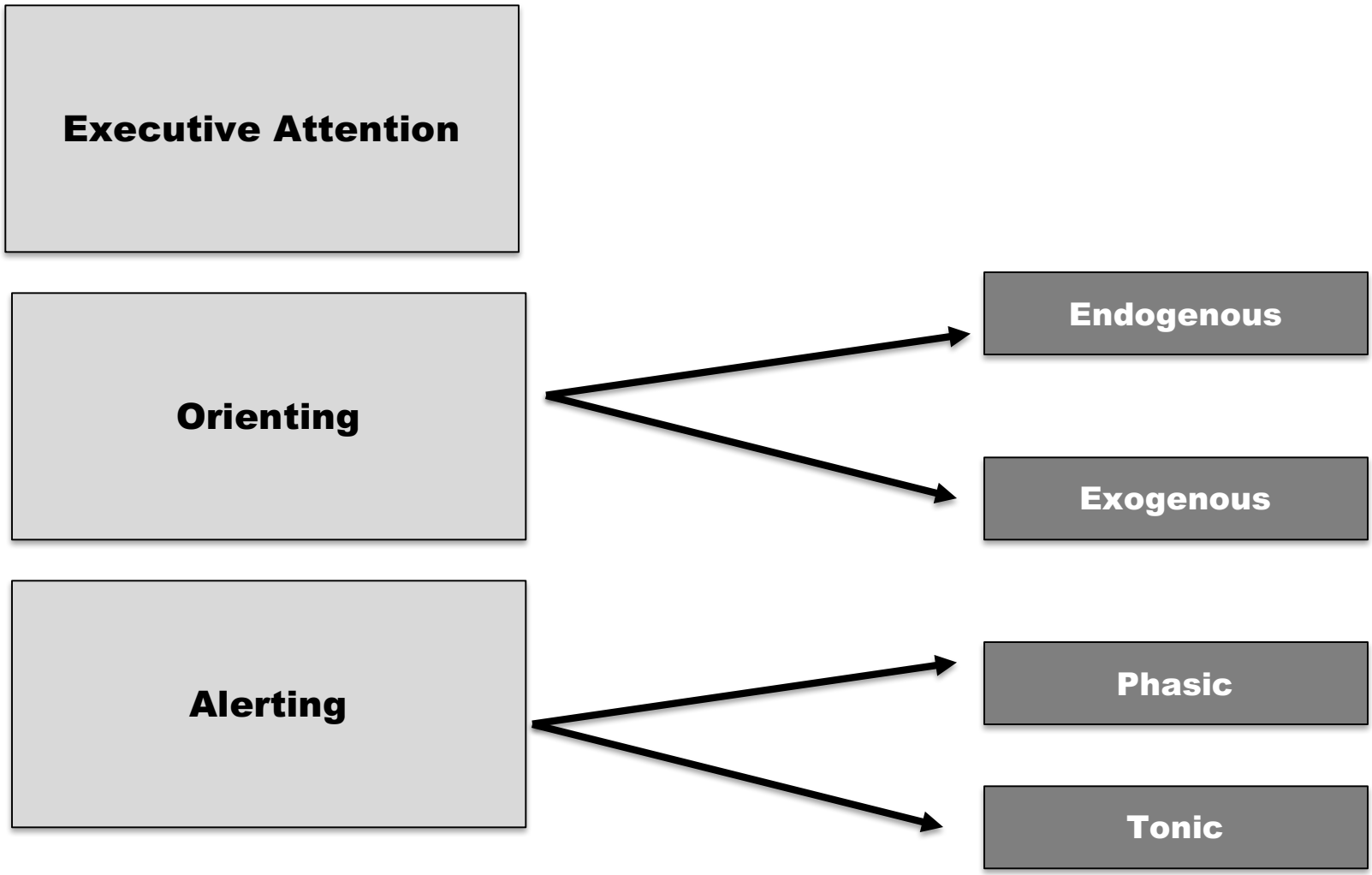

Figure 1. Theoretical framework of multi-component theory of attention proposed by Posner & Petersen (1990)

Figure 2. Hierarchical, three-tiered model of driving and cognitive impairment proposed by Michon (1985) and adapted by Barkley (2004)

Manuscript 1

Motor Vehicle Driving in High Incidence Psychiatric Disability: Comparison of Drivers with ADHD, Depression, and No Known Psychopathology

Paula A. Aduen, M.A.
University of Virginia

Michael J. Kofler, Ph.D.
Florida State University

Daniel J. Cox, Ph.D.
University of Virginia Health Systems

Dustin E. Sarver, Ph.D.
University of Mississippi Medical Center

Erin Lunsford, B.A.
University of Virginia

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Abstract

Although not often discussed in clinical settings, motor vehicle driving is a complex multitasking endeavor during which a momentary attention lapse can have devastating consequences. Drivers with high incidence psychiatric disabilities such as ADHD contribute disproportionately to collision rates, which in turn portend myriad adverse social, financial, health, mortality, and legal outcomes. However, self-referral bias and the lack of psychiatric comparison groups constrain the generalizability of these findings. The current study examined the unique associations among ADHD, Depression, and adverse driving outcomes, independent of self-selection, driving exposure, and referral bias. The Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study comprises U.S. drivers from six sites selected via probability-based sampling. Groups were defined by Barkley ADHD and psychiatric diagnosis questionnaires, and included *ADHD* (*n*=275), *Depression* (*n*=251), and *Healthy Control* (*n*=1,828). Individuals who endorsed Personality/psychotic/bipolar disorders (*n*=34) were excluded from the final sample. Primary outcomes included self-reported traffic collisions, moving violations, collision-related injuries, and collision fault (last 3 years). Accounting for demographic differences, ADHD but not Depression portended increased risk for multiple violations (OR=2.3) and multiple collisions (OR=2.2). ADHD but not Depression portended increased risk for collision fault (OR=2.1). Depression but not ADHD predicted increased risk for self-reported injury following collisions (OR=2.4). ADHD appears uniquely associated with multiple collisions, multiple violations, and collision fault, whereas Depression is uniquely associated with self-reported injury following a collision. Identification of the specific mechanisms underlying this risk will be critical to designing effective interventions to improve long-term functioning for drivers with high incidence psychiatric disability.

Motor Vehicle Driving in High Incidence Psychiatric Disability: Comparison of Drivers With ADHD, Depression, and No Known Psychopathology

The upsurge of research into adult attention-deficit/hyperactivity disorder (ADHD) reflects an improved understanding of the lifetime course of this chronic and potentially impairing neurodevelopmental disorder (Barkley et al., 2002; Klein et al., 2012). Prospective studies reveal that most children with ADHD continue to meet full diagnostic criteria in adolescence (70%-80%) and adulthood (46%-66%) (Barkley et al., 2002; Biederman et al., 2010; Mannuzza et al., 1993;). These findings are consistent with epidemiological estimates for childhood (5%; Polanczyk et al., 2007) relative to adult ADHD (4%; Biederman et al., 2010), and clearly position ADHD as a high incidence disability throughout the lifespan (Wilens, Faraone, & Biederman, 2004) when considered in the context of the disorder's broad impact on functioning.

In childhood, ADHD is associated with impairments in academic, peer, and family functioning (Bagwell et al., 2001; Heiligenstein et al., 1999; Pelham & Fabiano, 2008). Adult ADHD studies confirm continued impairments in these areas (Wilens, Faraone, & Biederman, 2004), and have identified two additional areas of concern: occupational functioning (Barkley & Fischer, 2011), and motor vehicle driving (Barkley & Cox, 2007; Jerome, Habinski, & Segal, 2006). Although not often discussed in the clinical setting, driving is a complex, cognitive-motor-perceptual, multitasking endeavor that involves controlling a multi-ton projectile through time and space while negotiating road, traffic, passenger, and technology demands (Cox, Madaan, & Cox, 2011). In this context, a momentary attentional lapse can have devastating consequences; U.S. car crashes are associated annually with over 34,000 deaths, 2.3 million non-fatal injuries, and $99 billion in costs. Converging data suggest that drivers with high incidence

disabilities such as ADHD disproportionately contribute to automobile collision rates, as well as moving violations and license suspensions/revocations (Cox, Madaan, & Cox, 2011).

Studies of drivers with ADHD consistently report that drivers have more citations and collisions, more expensive collisions, and are more likely to be at-fault for collisions, with relative risk ranging from 1.23 to 1.88 across meta-analyses (Cox, Madaan, & Cox, 2011; Vaa, 2003; 2014). A serious shortcoming of most studies, however, is their reliance on self-selected samples recruited specifically to examine the impact of ADHD on their driving behavior (Chang et al., 2014; Cox, Madaan, & Cox, 2011). This potential for self-referral bias and associated demand characteristics are significant confounds that constrain the external validity of previous findings. In addition, no study has compared drivers with ADHD to drivers with other clinical disorders (e.g., depression) – a critical omission given that drivers with depression also show increased collision risk based on driving simulator studies (Bulmash et al., 2006). Whether ADHD portends increased risk for adverse driving outcomes beyond other high incidence disorders such as depression remains unknown. Finally, fewer than 50% of previous studies reported annual miles/kilometers driven, despite the known association between exposure and collision/violation risk (Chang et al., 2014). Thus, the extent to which previous findings are attributable to participant perception, self-selection processes, comorbidity, exposure, or other high incidence psychopathology remains unknown.

The present study addressed these limitations by examining violations, collisions, collision-related injuries, and collision fault in a large, nationally representative sample of U.S. drivers with (a) ADHD, (b) Depression, and (c) no known psychopathology

participating in the Strategic Highway Research Program 2 (SHRP-2) Naturalistic Driving Study. SHRP-2 is a 6-center, prospective, naturalistic driving study (Antin et al., 2011). Importantly, drivers were not selected based on diagnostic status but rather completed diagnostic measures after study enrollment (Antin et al., 2011). Thus, the present study allows us to examine the extent to which two high incidence psychopathologies (ADHD, Depression) are associated with adverse driving outcomes, independent of the potential role of self-selection, demand characteristics, driving exposure, and referral bias.

We hypothesized that drivers with ADHD (Chang et al., 2014), and drivers with depression (Scott-Parker et al., 2013; Vassallo et al., 2008), would endorse more violations, collisions, collision-related injuries, and collision faults relative to Healthy Controls. No predictions were made regarding the relative risk for drivers with ADHD relative to drivers with Depression given the paucity of research.

Method

Design and Overview

The SHRP-2 Naturalistic Driving Study consists of 3,600 drivers from six U.S. sites (New York, Washington, Pennsylvania, Indiana, Florida, and North Carolina). A detailed description of study recruitment, participants, and methodology is provided in Antin and colleagues (2011). Briefly, participants were selected through a probability-based sampling approach and consented to have their vehicles outfitted with a sophisticated data acquisition system to capture day-to-day driving data continuously for 1-2 years. The current study is based on self-report data collected during the initial

evaluation that included driver demographic, driving history, and psychiatric screening questionnaires.

Measures

Barkley Adult ADHD Quick Screen (BAQS). The BAQS includes six items assessing self-reported ADHD symptoms on a 4-point Likert scale (0=Never/Rarely, 1=Sometimes, 2=Often, 3=Very Often); scores are summed across the six items and correlate .97 with the full, 18-item DSM-IV symptoms (Barkley, Murphy, & Fisher, 2008). The recommended BAQS cutoff score of 7 correctly identifies 93% of ADHD and 99% and non-ADHD adults (Barkley, Murphy, & Fisher, 2008).

Psychological Diagnoses Questionnaire. The psychological diagnoses questionnaire instructed participants to indicate if they currently met diagnosis for Depression, Anxiety, Bipolar Disorder, ADHD/ADD/Tourette's, or Psychotic or Personality Disorders. Participants selected all diagnoses that were applicable. Drivers who endorsed "ADHD/ADD/Tourette's" were included in the ADHD group unless they met the exclusion criteria below given the rarity of Tourette's Syndrome in adulthood (0.002% to 0.04%; Apter et al., 1993; Burd et al., 1989).

Driving History and Demographic Questionnaire. The driving history and demographic questionnaire assessed participant age, gender, marital status, and annual miles driven. Participants reported violation and collision frequency over the past 3 years (0, 1, 2+ collisions/violations) as well as severity and fault for up to two collisions. Endorsement of violations encompassed both moving and traffic violations.

Inclusion and Exclusion Criteria

Participants who did not complete the BAQS or the psychological diagnoses questionnaire (*n*=341) were excluded (final *N*=3,259; 90.5% of SHRP-2 drivers). Group membership was assigned based on the following criteria. Participants were included in the *ADHD Group* with a positive BAQS screen (7+) and/or self-reported ADHD, alone (*n*=229) or comorbid with anxiety (*n*=46; total *n* =275). Participants with positive BAQS screens who reported other clinical disorders but not ADHD (*n*=52) were excluded from the ADHD group as recommended because 83% of mood disorders screen positive on the BAQS (Barkley, Murphy, & Fischer, 2008). Participants were included in the *Depression Group* if they endorsed depression, alone (*n* =170) or comorbid with anxiety (*n*=81), but not ADHD (total *n*=251); no BAQS criteria were set for the Depression Group. Individuals with self-reported anxiety were included given its high comorbidity with both adult ADHD and Depression (Kessler et al., 2006; 2008). Individuals were assigned to the *Healthy Control Group* (no known psychopathology) based on negative BAQS screen (< 4) and no self-reported psychological diagnoses (*n*=1,828). Participants were excluded from all groups if they self-reported personality, psychotic, or bipolar disorders (*n*=32). The remaining 821 cases were excluded for failing to meet any group criteria (i.e., no self-reported depression and BAQS scores of 4-6 that fell between the Healthy Control maximum and ADHD minimum).

Analyses

Multinomial logistic regression was used to predict relative risk for collisions, violations, injuries, and collision fault for drivers with ADHD and drivers with Depression relative to drivers with no known psychopathology (Healthy Controls). An

additional multinomial logistic regression assessed relative risk for ADHD relative to Depression. These analyses predicted the maximum likelihood conditional probability of reporting 0, 1, or 2+ collisions; 0, 1, or 2+ violations; collision with injury (yes/no); and collision fault (yes/no) as a function of group membership. Results are expressed as odds ratios (OR); odds ratios with absolute values greater than 1.0 indicate increased (positive values) or decreased (negative values) risk relative to the comparison group.

Results

Preliminary Analyses

Data were available for over 99% of the 3,259 cases for all dependent and independent variables (range = 99.1% to 99.8%; N = 7 to 31 missing cases) with the exception of self-reported income (16.2% missing; N = 2,731 respondents)[a]. Chi-square tests supported a Missing At Random (MAR) assumption; the probability of missing data did not vary significantly as a function of group membership ($\chi^2[2]=1.02$; $p = .60$). The groups differed significantly in age, gender, education, marital status, average annual miles driven (all $p<.002$), and income ($p=.03$). Bonferroni-corrected post hocs revealed that ADHD drivers were overrepresented in the youngest age groups (ages 16-25) and underrepresented in the oldest age groups (ages 51+). Drivers with ADHD were also less likely to have a high school diploma or college degree, were overrepresented in the extreme income groups (< \$29K/year, > \$150K/year), and were less likely to be married (all $p<.05$). Drivers with depression were more likely to be female and report driving more than 20,000 miles/year (both $p<.05$). These demographic variables were included as covariates in all subsequent analyses (Table 1). Results are reported both before and after

[a] The pattern of results reported below did not change with Income excluded from the models; we therefore report results with Income included.

controlling for these factors given that most of these variables are known outcomes of ADHD (Barkley et al., 2002; Mannuzza et al., 1993) and Depression (Fergusson & Woodward, 2002; Harrington et al., 1990; Rao, Hammen, & Daley, 1999).

Traffic Violations (Last 3 Years)

As shown in Table 2 and Figure 1, ADHD and Depression were associated with a 56% and 43% increased risk for a single traffic violation (OR=1.56, 1.43), respectively. Drivers with ADHD experienced a 222% increased risk for multiple violations (OR=3.22), relative to a 76% increased risk for drivers with Depression. After correcting for demographic covariates, only drivers with ADHD remained significantly at risk for multiple violations (127% increased risk; OR=2.27). When compared to Depression, ADHD portended a significant, 83% to 85% increased risk for multiple violations (OR=1.83, 1.85).

Collisions (Last 3 Years)

Relative to Healthy Controls, ADHD was associated with an increased risk for a single collision (OR=1.41) and multiple collisions (OR=2.63) (Table 2, Figure 2). The ADHD group's increased risk for multiple collisions remained significant when controlling for demographic factors (OR=2.21). Depression was also associated with increased risk for multiple collisions (OR=1.72). The difference in relative risk between ADHD and Depression did not reach significance for single or multiple collisions.

Injuries From Collisions (Last 3 Years)

Among drivers reporting at least one collision[b], Depression portended a 125% increased risk for self-reported injury that was robust after accounting for demographic

[b] N = 91 drivers with suspected ADHD [33%], 73 drivers with self-reported Depression [29%], and 416 Healthy Control drivers [23%].

factors (OR=2.25). ADHD was not associated significantly with increased risk for self-reported injuries from collisions (Table 2, Figure 3).

Fault for Collisions (Last 3 Years)

Among drivers reporting at least one collision, ADHD was associated with a 112% increase in self-reported fault (OR=2.12) relative to Healthy Control but not relative to drivers with Depression. Depression was not associated with a significant increased risk for self-reported collision fault (Table 2, Figure 3).

Discussion

The current study used a large, nationwide sample to examine the relative risk of motor vehicle violations, collisions, collision-related injuries, and collision fault associated with ADHD and Depression relative to drivers with no known psychopathology. To our knowledge, this is the first study to compare drivers with multiple forms of high incidence psychopathology while also accounting for known risk factors of increased violation and collision rates. Using the nationally representative SHRP-2 sample of drivers, the present study addressed key limitations in our understanding of adverse driving outcomes for drivers with two forms of high incidence psychopathology. Importantly, drivers were not selected based on ADHD or Depression status but rather completed diagnostic screening measures after study enrollment (Antin et al., 2011). Thus, the present study allowed us to examine the extent to which ADHD and Depression are associated with adverse driving outcomes, independent of the potential role of self-selection bias, demand characteristics, exposure, and referral bias.

Results indicated that both ADHD and Depression portended increased risk for adverse driving outcomes, although the specific pattern of relative risk varied

considerably between the diagnostic groups. Specifically, both groups were associated with increased risk for a single collision and single violation relative to drivers with no known psychopathology. However, these relationships were no longer significant after controlling for known demographic correlates of adverse driving outcomes such as younger age, male gender, lower socioeconomic status indicators (SES; education, annual income), unmarried status, and increased driving exposure (i.e., more annual miles driven). Interestingly, however, several of these risk factors are known outcomes of ADHD (Barkley et al., 2002; Biederman et al., 2010; Kessler et al., 2008) and Depression (Fergusson & Woodward, 2002; Harrington et al., 1990; Rao, Hammen, & Daley, 1999). For example, longitudinal studies consistently implicate ADHD and Depression in decreased academic attainment, lower adult SES, unemployment, and increased interpersonal and marital difficulties (Barkley et al., 2002; Birmaher et al., 1996; Fergusson & Woodward, 2002; Mannuzza et al., 1993). Thus, we hypothesize that the influence of ADHD and Depression on single violation and collision risk may be at least partially indirect, such that these associated functional impairments of both ADHD and Depression may also increase the risk of adverse driving outcomes. Although we were unable to test this hypothesized mediation due to our cross-sectional, nonparametric data, the current findings suggest that future studies would benefit from examining the extent to which ADHD and Depression result in increased collisions and traffic violations directly (e.g., due to shared clinical symptoms), or indirectly through their influence on known correlates of adverse driving outcomes across time (Cox et al., 2012). In addition, the extent to which the similar magnitude risk associated with ADHD and Depression is due to shared mechanisms (e.g., inattention/concentration problems,

hyperactivity/psychomotor agitation, shared executive dysfunction profiles; Bulmash et al., 2006; Cox et al., 2012; Harvey et al., 2004; Snyder, 2013) or reflects equifinality secondary to disorder-specific processes (e.g., non-shared clinical symptoms) warrants further scrutiny.

ADHD and Depression were most strongly associated with risk for multiple violations and multiple collisions, although the specific risks varied across disorders. Specifically, ADHD but not Depression was a unique risk factor for multiple motor vehicle violations and collisions after accounting for the demographic factors described above. This increased risk was remarkable, such that drivers with ADHD were 2.3-3.2 times more likely to report multiple violations and multiple collisions relative to healthy control drivers (i.e., 130% to 220% increased risk). Furthermore, ADHD was associated with increased risk for multiple violations relative to drivers with Depression (OR = 1.8 to 1.9), whereas this increased risk failed to reach statistical significance for multiple collisions (OR = 1.5 to 1.6). These results are consistent with previous meta-analytic reviews indicating that ADHD is associated with increased risk for adverse driving outcomes (Chang et al., 2014), and extends this literature by indicating that this risk is most pronounced for multiple violations and collisions relative to single incidents.

Furthermore, the current study is the first to demonstrate increased risk for drivers with ADHD relative to drivers with another high incidence psychiatric disability also known to increase risk for motor vehicle collisions (Bulmash et al., 2006). These findings are consistent with a growing body of evidence implicating both ADHD and Depression in adverse driving outcomes (Bulmash et al., 2006; Cox et al., 2012), and extend this

literature by documenting the overlapping and disorder-specific risks across single and multiple adverse driving events.

Among drivers reporting at least one collision, ADHD and Depression were differentially associated with self-reported risk for collision injury and fault. With regards to collision fault, ADHD but not Depression predicted increased risk. Thus, we hypothesize that disorder-specific mechanisms may account for this finding. It is important to note, however, that this conclusion remains speculative; the current study was based on retrospective self-report, and the resultant nonparametric data limited our ability to examine specific driver behaviors or reasons for collisions. Previous simulator research, however, suggests that drivers with ADHD are more likely to collide with road obstacles compared to healthy control drivers (Biederman et al., 2007). Thus, one explanation may be that these drivers were disproportionately more likely to collide with inanimate objects rather than other vehicles, leaving little doubt regarding collision fault. In contrast, the only on-road study to prospectively record routine driving behavior for drivers with and without ADHD found that driver inattentive behaviors (e.g., eyes off road) tended to immediately precede collisions for drivers with ADHD (Cox et al., 2004; 2012). This suggests that inattentive symptoms – a symptom shared between ADHD and Depression – may be a key mechanism linking high incidence disability with collision fault. Alternatively, the findings may reflect the higher base rate of multiple collisions for drivers with ADHD (i.e., more opportunities to have been at-fault for at least one collision). Prospective research using continuous monitoring of routine driving is needed to definitively determine if and why drivers with ADHD are more likely to be at-fault for collisions. Finally, ADHD was not significantly associated with self-reported injury

following collisions. Rather, drivers with self-reported Depression reported being injured during a collision at significantly higher rates relative to healthy control drivers with at least one collision. Potential explanations for this pattern may be an attentional bias toward distress associated with depression (Gotlib et al., 2004), such that even minor injuries may take on increased salience in the driver's subjective experience. This increased emotional salience, in turn, is associated with increased rehearsal and consolidation of this aspect of the collision experience into long-term memory (Everaert et al., 2013). Similarly, depression has been associated with increased rates of somatic symptoms and medical utilization rates (Krause, Wiener, & Tait, 1994; McCauley, Carlson, & Calderon, 1991) that may further increase the perception and recall of injury for these drivers. Alternatively, it is possible that collision-related injuries predated the onset of depressive symptoms for many of these drivers given the current study's reliance on retrospective reporting and known association between chronic illness/pain and increased risk for depressive disorders (Fishbain et al., 1997; Krause, Wiener, & Tait, 1994).

Limitations

The present study is the first to examine adverse driving outcomes for drivers with multiple forms of high incidence psychiatric disability relative to drivers with no known psychopathology, while controlling for known correlates of collisions and risky driving. Despite these methodological refinements, the following caveats must be considered when interpreting the results. The current study relied exclusively on retrospective self-report data, and diagnostic status was based on self-report and responses to a well-validated measure. Thus, the extent to which the findings generalize

to adults with clearly defined ADHD and Depression is unknown. Nonetheless, the current study is the first to control for self-selection bias and the overall findings were highly consistent with previous studies using clinically-diagnosed samples. The shortcomings of retrospective self-report data are well documented (Gearing et al., 2006), and prospective studies are clearly needed to confirm the mechanisms by which ADHD, depression, and other high incidence disabilities lead to the adverse driving outcomes documented in the current study. Finally, the non-parametric, retrospective nature of the data precluded testing hypothesized mediating pathways. Nonetheless, the current findings reinforce previous studies documenting adverse driving outcomes for clinically diagnosed drivers with ADHD and drivers with depression, and provide important new data suggesting overlapping and unique driving outcomes across these two high incidence clinical disorders.

Clinical and Research Implications

Overall, the present results provide evidence that multiple high-incidence psychiatric disabilities – rather than a particular disorder – place drivers at a greater risk for a single violation and collision. However, ADHD and depression also pose unique driving hazards: ADHD appears to be uniquely associated with multiple violations, multiple collisions, and collision fault, whereas depression is uniquely associated with self-reported injury following a collision. Prospective, longitudinal studies with clinically defined samples are needed to definitively elucidate the mechanisms and processes linking these high incidence disabilities with adverse driving outcomes. Identification of the specific mechanisms – including both shared symptoms and disorder-specific processes – is critical to designing effective prevention, driver training, and technology-

enhanced accommodations to reduce the social, financial, health, mortality, and legal outcomes of motor vehicle collisions for drivers with high incidence disabilities such as ADHD and depression. Clinically, consideration of motor vehicle driving risk appears warranted when making treatment determinations and evaluating treatment response. Psychostimulants and manual transmission appear to reduce but not eliminate this risk for drivers with ADHD (Cox, Madaan, & Cox, 2011) and consideration of the timing of a patient's routine driving (e.g., afternoon/evening vs. late night) appears to be an important consideration when selecting among psychostimulants formulations (Cox et al., 2004).

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Table 1. Demographic and other risk factors: Relative risk for self-reported driving violations, collisions, injuries from collisions, and at-fault for collisions (last 3 years)

		Relative Risk Ratio			
	N	Violations (Last 3 Years)	Crashes (Last 3 Years)	Injuries from Collision	At-fault for Collision
Total	1,924				
Age					
Ages 16-17	136	2.94*	2.22	-1.67	3.59
Ages 18-20	307	2.34*	1.70*	-1.11	2.60*
Ages 21-25	351	2.35*	1.88*	1.40	3.64*
Ages 26-35	207	1.99*	1.45	1.79	2.20
Ages 36-50	230	1.28	-1.27	1.00	1.59
Ages 51-65	245	-1.15	-1.12	2.20	1.86
Ages 66-75	189	-1.23	-1.22	--	3.23*
Ages 75+	259	--	--	--	--
Gender					
Male	946	1.10	-1.11	-1.41	1.13
Female	978	--	--	--	--
Education					
Some high school	136	-1.66*	-1.40	1.44	-1.69
H.S. diploma/Some college	725	-1.07	-1.06	1.24	-1.46
College degree or higher	1,063	--	--	--	--
Annual Income					
Under $29K	389	2.07*	-1.23	-1.43	-1.49
$30K to $39K	283	1.65	-1.10	-1.56	-1.64
$50K to $69K	366	1.47	-1.12	-1.51	-1.68
$70K to $99K	393	1.47	-1.21	-1.40	-1.45
$100K to $149K	325	1.57	-1.18	-1.06	-1.53
$150K or higher	168	--	--	--	--
Marital Status					
Not Married	1180	1.22	1.03	2.14	-1.20
Married	744	--	--	--	--
Average Miles Driven/Yr					
< 5,000 miles/year	221	-1.41	-1.45*	1.23	-1.77
5K to 10K	511	-1.23	-1.35	1.19	-1.73
10K to 15K	596	1.18	-1.29	-1.37	-1.69
15K to 20K	282	1.35	-1.19	-1.32	-1.65
20K to 25K	126	1.55	-1.24	-1.25	-1.80
25K to 30K	72	1.09	-1.29	1.14	-1.78
> 30K miles/year	116	--	--	--	--

*95% confidence interval does *not* include 1.0 ($p < .05$); The last subgroup for each demographic variance serves as the reference group (indicated by the --). Total N reflects the 81.7% of ADHD, Depression, and Healthy Control (N=2,354) drivers with complete demographic and outcome data.

Table 2. ADHD and Depression: Relative risk for self-reported driving violations, collisions, injuries from collisions, and at-fault for collisions (last 3 years)

	Relative Risk Ratio			
	Relative to Healthy Control Drivers		Relative to Drivers with Self-Reported Depression	
	Raw	Corrected	Raw	Corrected
Violations (Last 3 Years)				
1 violation				
ADHD	1.56* (1.13, 2.16)	1.33 (0.91, 1.93)	1.09 (0.71, 1.68)	1.01 (0.60, 1.70)
Depression	1.43* (1.02, 1.98)	1.40 (0.97, 2.02)	--	--
2 or more violations				
ADHD	3.22* (2.25, 4.61)	2.27* (1.48, 3.49)	1.83* (1.10, 3.02)	1.85† (0.98, 3.55)
Depression	1.76* (1.15, 2.72)	1.20 (0.70, 2.06)	--	--
Collisions (Last 3 Years)				
1 collision				
ADHD	1.41* (1.03, 1.93)	1.25 (0.87, 1.78)	1.09 (0.72, 1.66)	1.04 (0.62, 1.75)
Depression	1.29 (0.93, 1.79)	1.24 (0.86, 1.79)	--	--
2 or more collisions				
ADHD	2.63* (1.69, 4.09)	2.21* (1.31, 3.74)	1.53 (0.83, 2.81)	1.59 (0.74, 3.45)
Depression	1.72* (1.02, 2.89)	1.55 (0.85, 2.82)	--	--
Injury from Collision				
ADHD	1.55 (0.81, 2.96)	1.67 (0.81, 3.48)	0.65 (0.29, 1.44)	0.63 (0.20, 2.01)
Depression	2.39* (1.27, 4.49)	2.25* (1.05, 4.82)	--	--
At-Fault for Collision				
ADHD	2.12* (1.34, 3.34)	1.65 (0.98, 2.78)	1.45 (0.78, 2.68)	1.24 (0.52, 2.97)
Depression	1.46 (0.89, 2.40)	1.47 (0.84, 2.60)	--	--

* 95% confidence interval does *not* include 1.0 ($p < .05$); † $p = .06$

Injury and at-fault from collision reflect relative risk among drivers reporting at least 1 collision; Corrected relative risk ratios are corrected values after accounting for known risk factors for adverse driving outcomes (age, gender, education, income, marital status, average annual miles driven)

Figure 1. Relative risk for traffic violations (last 3 years) for drivers with ADHD and Depression. Error bars reflect 95% confidence intervals. OR = odds ratio; an OR of 1.0 indicates no increased risk relative to Healthy Control drivers.

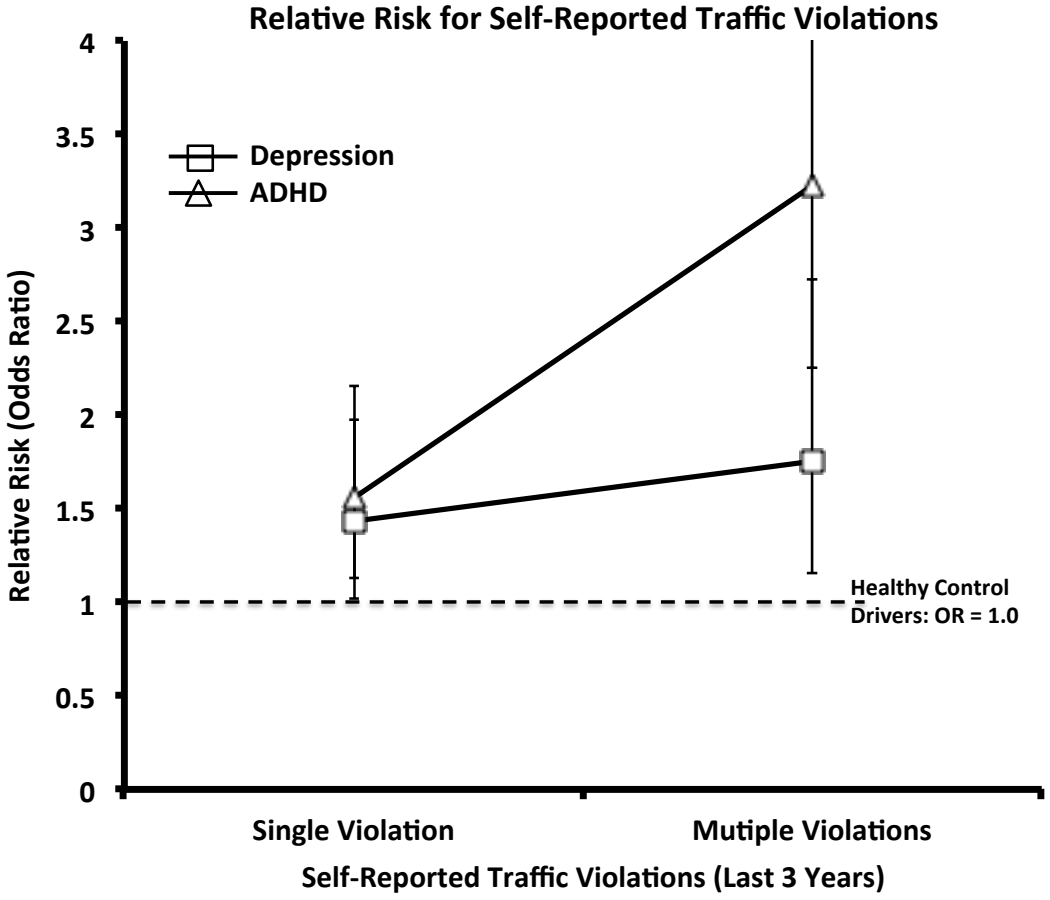


Figure 2. Relative risk for motor vehicle collisions (last 3 years) for drivers with ADHD and Depression. Error bars reflect 95% confidence intervals. OR = odds ratio; an OR of 1.0 indicates no increased risk relative to Healthy Control drivers.

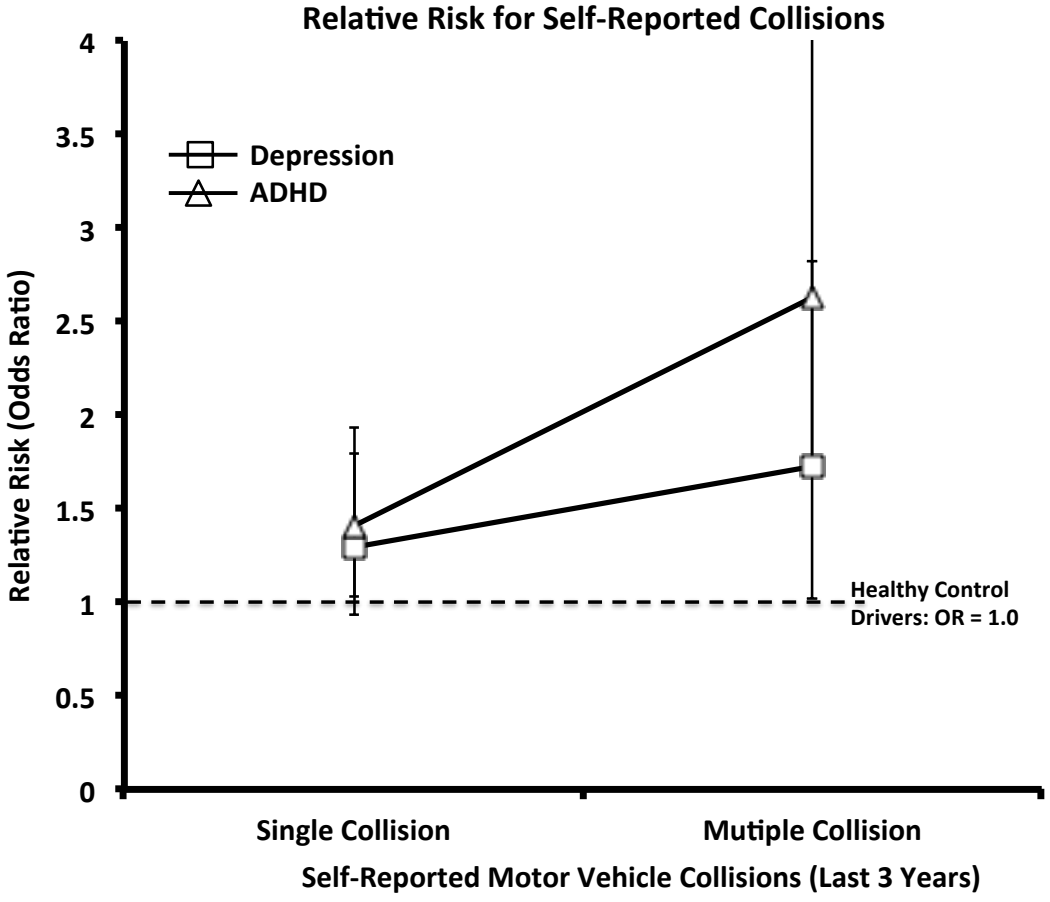
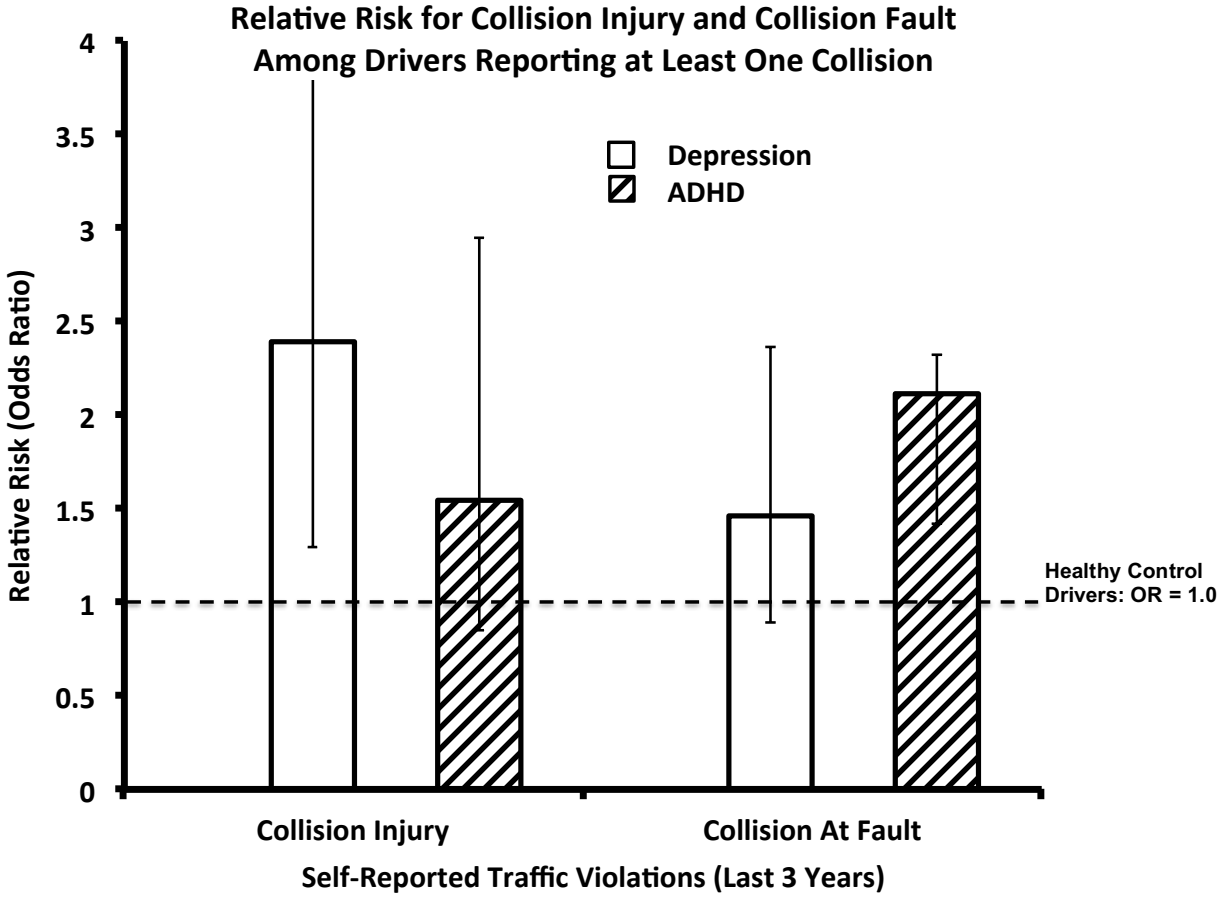


Figure 3. Relative risk for collision-related injury and collision fault among drivers reporting at least one collision (last 3 years). Error bars reflect 95% CIs. OR = odds ratio; an OR of 1.0 indicates no increased risk relative to Healthy Control drivers.



Manuscript 2

Prospective Crash Risk as a Function of ADHD Symptoms and Clinical Status

Paula A. Aduen, M.A.
University of Virginia

Michael J. Kofler, Ph.D.
Florida State University

Dustin E. Sarver, Ph.D.
University of Mississippi Medical Center

Erica Wells, M.Ed.
Florida State University

Elia Soto, B.A.
Florida State University

Daniel J. Cox, Ph.D.
University of Virginia Health Systems

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Abstract

Objective: Motor vehicle driving is a ubiquitous activity of daily living that cuts across gender, age, and socioeconomic status. ADHD is linked with adverse driving outcomes, but the paucity of prospective studies limits effect certainty. The current study provides the first large-scale evaluation of prospective crash risk as a function of ADHD (dimensionally and categorically). **Method:** Prospective monitoring of 3,226 drivers from six U.S. sites participating in the Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study. Drivers were assessed for ADHD symptoms and psychiatric status at study entry. Their vehicles were then outfitted with sophisticated data acquisition systems to continuously monitor routine driving from 'engine-on to engine-off' for 1-2 years (*M*=440 days/driver, *M*=9,528 miles/driver). Crashes/near-crashes were identified via software-based algorithms and double-coded validation (blinded to clinical status). Miles driven, days monitored, age, gender, education, and marital status were controlled. **Results:** Greater ADHD symptoms at study entry portended 5%-8% increased crash risk *per symptom* over the next 1-2 years (IRR=1.05-1.08). This risk corresponds to approximately 1 annual crash and 2 annual near-crashes *per driver* for drivers at the sample's maximum ADHD symptom severity. Analyses based on self-reported clinical status indicated similarly elevated rates for ADHD and Depression that were parsimoniously explained by both groups' elevated inattention/concentration symptoms. Risk was not attenuated by ADHD treatment-as-usual, but varied according to antidepressant treatment status. **Conclusions:** Previous studies have significantly underestimated the risk for vehicular crashes conveyed by ADHD. Results call for routine clinical monitoring and intervention, irrespective of reported crash history.

Prospective Driving Outcomes as a Function of ADHD Symptoms and Clinical Status

Motor vehicle driving is a ubiquitous activity of daily living that cuts across gender, age, and socioeconomic status (SES) (Di Milia et al., 2011), and is negatively impacted by psychiatric disorders such as ADHD (Fuermaier et al., 2015). Retrospective self-report, database/register reviews, and driving simulator data indicate that drivers with ADHD (Barkley & Cox, 2007; Cox, Madaan, & Cox, 2011; Fuermaier et al., 2015; Vaa, 2014) have higher rates of crashes, citations, insurance claims, loss of licenses, serious crash-related injuries, and traffic fatalities than healthy control drivers (Aduen et al., 2015; Chang et al., 2014; Jerome, Habinski, & Segal, 2006; Redelmeier, Chan, & Lu, 2010; Swensen et al., 2004). Their relative crash risk of 1.23 in the most recent meta-analysis (Vaa, 2014) has major public health implications when juxtaposed with the high prevalence of adult ADHD (4%) (Polanczyk et al., 2007).

However, the generalizability of these findings is limited by a paucity of prospective, on-road studies (Cox et al., 2004; Di Milia et al., 2013). Self-report is limited by informant memory and willingness (Knouse et al., 2005) and police/government records are limited to crashes on public roads and decisions to report the crash (drivers), send an officer (police dispatch), and file an official report (officer) (McCartt & Solomon, 2004). Further, national registers and hospital database reviews have been limited to crashes that involve death or severe road trauma (Chang et al., 2014).

Simulator studies address some of these limitations, but provide time-limited evaluation of driving skills under ideal conditions that may not correspond to on-road driving habits and in-car distractions (Barkley et al., 2005; Biederman et al., 2007; Cox et al., 2012). In addition, fewer than 50% of studies report miles/kilometers driven, despite

the known association between exposure and crash risk (Vaa, 2014). Finally, the correspondence between retrospective self-report and prospective crash risk is unknown, and only one study has directly compared ADHD with another form of high-prevalence psychiatric disability (Aduen et al., 2015). Thus, the extent to which previous findings are attributable to ADHD symptoms specifically, as opposed to participant perception, self-selection, exposure, or transdiagnostic risk remains unknown.

The current study addresses each of these limitations, and is the first large-scale, continuously-monitored assessment of adverse outcomes during routine driving as a function of ADHD symptoms and clinical status. Relative risk for crashes, near-crashes, and at-fault crashes/near-crashes was determined by outfitting vehicles with sophisticated data acquisition systems. A sample of 3,226 drivers across six U.S. sites were surveyed for prior crash involvement, then continuously monitored for over 5.5 million trips that spanned 1-2 years. Importantly, drivers were not selected based on ADHD symptoms or clinical diagnoses, but rather completed screening questionnaires at study enrollment. Analyses focus on prospective crash risk portended by ADHD symptoms, with secondary analyses examining risk as a function of clinical group designations identified for this sample at study entry (Aduen et al., 2015) and medication treatment. Correspondence between retrospective and prospective crash risk was also examined.

Method

Design and Overview

The Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study included 3,600 drivers from six U.S. sites (Bloomington, IN; Central PA; Tampa, FL; Buffalo, NY; Durham, NC; Seattle, WA). Technical reporting of study design and

recruitment, probability-based sampling, and methodological plans are found in Antin (2011). Sample characteristics and comparisons with the U.S. population of licensed drivers are provided in Antin (2015). Comparisons indicate close approximation to U.S. drivers for the sample. Detailed data reduction methods, software-based trigger algorithms and validation, vehicle sensor calibration, data reductionist training, and reliability are provided in Hankey, Perez, & McClafferty (2016). Sample demographics are shown in Table 1, and were controlled in all analyses.

Continuous Monitoring and Event Triggers

Each driver's car was outfitted with five high-speed video cameras, speed/brake monitors, accelerometers, and GPS to continuously capture routine driving from engine-on to engine-off for 1-2 consecutive years (Antin et al., 2011). Participants were protected by a national Certificate of Confidentiality and not required to report crashes or surrender crash-relevant evidence to authorities (Hankey, Perez, & McClafferty, 2016).

SHRP-2 collected approximately 2,000,000 gigabytes of data spanning 5,512,900 individual trips that occurred between 2010 and 2013. Software-based trigger algorithms and 100% double-coded manual validation identified 4,254 safety-critical events (SCE; 1,549 crashes, 2,705 near-crashes). These algorithms used kinematic and behavioral signatures previously identified as present with high probability during crashes (e.g., longitudinal deceleration < -0.65g, lateral acceleration >0.75g) (Hankey, Perez, & McClafferty, 2016). All SCEs were verified by comparing event videos with pre-recorded index images to ensure the consented participant was driving. Manual video review then verified if an SCE occurred. Verified events were coded by extensively trained data reductionists (100% SCEs coded by $\geq$2 coders; reliability=91%) (Antin et al.,

2011; Hankey, Perez, & McClafferty, 2016). Coders completed ~10 days of training, demonstrated 90% proficiency prior to coding, were retested frequently using the same 90% criterion, and completed ≤4 hour shifts (mandatory breaks/hour) to minimize fatigue-related errors. Coders were blind to driver clinical status (Hankey, Perez, & McClafferty, 2016).

Prospective Driving Outcomes

Primary outcomes included number of *crashes* (SCEs involving any contact between participant vehicle and fixed or moving object, at any speed where kinetic energy is measurably transferred or dissipated), *near-crashes* (SCEs requiring rapid, evasive maneuver by participant vehicle to avoid imminent crash), and *crash and near-crash fault* (observable evidence that the participant driver committed error leading to crash/near-crash) recorded during prospective monitoring.

Barkley Adult ADHD Quick Screen (BAQS)

The BAQS is a 6-item self-report questionnaire that assesses ADHD symptoms in adults on a 4-point Likert scale (0=never/rarely, 1=sometimes, 2=often, 3=very often; range=0-18). Psychometric support includes high internal consistency (α=.90), concurrent validity for self-reported (r=.97) and other-reported (r=.68) ADHD symptoms compared to full, 18-item DSM-based checklists, predictive validity for self-reported (r=.87) and other-reported impairment (r=.67), and high sensitivity (.93) and specificity (.97) for differentiating adults with ADHD from neurotypical adults (Barkley, Murphy, & Fischer, 2010).

Clinical Groups

Aduen (2015) identified 275 drivers with ADHD and 1,828 Healthy Control

Drivers based on self-reported clinical status at study entry. They also identified 251 drivers with Depression, who are included here to compare ADHD to another high-prevalence disorder (Kessler & Bromet, 2013) associated with attention/concentration problems (Austin, Mitchell, & Goodwin, 2001) and adverse driving outcomes (Wickens, Smart, & Mann, 2014). Clinical group comparisons were conducted using these psychiatric diagnoses (Aduen et al., 2015) and are considered exploratory because the naturalistic study design precluded clinical interviewing or tracking illness course/treatment efficacy during the prospective monitoring of driving outcomes.

Psychiatric Treatment

ADHD and antidepressant medications were queried at study entry and exit and used as a proxy for active treatment. Consistent with epidemiological estimates (Harman, Edlund, & Fortney, 2015; Polanczyk et al., 2007), 20.8% of ADHD and 61.0% of Depression group members reported disorder-specific medication treatment at one or both time points. Exploratory analyses were conducted by subdividing the ADHD and Depression groups into mutually exclusive categories: *Stable Unmedicated* (no reported medication that treats their identified disorder at either time point), *Started* (reported at exit but not entry), *Stopped* (reported at entry not exit), and *Stable Medicated* (reported at both time points).

Cell sizes were sufficient for exploratory analyses of antidepressant time course for the Depression group (Stable-Unmedicated=99; Started=98; Stopped=24; Stable-Medicated=30). ADHD medication was dichotomized based on medication at either time point (No=218; Yes=57) due to insufficient cell counts (Stable-Unmedicated=218; Started=43; Stopped=12; Stable-Medicated=2). The naturalistic study design precluded

monitoring of perceived medication efficacy, emergent effects, or timing in relation to crashes. Nevertheless, these analyses reflect the most extensive examination to date of treatment-as-usual's protective effects on prospective, objectively-documented motor vehicle crashes.

Data Analysis Overview

Negative binomial regressions predicted the maximum likelihood (MLE) conditional probability (incident rate ratios; IRR) of crash, near-crash, at-fault crash, and at-fault near-crash counts as a function of dimensional ADHD symptoms, controlling for total miles driven, days of continuous monitoring (exposure), age, gender, education, and marital status. Wald 95% CIs for each IRR were calculated (Valentine, Aloe, & Lau, 2015). IRRs ±1.0 indicate increased/decreased risk. To improve interpretability, IRRs are supplemented with estimates of risk per driver per year by computing estimated marginal means with time set to 365.25 days and miles driven set to the national average of 15,000 miles driven per year (National Highway Traffic Safety Administration, 2015). Exploratory analyses repeated these analyses, first substituting the categorical clinical groups (Aduen et al., 2015) (ADHD, Depression, Healthy Control) for BAQS scores, and finally subdividing the ADHD and Depression groups by medication status.

All models were superior to the null model (all omnibus likelihood ratio $\chi^2[14] \geq 218.01$, all $p<.0005$) and demonstrated adequate goodness-of-fit (all $\chi^2/df = 1.07\text{-}1.24$). The dispersion coefficient (negative binomial) was significantly greater than 0.0 for all models (all 95% Wald CIs exclude 0.0), supporting use of the negative binomial over Poisson distribution models.

Results

Preliminary Analyses

Missing data ranged from 0.1-0.9% for gender, age, education, and marital status and did not vary by clinical group (p=.60), supporting Missing at Random (MAR) assumptions. Education served as a proxy for socioeconomic status; income was not controlled due to high missing data (16.2%). Sample retention was excellent: 3,226 of 3,600 enrolled cases (89.6%) were followed prospectively and included in analyses. Of the 2,354 drivers assigned to a clinical or control group (Aduen et al., 2015), 2,329 (98.9%) were retained including 274 of 275 drivers with ADHD (99.6%), 249 of 251 drivers with Depression (99.2%), and 1,806 of 1,828 Healthy Control drivers (98.8%). These groups did not differ in miles driven *(M* miles=9527.9; p=.53), days of study participation (*M* days=440.49; p=.46), or performance on a driving knowledge questionnaire ($M_{correct}$=79.74%; p=.14). The ADHD group's vehicles were on average one model year older (*M*=2005.13, *SD*=4.73) than the Depression (*M*=2006.41, *SD*=4.24) and Healthy Control groups' vehicles (*M*=2006.36, *SD*=4.01) (both $p \leq .001$).

ADHD Symptoms

Greater ADHD symptoms at study entry portended 5%-8% increased risk *per symptom endorsement* for crashes (IRR=1.05, 95% Wald CI=1.02-1.09, p<.0005), at-fault crashes[c] (IRR=1.08, 95% Wald CI=1.04-1.11, p<.0005), near-crashes (IRR=1.06, 95% Wald CI=1.03-1.09, p<.0005), and at-fault near-crashes (IRR=1.07, 95% Wald CI=1.03-1.10, p<.0005). Annual number of expected crashes/near-crashes as a function of BAQS ADHD symptom score is depicted in Figure 1. Notably, risk increases *per*

[c] Gender, age, education, and marital status were excluded from the BAQS model predicting at-fault crashes and the clinical group models predicting at-fault crashes and at-fault near crashes to resolve singularities in the Hessian matrix associated with low cell counts. Total miles driven and total days of continuous monitoring remained controlled.

ADHD symptom endorsement; for example, a BAQS score of 17 predicts approximately 1 annual crash *per driver* (0.99 crashes/driver),[d] while a BAQS score of 0 predicts 1 crash per 2.4 drivers (0.41 crashes/driver). Inspection of Figure 2 indicates that these findings were highly consistent across age groups.

Clinical Groups

ADHD designation at study entry portended 46%-76% increased risk for crashes (IRR=1.46, 95% Wald CI=1.17-1.83, p=.001) and at-fault crashes (IRR=1.76, 95% Wald CI=1.38-2.25, p<.0005). ADHD also predicted 28%-66% increased risk for near-crashes (IRR=1.28, 95% Wald CI=1.04-1.58, p=.02) and at-fault near-crashes (IRR=1.66, 95% Wald CI=1.28-2.14, p<.0005). Figure 3 indicates that our data predict, on average, 0.65 annual crashes and 1.08 annual near-crashes per driver with ADHD. Figure 3 shows how these estimates vary as a function of miles driven per year; Figure 4 indicates that these findings were highly consistent across age groups.

Depression at study entry portended 34%-40% increased risk for crashes (IRR=1.34, 95% Wald CI=1.05-1.71, p=.02) and at-fault crashes (IRR=1.40, 95% Wald CI=1.07-1.84, p=.01). Depression predicted 52%-80% increased risk for near-crashes (IRR=1.52, 95% Wald CI=1.22-1.88, p<.0005) and at-fault near-crashes (IRR=1.80, 95% Wald CI=1.39-2.34, p<.0005). Figure 2 indicates that, on average, our data predict 0.60 annual crashes and 1.28 annual near-crashes per driver with Depression.

Treatment Status

[d] The range of BAQS scores in the sample was 0-17 (0-18 possible). A BAQS score of 0 reflects responses of never/rarely for all 6 items, whereas BAQS=17 occurs when 5 of 6 symptoms occur very often, and 1 symptom occurs often. A BAQS score of 8 would exceed the questionnaire's clinical screening cutoff of 7, and could be obtained via several item endorsement combinations (e.g., endorsements of Often on 4 items and Never on the remaining two items, endorsements of Often on 2 items and Sometimes on the remaining 4 items). This score of 8 predicts 0.62 crashes (1 crash per 1.61 drivers) and 1.17 near-crashes per year.

ADHD. Exploratory analyses of treatment correlates indicated that ADHD treatment-as-usual did not attenuate driving risk, as evidenced by increased crash risk for both untreated (IRR=1.36, 95% Wald CI=1.06-1.75, p=.02) and treated (IRR=1.86, 95% Wald CI=1.22-2.82, p=.004) drivers with ADHD. Both groups also demonstrated increased at-fault crash risk (unmedicated: IRR=1.57, 95% Wald CI=1.19-2.08, p=.001; medicated: IRR=2.43, 95% Wald CI=1.54-3.84, p<.0005) and at-fault near-crash risk (unmedicated: IRR=1.58, 95% Wald CI=1.18-2.10, p=.002; medicated: IRR=1.95, 95% Wald CI=1.19-3.20, p=.009).

Depression. Treatment-as-usual predicted reduced crash risk for medicated drivers with Depression, such that crash risk was detected only for the subgroup that discontinued antidepressants during the study (IRR=2.35, 95% Wald CI=1.29-4.27, p=.005; all other subgroups $p\geq$.24). At-fault crash risk was also specific to the subgroup that stopped antidepressants during the study (IRR=2.90, 95% Wald CI=1.47-5.73, p=.002; all other subgroups $p\geq$.17). Near-crash risk was detected in the stable unmedicated (IRR=1.59, 95% Wald CI=1.16-2.20, p=.004) and stable medicated groups (IRR=1.93, 95% Wald CI=1.13-3.31, p=.02), but not the subgroups that started (IRR=1.38, 95% Wald CI=0.99-1.92, p=.06) or stopped antidepressants (IRR=1.26, 95% Wald CI=0.65-2.44, p=.50).

Assessing Crash Risk: Retrospective Self-Report vs. Prospective Monitoring

A final comparison was made by comparing the retrospective self-report data for this sample from Aduen (2015) with the current study's prospectively documented crashes. Partial correlations adjusted for miles driven, days of continuous monitoring, and driver demographics (age, gender, education, marital status) indicated that self-reported

crash counts at study entry predicted crash counts during prospective monitoring (r=.10, p<.0005, n=1,743) for healthy control drivers, but were poor predictors of prospectively-identified crashes for drivers in the ADHD (r=-.002, p=.98, n=260) and Depression groups (r=-.01, p=.85, n=236).

Discussion

The current study was the first large scale, prospective, continuously-monitored assessment of real-world crash risk as a function of ADHD, controlling for a host of established risk factors (Mannuzza et al., 1993). Prospective monitoring indicated a robust association between ADHD symptoms and adverse driving outcomes. The 5%-8% increased risk per symptom endorsement indicates that, on average, drivers who screen positive for ADHD are expected to cause at least one biennial crash and one annual near-crash (based on at-fault crash and near-crash risk). This risk increases substantially as ADHD symptom severity increases, and predicts approximately one crash per year for drivers reporting the most severe ADHD symptoms.

Similarly, ADHD clinical status at study entry portended large magnitude risk for experiencing a crash (IRR=1.46) (Aduen et al., 2015). Further, these drivers are highly likely to commit the driving error(s) that directly lead to these crashes (at-fault crashes IRR=1.76). Examination of the confidence intervals indicates that these estimates were higher than expected based on the most recent meta-analysis (RR=1.23) (Vaa, 2014). Thus, our dimensional and categorical findings confirm that ADHD portends adverse driving outcomes (Cox, Madaan, & Cox, 2011; Fuermaier et al., 2015; Vaa, 2014) and extends previous findings by documenting that this risk is higher than previously estimated at both the symptom and clinical group levels.

Importantly, however, this risk did not appear unique to ADHD, but occurred at elevated rates for drivers with another high-prevalence psychiatric disability associated with attention/concentration problems (Austin, Mitchell, & Goodwin, 2011; Wickens, Smart, & Mann, 2014) (Depression, crash/at-fault crash IRR=1.34/1.40). Examination of risk across the continuum of ADHD symptoms – the study's primary predictor of interest – provides insight into this transdiagnostic risk. That is, the ratio of at-fault crash risk associated with ADHD vs. Depression (76% vs. 40% increased risk) is highly similar to the ratio of their self-reported ADHD symptoms (BAQS=7.4 vs. 3.4). We propose both inattentive and impulsive/hyperactive behavior as potential transdiagnostic mechanisms, given their status as core symptoms of both ADHD (reified 'attention problems' and 'hyperactivity/impulsivity') and Depression (reified 'concentration problems' and 'psychomotor agitation observable to others') (Austin, Mitchell, & Goodwin, 2001; Fuermaier et al., 2015). Combined with the finding that crash risk increases proportionately with increases in ADHD symptoms (Figure 1), these findings suggest that symptom frequency/severity may be more important than clinical status *per se* when assessing motor vehicle crash risk.

Comparing the at-fault data across the two clinical groups indicated that drivers with ADHD were more likely to cause a crash (IRR_{ADHD}=1.76 vs. $IRR_{Depression}$=1.40), whereas drivers with Depression were more likely to cause a near-crash ($IRR_{Depression}$=1.80 vs. IRR_{ADHD}=1.66). Beyond shared symptom profiles, this result also suggests disorder-specific differences in successfully recovering from presumed attentional lapses in time to avoid an imminent crash. Both groups experienced significantly more imminent crashes during prospective monitoring, but drivers in the

Depression group were somewhat more successful at avoiding these imminent crashes than drivers in the ADHD group.

The association between Depression and crash risk appears inconsistent with retrospective self-report from this sample , which documented this risk for ADHD but not Depression. The reason for this incongruence is not clear, but may be related to the overall poor correspondence between prior crashes and future crashes among drivers in the Depression and ADHD groups. Alternatively, exploratory analyses linked crash risk specifically to members of the Depression group who discontinued antidepressants during prospective monitoring. Medication results must be considered tentative, but protective effects of antidepressant treatment (Wingen, Ramaekers, & Schmitt, 2006) could explain this discrepancy given that these drivers were by definition taking medication when reporting prior crashes at study entry. We also considered Depression-specific explanations, but these appeared unlikely given evidence that these drivers appraise their driving performance more negatively than other drivers (Dorn & Matthews, 1995); Thames et al., 2011). Notably, the poor predictive validity of self-reported crashes for both clinical groups indicates that clinical monitoring may be warranted irrespective of patients' self-reported crash history.

Medication was not associated with reduced risk for drivers with ADHD, with relatively wide confidence intervals that limit comparative statements regarding crash risk between medicated (IRR=1.86) and unmedicated (IRR=1.36) ADHD subgroups. Although there is evidence that certain formulations may increase crash risk in certain environments (Cox et al., 2012; Randell, Charlton, & Starkey, 2016; Wingen, Ramaekers, & Schmitt, 2006), placebo-controlled studies are consistent in documenting reduced crash

risk when medication is metabolically active (Cox et al., 2004; Cox et al., 2012). Because ADHD medication has well-documented benefits for motor vehicle driving, the equivocal results for ADHD treatment-as-usual may reflect inconsistent adherence, interactions between unmedicated symptom severity and treatment status, and/or driving events that occur when medication is not metabolically active (Barkley & Cox, 2007; Cox, Madaan, & Cox, 2011). Alternatively, the trend toward increased risk in medicated drivers may reflect effects of unmeasured factors rather than causes, such that 75% of medicated drivers with ADHD (*n*=43 of 57) began treatment during the study monitoring period.

For Depression, the higher prevalence of medication treatment allowed us to separate medication status based on time course. We found that the increased risk for crashes was seen exclusively for drivers who discontinued antidepressant treatment during the study (IRR=2.35). To our knowledge, there have been no controlled studies documenting vehicular crash rates among patients who discontinue antidepressants. In the absence of such data, we suggest that the current findings call for routine clinical monitoring of driving behaviors – particularly when patients discontinue antidepressant medication.

Limitations

The current study was the first to prospectively track crash risk as a function of clinical status in a large sample of drivers using continuous, on-road monitoring. The following caveats must be considered. ADHD symptoms were based on a well-validated ADHD screening measure (93% sensitivity, 99% specificity) (Barkley, Murphy, & Fischer, 2010) whereas clinical group assignment was based on self-reported current diagnosis rather than gold-standard psychiatric interviewing (Aduen et al., 2015). We

were unable to track symptom course during prospective vehicle monitoring. Although these methods are comparable to other large-scale epidemiological studies (Polanczyk et al., 2007), generalizability is likely limited to clinically- rather than stringent research-defined ADHD and Depression. Thus, while the results exhort routine clinical monitoring, implications for putative etiological mechanisms are less clear. Participants were protected by a national Certificate of Confidentiality; thus, correspondence with police, hospital, and/or DMV recordkeeping is unknown.

Further, we were unable to track the course of Depression during prospective monitoring. Epidemiological evidence indicates that 20% of Depression cases are chronic across the two-year period covered in the current study (Spijker et al., 2002) and an additional 33%-50% experience recurrent episodes in a given year (Kessler & Bromet, 2013). Nevertheless, the proportion of these drivers who were depressed and/or medicated at the time of a crash/near-crash is unknown, and uncertainty regarding medication and symptom time course precludes causal attributions. Still, pharmacoepidemiological studies frequently use prescription use as a proxy for active treatment (Cox et al., 2004; Cox et al., 2012). For clinical practice, we interpret these findings to indicate that clinicians should monitor crash risk irrespective of self-reported crash history and potential symptom remission. Finally, we were unable to examine proximal risk factors for crashes, such as *in situ* driver behaviors, cell phones, substance use, or whether medication was active at the time of a crash (Cox, Madaan, & Cox, 2011). The naturalistic study design precluded clinical interviewing regarding perceived medication efficacy, emergent effects, or timing in relation to crashes, and thus informs protective effects of medication treatment-as-usual rather than optimal dosing.

Nevertheless, these analyses reflect the most extensive examination to date of treatment-as-usual's protective effects on prospective, objectively documented motor vehicle crashes.

Clinical and Research Implications

Results confirm that ADHD and Depression are significant risk factors for adverse driving outcomes, and indicate that this risk is greater than previously estimated – particularly for being involved in, and culpable for, crashes and near-crashes. Notably, this risk appears proportional to ADHD symptom severity, rather than an outcome of clinical status *per se*. Clinically, routine monitoring of driving risk is warranted. Psychostimulants and manual transmission may reduce but not eliminate risk for ADHD drivers (Cox, Madaan, & Cox, 2011), and assessing daily driving routines (e.g., afternoon/evening vs. late night) has important implications for selecting among psychostimulant formulations (Cox et al., 2012).

Future studies are needed to identify specific, in-car behaviors that portend this risk, and determine why drivers with elevated but less severe ADHD symptoms – such as those with Depression – have greater success with regard to evasive actions that avoid imminent crashes. Determining whether similar behaviors precede crashes between clinical groups and across ADHD severity levels will be helpful for developing transdiagnostic and disorder-specific interventions to reduce adverse driving outcomes. In particular, the omnipresence of cellphones, social media access, and Wi-Fi-connected vehicles may simultaneously provide both serious risk (e.g., distracted driving) and golden public health opportunity for intervention (e.g., real-time monitoring/intervention) (El Farouki et al., 2014; Jenkins et al., 2017; Reimer et al., 2010). Understanding how

transdiagnostic and disorder-specific traits (e.g., core symptoms, neuropsychological profiles) and states (e.g., reaction to cell phone ringing) contribute to crash risk has the potential to inform clinical decision-making, vehicle adaptations, and intervention development to improve public safety (Stavrinos et al., 2015).

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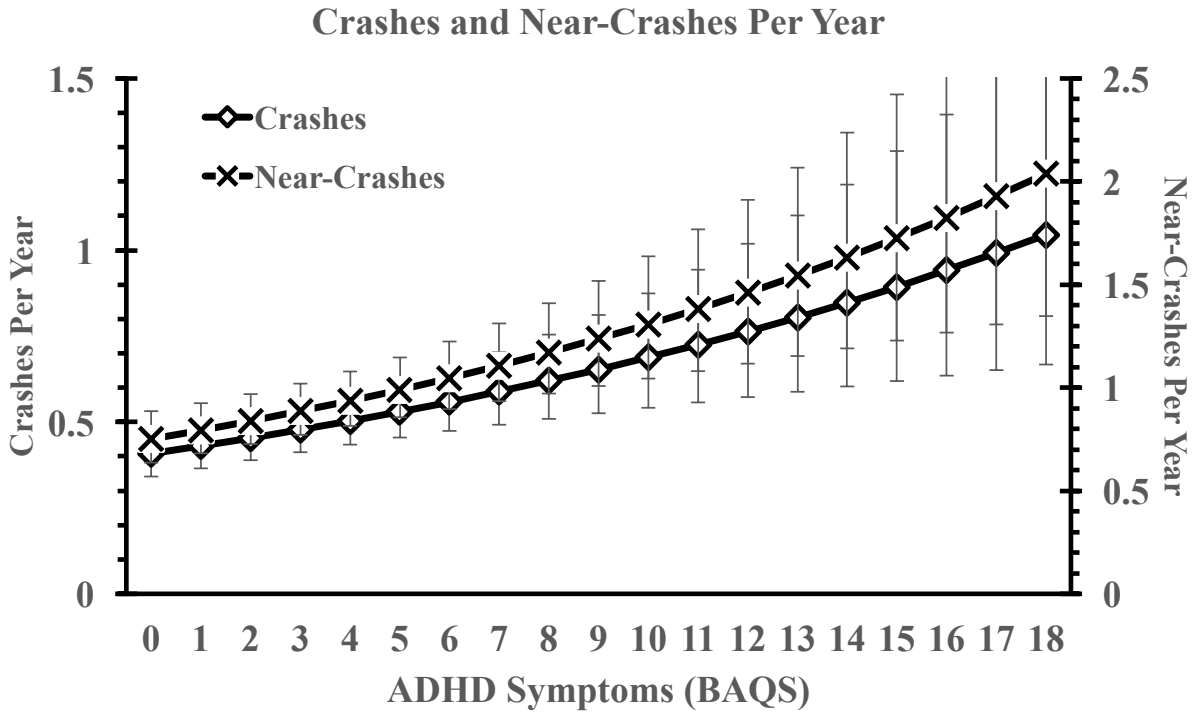
Table 1. Sample demographics.

	Overall Sample (N=3,226)		ADHD (N=274)		Depression (N=249)		Healthy Control (N=1,806)		Clinical Subgroup Chi-square
	M	SD	M	SD	M	SD	M	SD	
Miles Driven	9527.9	7315.8	9874.2	7346.9	9716.6	6846.1	9390.9	7510.0	p=.53, *ns*
Days Monitored	440.49	210.65	423.39	202.68	442.17	210.34	439.85	213.36	p=.46, *ns*
BAQS ADHD Score	3.20	2.18	7.43	2.57	3.39	1.63	1.86	1.01	p<.0005
Percent involved in									
No crashes	70.3%		58.8%		64.7%		72.8%		p<.001
Single crash	19.9%		23.4%		21.7%		19.1%		
Multiple crashes	9.8%		17.9%		13.7%		8.1%		
No near-crashes	61.7%		52.2%		52.2%		64.4%		p<.001
Single near-crash	21.7%		25.5%		24.5%		20.8%		
Multi. near-crashes	16.6%		22.3%		23.3%		14.8%		
Age Group	N	%	N	%	N	%	N	%	p<.005
16-17	258	8.0	40	14.7	13	5.2	126	7.0	
18-20	520	16.1	71	26.0	39	15.7	248	13.8	
21-25	597	18.5	77	28.2	53	21.3	280	15.5	
26-35	327	10.1	25	9.2	25	10.0	192	10.6	
36-50	349	10.8	25	9.2	38	15.3	198	11.0	
51-65	383	11.9	11	4.0	37	14.9	234	13.0	
66-75	345	10.7	12	4.4	28	11.2	213	11.8	
75+	442	13.7	12	4.4	16	6.4	312	17.3	
Not reported	5	0.2	1	0.004	0	0.0	3	0.002	
Gender									p<.005
Male	1537	47.6	131	48.3	75	30.4	900	50.3	
Female	1661	51.5	140	51.7	172	69.6	890	49.7	
Missing	28	0.9	3	0.01	2	0.001	16	0.001	
Education									p<.005
Some high school	271	8.4	39	14.3	14	5.7	126	7.0	
H.S. graduate	1241	38.5	118	43.2	100	40.5	660	36.8	
College degree +	1692	52.4	116	42.5	133	53.8	1006	56.1	
Not reported	22	0.7	1	0.003	2	0.001	14	0.008	
Marital Status									p<.005
Not Married	1989	61.7	211	77.9	162	65.3	1054	58.9	
Married	1207	37.4	60	22.1	86	34.7	734	41.1	
Not reported	30	0.9	3	0.01	1	0.004	18	0.001	
Annual Income									p=.04
Under $29K	556	17.2	60	21.9	52	20.9	282	15.6	
$30K to $39K	378	11.7	26	9.5	27	10.8	233	12.9	
$50K to $69K	537	16.6	36	13.1	39	15.7	297	16.4	
$70K to $99K	551	17.1	36	13.1	44	17.7	316	17.5	
$100K to $149K	462	14.3	37	13.5	36	14.5	258	14.3	
$150K or higher	219	6.8	28	10.2	14	5.6	133	7.4	
Not reported	523	16.2	51	18.6	37	14.9	287	15.9	

Note: *BAQS = Barkley Adult ADHD Quick Screen*.

Figure 1. Crash and near-crash risk as a function of ADHD symptoms. Values reflect estimated marginal means for incidents per year, controlled for age, gender, education, and marital status. Per year was defined for days of continuous monitoring=365.25 and total miles driven=15,000. Error bars reflect 95% Wald confidence intervals (CIs).



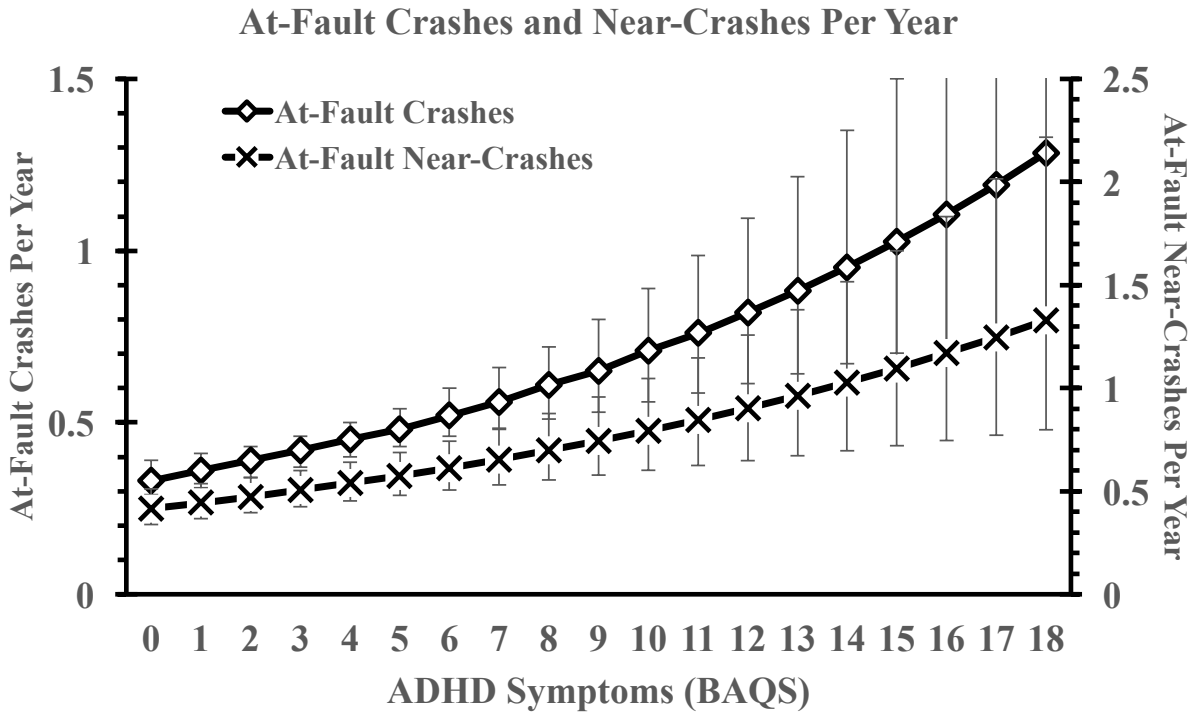
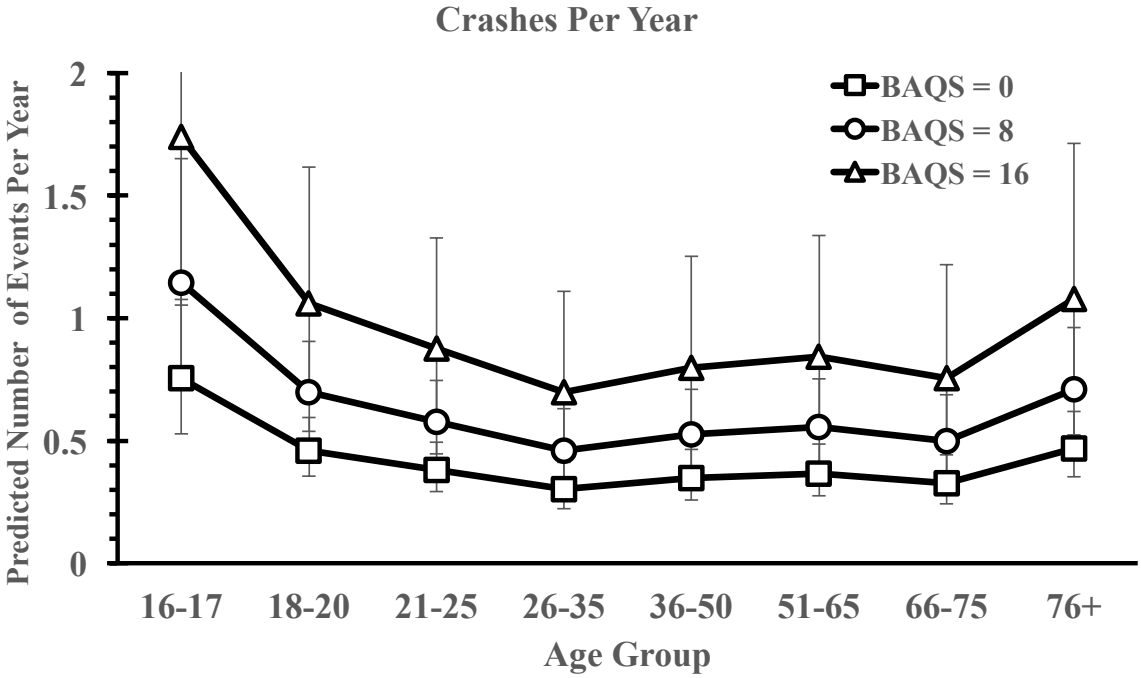


Figure 2. Crash and near-crash risk as a function of ADHD symptoms (BAQS) and age group. BAQS scores were selected to be representative and equidistant. BAQS=0 indicates no ADHD symptoms, BAQS=8 exceeds the clinical cut-off for ADHD of >7, and BAQS=16 indicates high severity ADHD symptoms. Values reflect estimated marginal means for incidents per year, controlled for gender, education, and marital status. Per year was defined for days of continuous monitoring=365.25 and total miles driven=15,000. Error bars reflect 95% Wald CIs.



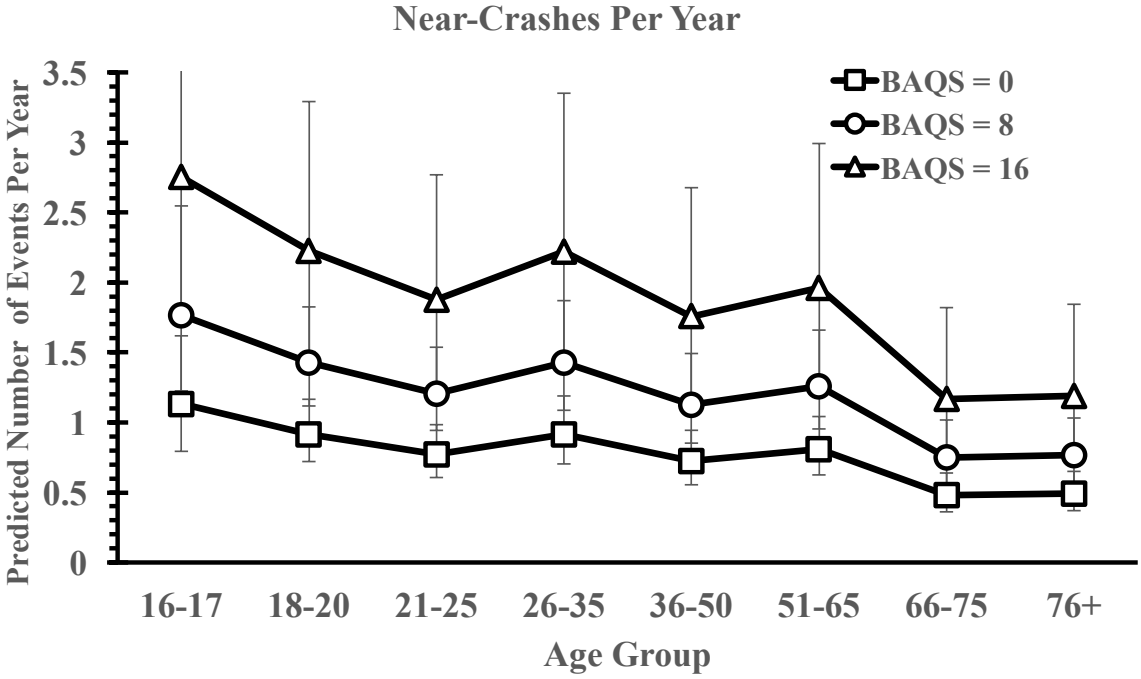
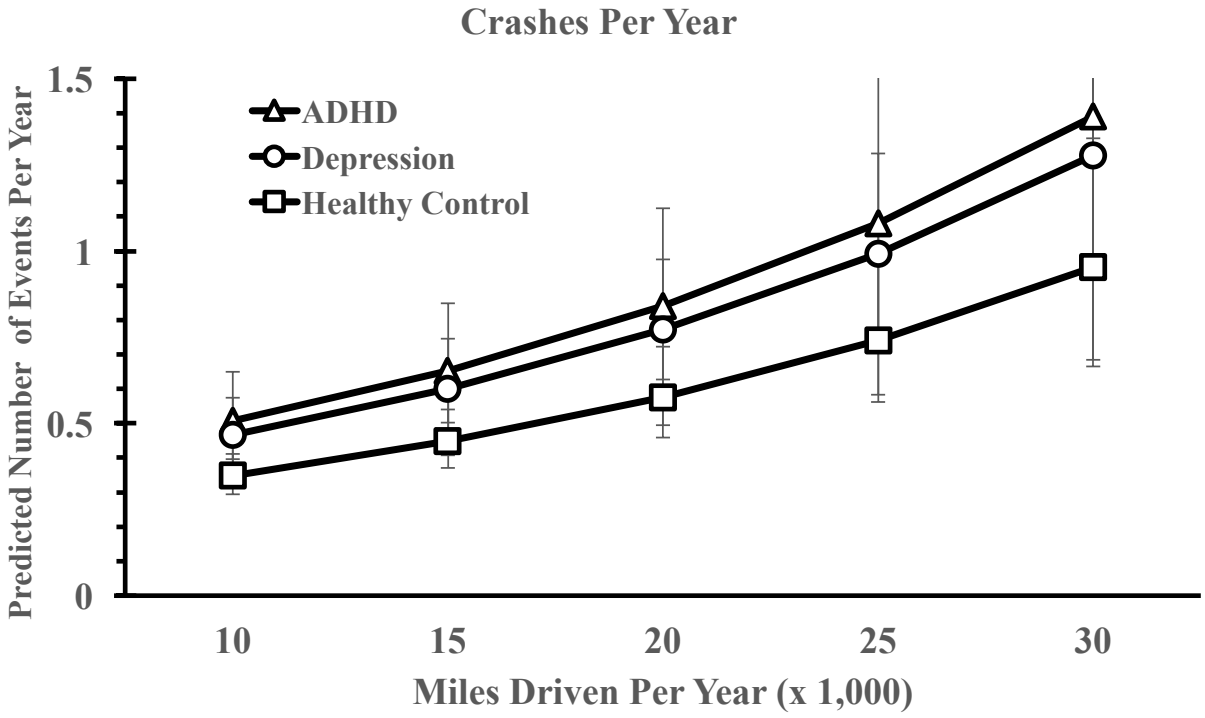


Figure 3. Crash and near-crash risk as a function of clinical group and exposure (miles driven per year), controlled for age, gender, education, and marital status. Values reflect estimated marginal means for incidents per year, defined for days of continuous monitoring=365.25. Error bars reflect 95% Wald confidence intervals.



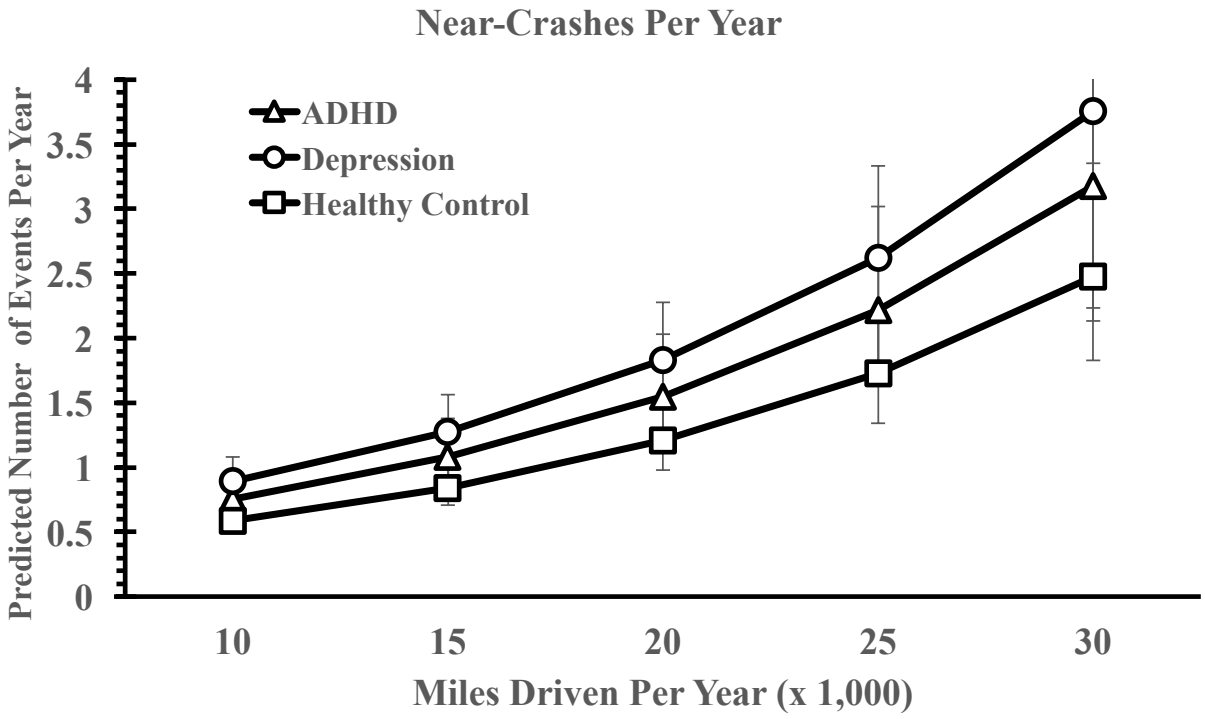
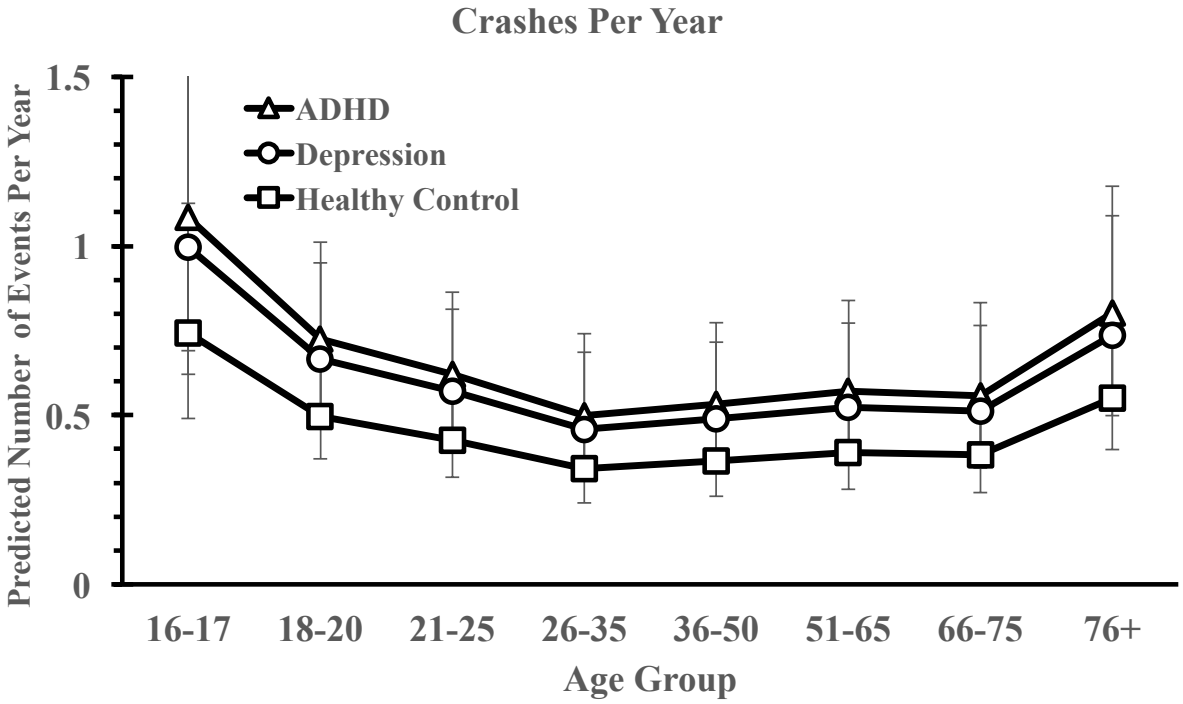
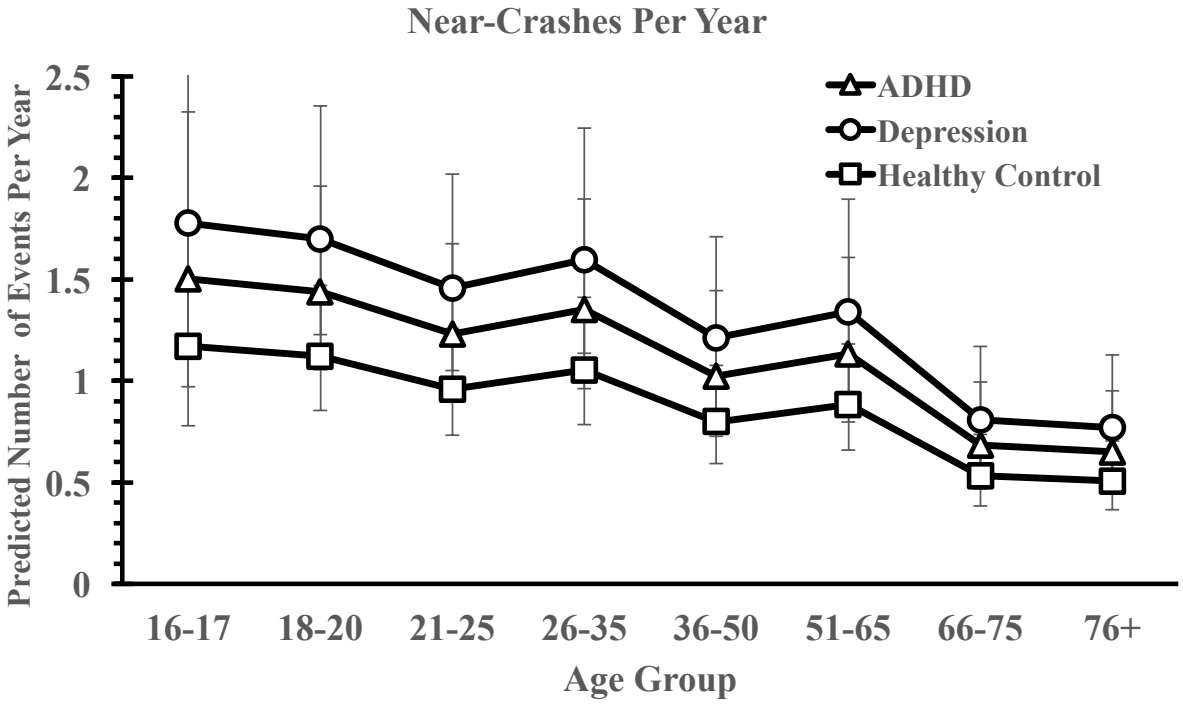


Figure 4. Values reflect estimated marginal means for incidents per year, defined for days of continuous monitoring =365.25 and miles driven =15,000. Error bars reflect 95% Wald confidence intervals.





Manuscript 3

The Role of Visual Attention in Predicting Crash Risk in Drivers with ADHD

Paula A. Aduen, M.A.
University of Virginia

Michael J. Kofler, Ph.D.
Florida State University

Catherine Bradshaw, Ph.D.
University of Virginia

Dustin Sarver, Ph.D.
University of Mississippi Medical Center

Daniel J. Cox, Ph.D.
University of Virginia Health Systems

Manuscript in Preparation for Submission to Peer-Reviewed Journal

Abstract

Objective: Drivers with ADHD disproportionately contribute to high rates of motor vehicle accidents, with a 5%-8% increase in crash risk associated with each increase in ADHD symptom. Inattention, one of the core symptoms of ADHD, is hypothesized to be one of the primary causes of motor vehicle violations and accidents. The current study examines whether disinhibition and sub-components of attention are cognitive pathways through which driving risk is conveyed in drivers with ADHD. **Method:** Prospective monitoring of crash risk for up to 2 years in 3,226 drivers from six U.S. sites participating in the Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study. At study entry, drivers were assessed for ADHD symptoms and completed the Conners' CPT-II. Utilizing a bias-corrected bootstrapping mediation procedure to estimate all effects, primary models involved four CPT-II derived variables mediating relations between ADHD symptoms and future crash risk. Miles driven, days monitored, age, gender, education, and marital status were controlled. **Results:** ADHD symptoms exerted an indirect effect on future crash, near-crash, and at-fault crash/near-crash risk through its association with Endogenous Orienting. Endogenous Orienting predicted future crashes and at-fault crashes/near-crashes while Vigilance Decrements portended future near-crashes. ADHD symptoms predicted all markers of future crash risk, higher levels of Disinhibition, Endogenous Orienting, and Arousal Decrements. **Conclusions:** Results suggest that orienting attention mediates the relationship between ADHD symptoms and future crash risk. Importantly, a 14-minute visual-attention and inhibition task predicted future crash risk 1 to 2 years following initial assessment. Identifying inattention as a key mechanism of driving risk has significant public health and clinical implications.

The Role of Visual Attention in Predicting Crash Risk in Drivers with ADHD

The National Highway Traffic Safety Administration estimates that approximately 33,963 motor vehicle related deaths occur per year, making injury or fatality due to traffic accidents one of the leading causes of death in the United States (National Highway Traffic Safety Administration, 2014). Drivers with high incidence psychiatric disabilities disproportionately contribute to the high rates of adverse driving outcomes. A recent meta-analysis indicated that drivers with Attention-Deficit/Hyperactivity Disorder (ADHD) are 1.23 times more at risk for involvement in a motor vehicle accident, with previous reviews reporting greater risk (RR=1.54-1.88) (Barkley & Cox, 2007; Vaa, 2014). In fact, studies examining driving behavior in ADHD have suggested that drivers with ADHD report more frequent crashes and a higher number of traffic violations (Barkley, 2004; Fischer et al., 2007; Vaa, 2014), with evidence suggesting that these rates do not decline in adulthood (Kay, Michaels, & Pakull, 2009). Further, drivers with ADHD are more likely to have a significant history of drivers' license suspension or revocation, report more severe crashes, and found to be culpable for driving errors that lead to traffic accidents (Aduen et al., 2015; Jerome, Segal, & Habinski, 2006; Vaa, 2014). In the context of these findings, driving impairment emerges as an associated functional outcome of adolescent and adult ADHD (Barkley, 2004), thus warranting further scrutiny of how core behavioral and cognitive features of ADHD may contribute to increased crash risk. Understanding how ADHD-related behavioral and cognitive sequelae relate to increased crash risk has the potential to inform prevention and intervention initiatives for drivers with high incidence psychopathology.

ADHD as a Risk Factor for Adverse Driving Outcomes

Analysis of specific driving behaviors in simulated driving environments suggests that both adolescent and adult drivers with ADHD show poorer vehicle control, a pattern of unsafe driving behaviors (e.g., less defensive driving, more abrupt acceleration and deceleration), and greater driving errors (e.g., more frequent lane departures, speeding) (Biederman et al., 2007; Groom et al., 2015; Merkel et al., 2016; Reimer et al., 2006). A prevalent finding suggests that inattention appears to be a primary contributor to motor vehicle accidents and violations among drivers with ADHD (Dingus et al., 2016; Fuermaier et al., 2015). Drivers with ADHD are also more likely to allocate their attention to in-vehicle distractors (Pope, Bell, & Stavrinos, 2017; Reimer et al., 2010), which is problematic given that attentional lapses as short as two seconds have been shown to result in severe or fatal driving outcomes (Horrey & Wickens, 2006). Individuals with ADHD are less likely to sustain focus for longer periods of driving, resulting in greater susceptibility for distraction, less monitoring of changing road conditions and traffic demands, and extended glances away from the roadway (Biederman et al., 2007; Fuermaier et al., 2015; Kingery et al., 2015).

The literature has also highlighted disinhibition as a contributor of driving errors that lead to increased crash risk. Disinhibition has been associated with higher frequency of crashes, traffic violations, and risky driving behaviors in simulated high stress driving scenarios (Barkley & Cox, 2007; Bioulac et al., 2016; Groom et al., 2015). However, findings linking disinhibition to poor driving performance have been inconsistent (Biederman et al., 2007; Reimer et al., 2006), suggesting that inattention may have a more prominent role in predicting driving errors and crash risk.

Impairments in attention and disinhibition are well documented in the adult ADHD literature (Barkley, Murphy, & Fischer, 2008; Biederman, Mick, & Faraone, 2000; Woods, Lovejoy, & Ball, 2002). Given their prominent role in contributing to crash risk, (Barkley, 2004; Barkley & Cox, 2007; Fuermaier et al., 2015), it is unsurprising that drivers with ADHD are at a heightened risk for adverse driving outcomes. Methods of assessing the question of driving impairment in ADHD have ranged from population-based registers (e.g., official hospital, insurance, and car insurance records), self-reported driving outcomes to simulated driving paradigms and assessment of on-road driving behavior. Despite methodological heterogeneity, findings have been consistent in highlighting driving risk as an emerging functional impairment associated with adolescent and adult ADHD (Barkley & Cox, 2007; Chang et al., 2014; Vaa, 2014). Identifying this area of impairment has significant clinical and public health implications, given drivers with ADHD disproportionately contribute to existing high rates of motor vehicle crashes (Barkley & Cox, 2007; Vaa, 2014). In the context of these findings, there is a critical need to elucidate the contributing factors and underlying pathways that convey increased driving risk for individuals with ADHD.

Model of Driving Performance and Cognition

Building on Michon's (1985) hierarchical model of driving and cognition, Barkley (2004) posited a potential framework to understand how inattention, hyperactivity, and impulsivity interfere with driving performance. This model captures the complexity of the routine task of driving by highlighting the integral role of simple and complex cognitive mechanisms at each level of the multi-dimensional task. Briefly, this model is composed of three hierarchical levels of driving competency- *operational,*

tactical, and strategic- that increase in complexity in terms of cognitive load and susceptibility to disruption. The *operational level* involves immediate vehicle control (e.g., steering, braking, shifting gears). Postulated underlying mechanisms include attention, concentration, reaction time, visual scanning, spatial perception and orientation, visual-motor integration, processing speed, and motor coordination (Barkley, 2004). The *tactical level* follows and involves negotiation of traffic and in-vehicle demands, with underlying cognitive mechanisms of set-shifting, visual tracking, and flexibility (Ranney, 1994). The *strategic level* is the most complex and involves higher-order planning abilities, goal-directed behavior, and working memory. A key component of this model is its emphasis on the permeating impact of inattention and disinhibition on each level of driving performance (Barkley, 2004; Barkley & Cox, 2007). As such, neurocognitive processes of inattention and disinhibition are positioned as likely candidate mechanisms underlying driving risk in ADHD, given established associations with ADHD behavioral symptoms (Biederman et al., 2007; Hervey, Epstein, & Curry, 2004; Woods, Lovejoy, & Ball, 2002) and adverse driving outcomes (Barkley, 2004; Fuermaier et al., 2015; Groom et al., 2015; Reimer et al., 2010).

Neurocognitive Mechanisms of Attention and Inhibitory Control

Attention. Inattention has been hypothesized as the chief contributor of traffic crashes and violations, with even a momentary lapse of attention resulting in possibly disastrous consequences (Dingus et al., 2016; Horrey & Wickens, 2006; Lam, 2002). Attention is a complex, multi-component construct that can be parsed into separate but interrelated neural subsystems and functions (Posner & Petersen, 1990; Riccio et al., 2002). Three attention networks frequently emerge, the *alerting* network, the *orienting*

network, and the *executive* attention network, each associated with distinct neural areas and carrying functionally separate sub-processes of attention (Posner & Petersen, 1990; Petersen & Posner, 2012).

Alerting refers to the concept of arousal and is responsible for enhancing physiological activation to maintain a state of high awareness to incoming stimuli (Posner & Petersen, 1990; Strum et al., 1999). Alerting is conceptualized as a foundational aspect of attentional capacity and a prerequisite to more complex attentional processes (Cohen, 2014; Sturm et al., 1999). Its function has been associated with lateralized right-hemisphere frontal and posterior parietal cortices, the locus coeruleus, and brain stem, and is primarily reliant on noradrenergic systems (Petersen & Posner, 2012; Posner, 2008; Samuels & Szabadi, 2008; Strum & Willmes, 2000). Posner & Petersen (1990) further dichotomized arousal into *tonic alertness* and *phasic alertness* to differentiate between: *a)* an individual's trait level of psychophysiological arousal and *b)* increases in alertness following an external cue or warning, respectively. The term tonic alertness is often used interchangeably with sustained attention/vigilance to describe decrements in attention over time, while phasic alertness characterizes the basic orienting response (Oken, Salinsky, & Elsas, 2006).

Studies have assessed the broad construct of alertness through lengthy, monotonous sustained vigilance tasks (Posner, 2008). Varying the presentation rate of sensory stimuli (interstimulus interval; ISI), during these sustained vigilance tasks has been found to reliably assess alertness level in both children and adults (Kuntsi et al., 2005; van der Meere, 2005; Wiersema et al., 2006). Separate subdomains of alertness are measured through manipulations of these paradigms, with *tonic alertness* assessed

through reaction time to sensory (visual, auditory) stimuli and *phasic alertness* assessed through changes in reaction time as a function of an external change in the task or sensory warning stimulus.

Males with ADHD appear to generally have increased variability in response time irrespective of stimulus presentation rate (e.g., faster, slower), suggestive of broader deficits in arousal (Cohen, 2014; Wiersema et al., 2006). Meta-analyses examining alertness in ADHD have concluded that ADHD is not consistently characterized by dysfunction in tonic alertness (Huang-Pollock & Nigg, 2003). However, adults with ADHD have been shown to have slower response times with longer interstimulus intervals, providing evidence for phasic arousal decrements as a function of increased task duration (Wiersema et al., 2006). Conclusively, studies suggest general arousal deficits in ADHD, which may be more apparent during monotonous, sustained tasks, and as such may contribute to broader impairment in sustained attention and other attention subsystems (Epstein et al., 1997; Posner & Petersen, 1990; Tucha et al., 2015; 2008; Woods, Lovejoy, & Ball, 2002).

Orienting refers to the detection of external sensory input and the ability to give priority to salient stimuli (Posner & Petersen, 1990). Orienting has been further characterized as either *exogenous* or *endogenous* to differentiate between reflexive/automatic orientation (e.g., bottom-up processing) to a salient sensory cue in the environment and controlled/voluntary (e.g., top-down processing) orientation toward an object, respectively (Berger, Henik, & Rafal, 2005; Jonides, 1981; Posner, 1980). Studies have linked orienting of attention to frontal eye fields, superior parietal lobe, temporal parietal junction, superior colliculus, and the thalamic reticular nucleus (Posner &

Petersen, 1990; Petersen & Posner, 2012), and have been associated with cholinergic systems (Petersen & Posner, 2012; Voytko et al., 1994). Anatomically distinct neural networks have been distinguished that align with *exogenous* and *endogenous* orienting of attention. Specifically, the locus coeruleus, superior parietal cortex, pulvinar, and superior colliculus, has been associated with exogenous, automatic orienting while the anterior cingulate gyrus, supplementary motor cortex, and mid-prefrontal cortex have been linked to endogenous, voluntary orienting (Berger & Posner, 2000; Posner & Raichle, 1994).

Tasks assessing orienting processes include simple detection designs or predictive designs that involve presenting a cue in the location where a target stimulus will appear (Huang-Pollock & Nigg, 2003). Primary outcomes of interest in these tasks include reaction time as well as omissions and anticipatory responses for exogenous and endogenous orienting, respectively (Novak, Solanto, & Abikoff, 1995; Fan et al., 2005). Studies examining orienting of attention have provided the most evidence for dysfunction in endogenous orienting in samples of children and adults with ADHD (d= 0.30-1.32) (Nigg, Swanson, & Hinshaw, 1997; Novak, Solanto, & Abikoff, 1995). Nevertheless, in their review of the literature, Huang-Pollock and Nigg (2003) reported that evidence is inconsistent for deficits in endogenous, voluntary orienting in ADHD. Conversely, findings have been more conclusive regarding intact exogenous, automatic orienting in ADHD (Aman et al., 1998; Epstein et al., 1997; Perchet et al., 2001).

Executive attention describes attentional mechanisms responsible for resolving conflict between opposing responses, including monitoring and response selection processes (Posner & Petersen, 1990). These executive control processes of attention are

responsible for voluntary control and processing of attention in space (Posner & Raichle, 1994). Several processes commonly attributed to broader executive functions (EF), such as interference control, are subsumed within this sub-component of attention (Posner & DiGirolamo, 1998). Executive attention mechanisms are associated with the prefrontal and lateral ventral cortices, anterior cingulate, supplementary motor cortex, and basal ganglia (Botvinick et al., 2001; Fan et al., 2005) and have been linked to dopaminergic systems. Executive attention has historically been assessed through measures involving competing response selection, such as Stroop and Color-Word Inhibition tasks. Consistent findings have implicated impairment in executive attention in ADHD throughout the lifespan (Berger & Posner, 2000; Durston & Konrad, 2007; Mullane et al., 2009),

Inhibitory control. *Inhibitory control* refers to a set of interrelated cognitive processes that underlie the ability to withhold (action restraint) or stop (action cancellation) an on-going behavioral response (Alderson et al., 2007; Schachar et al., 2000). These processes have been linked to the septo-hippocampal system with associated projections to the inferior frontal cortex (Quay, 1997), and to fronto-basal-ganglia circuitry (Aron et al., 2007). Inhibitory control has been classically assessed by go/no-go or stop-signal tasks. Go/no-go tasks differ from stop-signal tasks in that they require a continuous response pattern that is only interrupted when a stimulus signals to inhibit responding. Adults with ADHD have demonstrated poorer performance on response inhibition tasks compared to adults with no known psychopathology and adults with anxiety (Epstein et al., 2001). Nevertheless, studies examining differences in inhibition between ADHD, other clinical groups, and healthy control groups have failed

to consistently replicate these findings (Lijffijt et al., 2005; Nigg, 2001), with recent meta-analyses concluding that inhibition processes are generally intact in ADHD (Alderson et al., 2007).

Current Study

Models of driving risk (Barkley, 2004; Barkley & Cox, 2007; Michon, 1985) postulate that cognitive vulnerabilities underlie poor driving performance. Given evidence that processes critical to driving performance, such as attention and inhibition, are often compromised in individuals with high incidence psychopathology, it is unsurprising that drivers diagnosed with ADHD disproportionately contribute to high automobile collision rates (Barkley, 2004; Barkley & Cox, 2007; Fuermaier et al., 2015; Vaa, 2014). Driving impairment has emerged as a key functional outcome of ADHD, with greater symptoms of inattention, hyperactivity, and impulsivity portending a 5%-8% increase in crash risk per symptom across a 1-2 year period (Aduen et al., *Under Review*). In the context of these robust findings, it is of significant public health and clinical importance to better understand the underlying mechanisms through which risk is transmitted.

The current study examined whether impairments in attention and inhibition, as measured by the Conners' Continuous Performance Test, Second Edition (CPT-II; Conners, 2000), explain relations between ADHD symptoms and future risk for objective, criterion-based crashes and near-crashes. Described as a go/no-go paradigm, the CPT-II assesses inhibitory control as well as multiple subcomponents of attention (Bytoft et al., 2017; Egeland & Kovalik-Gran, 2010a; Egeland & Kovalik-Gran, 2010b) and has been deemed to possess ecological validity with motor vehicle driving due to the

shared monotonous nature of each task (Barkley et al., 2002). The CPT-II manipulates the interstimulus interval (ISI) within a fixed task duration and go/no-go ratio, resulting in performance markers that have been shown to diffusely align with ADHD symptoms of inattention, hyperactivity, and impulsivity (Barkley, 2004; Epstein et al., 1997). Individuals with ADHD have been documented to have poorer CPT-II performance (Barkley, 1991; Epstein et al., 2003) as evidenced by variable or impaired reaction time, omission errors, mean Hit Reaction Time (HRT), and signal detection measures (D Prime; Beta) (Biederman et al., 2007; Epstein et al., 2001). Importantly, significant variation exists across studies regarding what CPT-II parameters are used to assess for inattention and disinhibition, with most studies relying on clinical assumptions and face validity (e.g., omission errors as a proxy for inattention, commission errors as a proxy for impulsivity) of each variable rather than empirically-derived indicators, such as latent factor scores (Barkley, 1991; Epstein et al., 2001).

Through its prospective and longitudinal design, the Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study is particularly well suited to deciphering the extent to which previously identified links between ADHD symptoms and driving risk may be conveyed via neurocognitive pathways of inattention and disinhibition. Findings from past studies using neuropsychological task performance to predict driving risk in varied clinical groups have been mixed (Barkley et al., 1993; Biederman et al., 2006; Bioulac et al., 2016; Leon-Dominguez et al., 2016). Notably, however, most studies have relied on single markers of performance on the CPT-II (e.g., omissions, commissions) rather than using empirically-derived factors to better assess cognitive constructs of attention or inhibition (Bytoft et al., 2016; Egeland & Kovalik-Gran, 2010a;

Miyake et al., 2000). Further, existing studies relating neuropsychological functioning to driving performance have had methodological confinements including cross-sectional designs, driving simulator paradigms, or relatively brief on-road assessments that limit generalizability of results.

Guided by Posner's (1980) model of attention and in the context of previous literature documenting attention and inhibition deficits in ADHD using neuropsychological measures (Biederman et al., 2006; Epstein et al., 2003; Hervey, Epstein, & Curry, 2004), we hypothesized that ADHD symptoms would be associated with deficits in vigilance (i.e., phasic alertness) (Wiersema et al., 2006), orienting (Nigg, Swanson, & Hinshaw, 1997), but not disinhibition (Alderson et al., 2007) or arousal (i.e., tonic alertness) (Huang-Pollock & Nigg, 2003). It was also predicted that performance on the CPT-II would be related to adverse driving outcomes given past studies showing an association between neuropsychological test performance and driving (Barkley, 2004; Lincoln & Radford, 2013). Consistent with previous literature, we hypothesized that ADHD symptoms would portend increased risk for future adverse driving outcomes and that this association would be mediated by attention as measured by derived factors from the CPT-II (Dingus et al., 2016; Fuermaier et al., 2015).

Methods

SHRP-2 Design and Overview

The Strategic Highway Research Program (SHRP-2) Naturalistic Driving Study included 3,600 drivers from six U.S. sites (Bloomington, IN; Central PA; Tampa, FL; Buffalo, NY; Durham, NC; Seattle, WA). Technical reporting of study design and recruitment, probability-based sampling, and methodological plans are found in Antin

(2011). Sample characteristics and comparisons with the U.S. population of licensed drivers are provided in Antin (2015). Comparisons indicate close approximation to U.S. drivers for the sample. Detailed data reduction methods, software-based trigger algorithms and validation, vehicle sensor calibration, data reductionist training, and reliability are provided in Hankey, Perez, & McClafferty (2016). Sample demographics are shown in Table 1, and were controlled in all analyses**.** Each driver's car was outfitted with five high-speed video cameras, speed/brake monitors, accelerometers, and GPS to continuously capture routine driving from engine-on to engine-off for 1-2 consecutive years (Antin et al., 2011). Participants were protected by a national Certificate of Confidentiality and not required to report crashes or surrender crash-relevant evidence to authorities (Hankey, Perez, & McClafferty, 2016). Upon study entry, drivers completed a driving history and demographic questionnaire, the Barkley Adult ADHD Quick Screen (BAQS), and the Conners' Continuous Performance Test- Second Edition (CPT-II; Conners, 2000).

Continuous Monitoring and Event Triggers

SHRP-2 collected approximately 2,000,000 gigabytes of data spanning 5,512,900 individual trips that occurred between 2010 and 2013. Software-based trigger algorithms and 100% double-coded manual validation identified 4,254 safety-critical events (SCE; 1,549 crashes, 2,705 near-crashes). These algorithms used kinematic and behavioral signatures previously identified as present with high probability during crashes (e.g., longitudinal deceleration < -0.65g, lateral acceleration >0.75g) (Hankey, Perez, & McClafferty, 2016). All SCEs were verified by comparing event videos with pre-recorded index images to ensure the consented participant was driving. Manual video

review then verified if an SCE occurred. Verified events were coded by extensively trained data reductionists (100% SCEs coded by ≥2 coders; reliability=91%) (Antin et al., 2011; Hankey, Perez, & McClafferty, 2016). Coders completed ~10 days of training, demonstrated 90% proficiency prior to coding, were retested frequently using the same 90% criterion, and completed ≤4 hour shifts (mandatory breaks/hour) to minimize fatigue-related errors. Coders were blind to driver clinical status (Hankey, Perez, & McClafferty, 2016).

Prospective Driving Outcomes

Primary outcomes included number of *crashes* (SCEs involving any contact between participant vehicle and fixed or moving object, at any speed where kinetic energy is measurably transferred or dissipated), *near-crashes* (SCEs requiring rapid, evasive maneuver by participant vehicle to avoid imminent crash), and crash and near-crash *fault* (observable evidence that the participant driver committed error leading to crash/near-crash) recorded during prospective monitoring.

Barkley Adult ADHD Quick Screen (BAQS)

The BAQS is a 6-item self-report questionnaire that assesses ADHD symptoms in adults on a 4-point Likert scale (0=never/rarely, 1=sometimes, 2=often, 3=very often; range=0-18). The questionnaire has items relating to attention (e.g., easily distracted), organization (e.g., organization of tasks and activities, losing items), and impulsivity (e.g., difficulty waiting turn, restlessness). Psychometric support includes high internal consistency (α=.90), concurrent validity for self-reported (r=.97) and other-reported (r=.68) ADHD symptoms compared to full, 18-item DSM-based checklists, predictive validity for self-reported (r=.87) and other-reported impairment (r=.67), and high

sensitivity (.93) and specificity (.97) for differentiating adults with ADHD from neurotypical adults (Barkley, Murphy, & Fischer, 2010).

Demographic Questionnaire and Driving History

Upon enrollment in SHRP-2, participants completed the driving demographic questionnaire, which assessed participant age, gender, educational level, income, and marital status. The driving history questionnaire also assessed vehicle year and estimated annual miles driven.

Clinical Groups

Aduen (2015) identified 275 drivers with ADHD and 1,828 Healthy Control Drivers based on self-reported clinical status at study entry. They also identified 251 drivers with self-reported diagnoses of Depression, who are included here to compare ADHD to another high-prevalence disorder (Kessler & Bromet, 2013) associated with attention/concentration problems (Austin, Mitchell, & Goodwin, 2001) and adverse driving outcomes (Wickens, Smart, & Mann, 2014). Clinical group comparisons were conducted using these psychiatric diagnoses (Aduen et al., 2015) and are considered exploratory because the naturalistic study design precluded clinical interviewing or tracking illness course/treatment efficacy during the prospective monitoring of driving outcomes.

Psychiatric Treatment

ADHD and antidepressant medications were queried at study entry and exit and used as a proxy for active treatment. Consistent with epidemiological estimates (Polanczyk et al., 2007), 20.8% of ADHD and 61.0% of Depression group members reported disorder-specific medication treatment at one or both time points. Medication

status was analyzed irrespective of clinical group (Medicated ADHD/Depression=255; Unmedicated ADHD/Depression=269). Cell sizes were sufficient for exploratory analyses of antidepressant time course for the Depression group (Stable-Unmedicated=99; Started=98; Stopped=24; Stable-Medicated=30). ADHD medication was dichotomized based on medication at either time point (No=218; Yes=57) due to insufficient cell counts (Stable-Unmedicated=218; Started=43; Stopped=12; Stable-Medicated=2). The naturalistic study design precluded monitoring of perceived medication efficacy, emergent effects, or timing in relation to crashes. Nevertheless, these analyses reflect the most extensive examination to date of treatment-as-usual's protective effects on prospective, objectively-documented motor vehicle crashes.

Conners' Continuous Performance Test- Second Edition

The Conners' Continuous Performance Test- Second Edition (CPT-II; Conners, 2000) is a 14-minute computerized visual-motor task that requires participants to rapidly and accurately respond to letters that continuously appear on the screen. Participants respond by pressing the spacebar for every letter (target) except 'X' (non-target). When the letter 'X' appears, participants are instructed to interrupt their continuous motor response and inhibit responding. As with go/no-go paradigms, the CPT-II establishes a pre-potent, ongoing response whereby performance on 'no-go' trials serves as an index of inhibitory control (Quay, 1997; Soreni et al., 2009). The task presents 360 letters, one at a time, for 18 consecutive blocks (6 blocks divided into three sub-blocks). Both target and non-target stimuli are shown for 250 milliseconds and appear on the screen with interstimulus intervals (ISIs) varying between 1, 2, or 4 seconds within each block. The

CPT-II utilizes a high target-to-nontarget ratio, 90% of presented stimuli are 'go' trials ('X' appears during only 10% of trials) (Conners, 2000).

Completion of the task calculates and records 12 indices: Omission Errors (targets to which the subject failed to respond), Commission Errors (non-targets to which the subject erroneously responded), Hit Reaction Time (Hit RT; reaction time to all non-"X" letters across six time blocks), Hit Reaction Time Standard Error (Hit RT SE; consistency of reaction time), Variability of Standard Error (response time consistency for each sub-block), Detectability (*d*'; discrimination between targets and non-targets), Perseverations (reaction time <100ms), Response Style (Beta; function of speed/accuracy with higher scores indicative of cautious response style), Hit Reaction Time by Block (HIT RT Block Change; change in reaction time across duration of test), Hit Standard Error by Block (Hit SE Block Change; changes in response consistency across duration of test), Reaction Time by Inter-Stimulus Interval (Hit RT ISI Change; change in average reaction times at 1, 2, or 4 second ISIs), and Standard Error by Inter-Stimulus Interval (Hit SE ISI Change; consistency of reaction times at 1, 2, or 4 ISIs). Raw scores are converted to T-Scores based on age and gender (national standardization sample N= 2,521; Conners, 2000).

CPT-II indices have been found to have adequate split-half reliability for most variables ranging between 0.66 to 0.95. However, test-retest reliability estimates over a three-month period have been modest and variable ranging from 0.05 to 0.92, suggesting that the CPT-II alone should not be used alone to clinically diagnose ADHD (Conners & MHS Staff, 2000; Soreni et al., 2009). The following test-retest reliabilities have been reported across adolescent and adults studies: Omission Errors (r=.84), Commission Errors (r=.72), Perseverations (r=.48), HRT (r=.76), HRT SE (r=.63), Variability

(*r*=.48), D Prime (*r*=.33), Beta (*r*=.63), Detectability (*r*=.76), Hit SE ISI Change (*r*=.05), Hit SE Block Change (*r*=.08), and Hit RT Block Change (*r*=.28; Conners & MHS Staff, 2000; Homack & Riccio, 2006; Soreni et al., 2009). Time-related changes (e.g., administration order) have been found to have salient effects on the repeated assessment of attention. Individuals with ADHD are more susceptible to these time-related task effects, such as fatigue, compared to individuals without ADHD, which may contribute to instability of performance over time (Erdodi & Lajiness-O'Neill, 2014; Erdodi, Lajiness-O'Neill, & Saules, 2010). Nevertheless, the CPT-II accurately discriminates between individuals with and without ADHD (Epstein et al., 2003; Seidel & Joschko, 1990).

Neurocognitive Factor Construction

The majority of studies that have used the Conners CPT (Conners, 2000) to examine aspects of attention and inhibition have used specific variables (i.e., omission and commission errors, detectability) produced by the task, rather than empirically-derived factors (Barkley, 1991; Epstein et al., 2003). Using a factor reduction approach rather than single makers of performance has the advantage of providing more accurate estimates of higher-order neurocognitive abilities through isolating reliable variance among related variables (Miyake et al., 2000). The psychometric structure of the Conners CPT-II varies across published reports, with evidence supporting three (Conners, 2000), four (Conners, 2014), and five (Egeland & Kovalik-Gran, 2010a; Bytoft et al., 2017) factor solutions based on exploratory models.

To date, only one study has published on a five-factor solution (Focus, Sustained Attention, Hyperactivity/Impulsivity, Vigilance, Change in Control) for the CPT-II (Conners, 2000) in a clinically heterogeneous (Outpatient=310; Inpatient=66) sample

ranging from ages 14 to 77 (Egeland & Kovalik-Gran, 2010a; Egeland & Kovalik-Gran, 2010b). Importantly, the authors excluded the Detectability (*d')* variable and created additional variables (e.g., change in omissions, change in commissions) to improve the fit of the model, which limits the generalizability of this factor structure. These changes prove to be problematic given that the Detectability variable is an important marker for attentiveness, specifically for assessment of alerting attention (Cohen, 2014; Conners, 2000; Soreni et al., 2009), and because the psychometric properties of their created variables are unknown.

Evidence has been inconsistent regarding the validity of this factor structure. To our knowledge no study has successfully replicated a previously published Conners CPT factor structure despite multiple attempts (Bytoft et al., 2017; Vertinski et al., 2014). Bytoft and colleagues (2017) produced a four-factor structure that aligned moderately with the first four factors of Egeland and colleagues (2010a; 2010b), but they were unable to replicate the Change in Control factor because change in omission and commission variables were unavailable. As such, their fifth factor was re-labeled *Response Style* and was comprised of only one factor loading, which affects accurate estimation of the construct (Kline, 2016). Similarly, Vertinski and colleagues (2014) explored Egeland & Kovalik-Gran's (2010a) five-factor model, in addition to a one-, three-, and four-factor solution, in heterogeneous clinical pediatric samples. This group found that all *a priori* factor structures were misspecified to the data, even after excluding variables, such as omission errors and Beta, to improve model fit. Conclusively, considerable debate continues to exist regarding the factor structure of this widely used test.

Given inconsistent findings regarding the CPT-II's factor structure, we first used confirmatory factor analyses (CFA) to test each of the previously reported three-, four-, and five-factor models, as well as an *a priori* specified one-factor model using *MPlus* v7.4 (Muthén & Muthén, 2015). Results indicated that the three-, four-, and five-factor models were misspecified for the data, characterized by large negative residual variances across factors. Inspection of fit indices for the single-factor model suggested poor fit to the data (χ^2 (45)=21,340.11, p<.001; RMSEA=.389 [90%CI: .384-.394]; CFI=.301, TLI=.146). As such, principal component analysis (PCA) was conducted to identify the structure of the CPT-II observed variables and derive uncorrelated factor scores for the current study's primary mediation analyses. Prior to this analysis, intercorrelations between variables of interest were examined, data was screened for outliers, and assumptions were tested. The Kaiser-Meyer-Olkin measure verified sampling adequacy for the analysis, KMO = 0.64, which is considered acceptable (Hutcheson & Sofroniou, 1999). All KMO values for individual variables were inspected and found to be greater than the acceptable limit of 0.50 (Field, 2009). Bartlett's test of sphericity $\chi^2(66) = 17119.67$, $p < .0001$, indicated that correlations between items were sufficiently large for PCA.

PCA was conducted on the 12 CPT-II variables with an orthogonal rotation (Varimax). Both theoretical and empirical evidence were considered when deciding on the number of factors to retain. Results were evaluated against the following criteria: a) unrotated factors required to satisfy Kaiser's (1958) criterion of eigenvalues greater than 1.00; b) accepted configurations had to account for an appreciable percentage of total score variance (i.e., ≥ 50%); c) solutions must meet Cattell's (1966) scree test; d) each

rotated factor included at least two appreciable factor loadings (i.e., ≥ 0.40; Stevens, 2002); and e) the final solution should be compatible with theoretical models of the mental processes involved in go/no-go tasks that vary stimulus presentation rates over an extended duration (Huang-Pollock et al., 2012; Soreni et al., 2009).

An initial analysis was run to obtain eigenvalues for each factor in the data. Four factors were retained that had eigenvalues over Kaiser's (1985) criterion of greater than 1.00 and in combination explained 69.95% of the variance. Given the large sample size and the convergence of the scree plot and Kaiser's criterion on four components, this is the number of components that were retained in the final analysis. Varimax rotated component loadings suggest four distinct neurocognitive variables including Disinhibition, Endogenous Orienting, Arousal Decrements, Vigilance Decrements (Table 2). The Disinhibition factor explained 26.47% of the variance with high loadings from Commission, Detectability (*d'*), HRT, and Response Style (Beta). The Endogenous Orienting factor explained 19.38% of the variance with high loadings from Variability, HRT SE, Perseverations, and Omissions. Arousal Decrements and Vigilance Decrements explained 12.81% and 11.29% of the variance, receiving high loadings from HRT ISI, HSE ISI and HRT Block Change and HRT SE Block Change, respectively. Factor scores were saved using the Bartlett (1993) method. Bartlett scores are computed using maximum likelihood methods that yield unbiased estimates of true factor scores (DiStefano, Zhu, & Mindrila, 2009). As such, the four neurocognitive variables were uncorrelated by design (r_{all}=.00; DiStefano, Zhu, & Mindrila, 2009; Gorsuch, 1990).

Factor labels in the present study were selected to be consistent with terminology implemented in the ADHD and cognitive literature. For example, the first factor was

labeled *Disinhibition* rather than Impulsivity to better capture the cognitive construct of response inhibition assessed through commission errors (Congdon et al., 2012; Epstein et al., 2001; van der Meere, 2002). The second factor, characterized as Inattention by the CPT-3 (Conners, 2014), was labeled *Endogenous Orienting* to specify the subcomponent of attention measured (Berger, Henik, & Rafal, 2005; Posner & Petersen, 1990) and distinguish it from the Vigilance Decrement factor that indexes changes in alertness over time (Huang-Pollock & Nigg, 2003; Woods, Lovejoy, & Ball, 2002). Given that both omission errors and anticipatory responses (Perseverations) were among the variables that loaded onto the Orienting factor, this construct was determined to most accurately describe endogenous as opposed to exogenous orienting (Carter et al., 1995; Huang-Pollock & Nigg, 2003; Swanson et al., 1991). Lastly, CPT-3 (Conners, 2014) factors of Sustained Attention and Vigilance were re-labeled *Arousal Decrements* and *Vigilance Decrements* in the current study given that sustained attention and vigilance are often used interchangeably in the literature (Oken, Salinsky, & Elsas, 2006). The *Arousal Decrements* variable is consistent with literature investigating arousal deficits in ADHD through manipulation of ISIs (Oken, Salinsky, & Elsas, 2006; Raymaekers et al., 2007; van der Meere, 2005), while *Vigilance Decrements* describes reductions in attention as a function of time (Cohen, 2014).

The factor loadings obtained in the present study broadly align with the updated normative sample factor structure of the CPT-3 (Conners, 2014), with notable exceptions. For example, Detectability (*d'*) loaded onto the Disinhibition (Impulsivity; CPT-3) rather than the Endogenous Orienting (Inattention; CPT-3) factor, and Perseverations loaded onto the Endogenous Orienting (Inattention; CPT-3) rather than the Disinhibition

(Impulsivity; CPT-3) factor. Lastly, Response Style (Beta) loaded onto the Disinhibition factor in the current study but was not included in the CPT-3 (Conners, 2014). Factors loadings within the CPT-3's Sustained Attention and Vigilance factors were consistent with our Vigilance Decrement (HRT Block Change, HRT SE Block Change) and Arousal Decrement (e.g., HRT ISI, HSE ISI) factor loadings, with the exception that the CPT-3 factors included additional variables that index changes in Omissions and Commissions by Block and ISI.

Mediation Analyses

Bias-corrected, bootstrapping mediation was conducted using PROCESS (Hayes, 2013) and 10,000 bootstrapped samples. Only observed variables were included. Each model included one predictor (BAQS Score), four neurocognitive mediators (Disinhibition, Endogenous Orienting, Arousal Decrements, Vigilance Decrements) and one outcome variable. Separate models were analyzed for each adverse driving outcome (Crashes, Near-Crashes, Crash/Near-Crash Fault; Figure 1). Exploratory analyses repeated these analyses, substituting the categorical, dummy-coded clinical groups (ADHD, Depression, Healthy Control) and medication status (Medicated/Unmedicated drivers with ADHD/Depression) for BAQS scores (Aduen et al., 2015).

In mediation, *total effects* represent relations between ADHD symptoms and adverse driving outcomes prior to accounting for the four neurocognitive factors (paths $c_{1\text{-}4}$; Figure 1). *Direct effects* include ADHD symptoms predicting neurocognitive abilities (a pathways), and neurocognitive performance predicting adverse driving outcomes after accounting for ADHD symptoms (b pathways). The residual differences in effect magnitude before (c pathways) and after (c' pathways) accounting for

neurocognitive performance reflects *indirect effects* of ADHD symptoms on adverse driving outcomes (ab pathways). *Effect ratios* (indirect/total effect) estimate the proportion of each total effect attributable to each ADHD symptom's influence on neurocognitive performance (which in turn influence adverse driving outcomes; i.e., indirect effects; Shrout & Bolger, 2002).

Data Analysis Overview

Partial correlations were conducted to assess the strength and relation between predictors, mediators, and outcomes while controlling for demographic and driving-relevant covariates (Table 3). Bias-corrected, bootstrapped mediation (Hayes, 2009; Williams & MacKinnon, 2008) was implemented to examine the extent to which ADHD symptoms (BAQS) exert direct effects on future adverse driving outcomes (crash count, near-crash count, at-fault crashes/near-crashes), exert indirect effects through neurocognitive factors (Disinhibition, Endogenous Orienting, Arousal Decrements, Vigilance Decrements), exert both direct and indirect effects, or fail to portend adverse future driving outcomes (Williams & MacKinnon, 2008). Additional exploratory models were analyzed with clinical groups, previously established by Aduen (2015), as well as medication status as separate predictors. These analyses were exploratory in nature due to the naturalistic study design, which precluded rigorous diagnostic processes (e.g., clinical interviewing, tracking of illness and treatment).

Results

Preliminary Analyses

Missing data ranged from 0.1-0.9% for gender, age, education, and marital status and did not vary by clinical group (p=.60), supporting Missing at Random (MAR) assumptions. Education served as a proxy for socioeconomic status; income was not

controlled due to high missing data (16.2%). Sample retention was excellent: 3,226 of 3,600 enrolled cases (89.6%) were followed prospectively and included in analyses.

Of the 2,354 drivers assigned to a clinical or control group, 329 (98.9%) were retained including 274 of 275 drivers with ADHD (99.6%), 249 of 251 drivers with Depression (99.2%), and 1,806 of 1,828 Healthy Control drivers (98.8%). These groups did not differ in miles driven (M=9527.9 miles; p=.53), days of study participation (M=440.49 days; p=.46), or performance on a driving knowledge questionnaire ($M_{correct}$=79.74%; p=.14). The ADHD group's vehicles were on average one model year older (M=2005.13, SD=4.73) than the Depression (M=2006.41, SD=4.24) and Healthy Control groups' vehicles (M=2006.36, SD=4.01) (both $p\leq$.001). All CPT-II variables were screened for univariate/multivariate outliers and tested against p<.001, resulting in four identified outliers that were subsequently recoded as missing.

Partial correlations. As shown in Table 3, ADHD symptoms (BAQS) covaried with concurrently assessed CPT-II Disinhibition (r=.07, p<.001), Endogenous Orienting (r=.09, p<.001), and Arousal Decrements (r=.04; p=.02), but not Vigilance Decrements (r=-.01, p=.44) when controlling for age, gender, education, marital status, time in study, and miles driven. ADHD symptoms prospectively predicted crashes (r=.06, p=.001), near-crashes (r=.05, p=.003), and at-fault crashes/near-crashes over a 1-2 year period (r=.07, p<.001). CPT-II Endogenous Orienting portended future crashes (r=.04, p=.02) and future at-fault crashes/near-crashes (r=.05, p<.05). CPT-II Vigilance Decrements predicted future near-crashes (r=-.04, p=.03).

Mediation Results

Based on significant relations between the primary predictor of interest (BAQS Score), neurocognitive mediators (Disinhibition, Endogenous Orienting, Arousal Decrements, Vigilance Decrements), and adverse driving outcomes (crashes, near-crashes, and at-fault crashes/near-crashes), separate mediation models were analyzed for each of the three primary adverse driving outcomes. Further, exploratory mediation models were analyzed that replaced BAQS with dummy-coded Clinical Group variables (ADHD, Depression, Healthy Control) as the predictor, given clinical group differences in neurocognitive factors and adverse driving outcomes. Lastly, medication effects were explored, placing Medicated and Non-Medicated ADHD/Depression as predicting each separate adverse driving outcome and mediated by the four parallel neurocognitive factors. All models controlled for age, gender, education, marital status, time in study, and miles driven. Results are organized by pathway.

Continuous ADHD Symptoms (BAQS)

Total Effects (c pathways). As shown in Figure 1, greater ADHD symptoms at study entry portended increased risk for future crashes (β=.03 p=.001), near-crashes (β=.04, p=.003), and at-fault crashes/near-crashes (β=.05; p=.0001).

Direct Effects of ADHD Symptoms on CPT-II Neurocognitive Factors (a pathways). Greater ADHD symptoms predicted higher levels of Disinhibition (β=.03, p=.0001), lower Endogenous Orienting (β=.04, p<.001), and Arousal Decrements (β=.02, p=.02), but not Vigilance Decrements (p=.44).

Direct Effects of CPT-II Neurocognitive Factors on Future Driving Outcomes (b pathways). Accounting for ADHD symptoms, Endogenous Orienting at study entry predicted future crashes (β=.04, p=.04) and at-fault crashes/near-crashes (β=

.07, *p*=.03). Only Vigilance Decrements predicted number of near-crashes (*β*= -.06, *p*=.03). None of the other neurocognitive factors significantly predicted number of crashes (*all p*>.16), near-crashes (*all p*>.11), and at-fault crashes/near-crashes (*all p*>.18).

Indirect Effects of ADHD Symptoms on Future Driving Outcomes (ab pathways). ADHD symptoms exerted an indirect effect on future crash risk (*β*=.001 ER=.06; 95%CI= .0002-.003), near-crash risk (*β*=.002 ER= .05; 95%CI=.0000-.005), and at-fault crash/near-crash risk (*β*=.002; ER= .05; 95%CI=.0004-.005) through its association with Endogenous Orienting. No additional indirect effects were detected (All 95%CI Include Zero).

Residual Effects of ADHD Symptoms on Future Driving Outcomes (c' pathways). After accounting for the effects described above, self-reported ADHD symptoms continued to predict risk for future crashes (*β*=.02; *p*=.002), near-crashes (*β*=.04; *p*=.005), and at-fault crashes/near-crashes (*β*=.05; *p*=.0001).

Sensitivity Analyses

Clinical Group

Total Effects (c pathways). Drivers with ADHD (*β*=.35, *p*=.001) and Depression (*β*=.40, *p*=.0003) both had a higher likelihood of experiencing at-fault crashes/near-crashes compared to Healthy Control drivers. Interestingly, ADHD at study entry portended risk for experiencing future crashes (*β*=.22, *p*=.001) but not near-crashes (*p*=.06), whereas Depression at study entry predicted risk for future near-crashes (*β*=.33, *p*=.002) but not crashes (*p*=.11) when compared to drivers with no known psychopathology. Differences between drivers with ADHD and Depression in future

crashes, near-crashes, and at-fault crashes/near-crashes did not reach significance (*all* $p>.31$).

Direct Effects of Clinical Group on CPT-II Neurocognitive Factors (a pathways). Both drivers with ADHD ($\beta=.22$, $p=.0004$) and Depression ($\beta=.14$, $p=.02$) demonstrated significantly reduced Endogenous Orienting compared to Healthy Control drivers. Drivers with ADHD demonstrated worse Disinhibition ($\beta=.14$, $p=.03$) and Arousal Decrements ($\beta=.16$, $p=.01$), but not Vigilance Decrements ($p=.44$) compared to Healthy Control drivers. Drivers with Depression demonstrated more Vigilance Decrements than drivers with ADHD ($\beta=.29$, $p=.002$) and no known psychopathology ($\beta=-.20$, $p=.004$). For drivers with Depression, differences in Disinhibition ($p=.97$; $p=.34$) and Arousal Decrements ($p=.37$; $p=.17$) did not reach significance when compared to Healthy Control and ADHD drivers, respectively. Differences between drivers with ADHD and Depression on Endogenous Orienting did not reach significance ($p=.85$).

Direct Effects of CPT-II Neurocognitive Factors on Future Driving Outcomes (b pathways). Neurocognitive factors did not uniquely predict crash count (*all* $p>.07$), near-crash count (*all* $p>.11$), or at-fault crashes/near-crashes (*all* $p>.11$) in all models controlling for clinical groups.

Indirect Effects of Clinical Group on Future Driving Outcomes (ab pathways). Clinical groups did not exert indirect effects on future crash, near-crash, or at-fault crash/near-crash risk via any of the neurocognitive variables (all $\beta<.001$; all 95%CI Include Zero).

Residual Effects of Clinical Group on Future Driving Outcomes (c' pathways). After accounting for effects described above, ADHD at study entry continued to portend risk for future crashes (β=.21, p=.001) and at-fault crashes/near-crashes (β=.35, p=.001), but not near-crashes (β=.19, p=.05) when compared to Healthy Control Drivers. In contrast, Depression continued to predict risk for near-crashes (β=.32, p=.003) and at-fault crashes/near-crashes (β=.39, p=.001), but not crashes (p=.12) when compared to Healthy Control Drivers. No significant differences between drivers with ADHD and Depression emerged in crashes (p=.41), near-crashes (p=.36), or at-fault crashes/near-crashes (p=.55).

Medication Status

Total Effects (c pathways). Drivers with ADHD/Depression on medication experienced more crashes (β=.23, p=.01), at-fault crashes/near-crashes (β=.36, p=.02), but not near-crashes (β=.29, p=.07) compared to non-medicated drivers. Medicated drivers with ADHD did not differ from non-medicated drivers with ADHD on any driving outcomes (*all* p>.08). Only drivers with Depression who stopped medication experienced more crashes (β=.57, p=.01). Other antidepressant subgroups did not differ from one another significantly across crashes, near-crashes, or at-fault crashes/near-crashes (*all* p>.32).

Direct Effects of Medication Status on CPT-II Neurocognitive Factors (a pathways). Drivers with ADHD/Depression on medication did not differ from non-medicated drivers on Disinhibition (p=.40), Endogenous Orienting (p=.10), Arousal Decrements (p=.51), or Vigilance Decrements (p=.22). Medicated drivers with ADHD did not differ from non-medicated drivers with ADHD on any neurocognitive factors (*all*

p>.41). Drivers with Depression who started antidepressants demonstrated less Disinhibition compared to other antidepressants subgroups (β=-.31, *p*=.03). Differences among subgroups did not emerge on Endogenous Orienting (*all p*>.08), Arousal Decrements (*all p*>.15), or Vigilance Decrements (*all p*>.33).

Direct Effects of CPT-II Neurocognitive Factors on Future Driving Outcomes (b pathways). Neurocognitive factors did not predict crash count (*all p*>.14), near-crash count (*all p*>.45), or at-fault crashes/near-crashes (*all p*>.45) when drivers with ADHD/Depression on medication were compared to non-medicated drivers. Similarly, neurocognitive factors did not predict future crash risk in models comparing medicated to non-medicated drivers with ADHD (*all p*>.13). Differences did not emerge in models comparing antidepressant subgroups (*all p*>.12).

Indirect Effects of Medication Status on Future Driving Outcomes (ab pathways). Medication status did not exert an indirect effect on future crash, near-crash, or at-fault crash/near-crash risk when drivers with ADHD/Depression on medication were compared to non-medicated drivers (All 95%CI Include Zero). Results were consistent when comparing medicated and non-medicated drivers with ADHD (All 95%CI Include Zero) and Depression (All 95%CI Include Zero) separately.

Residual Effects of Medication Status on Future Driving Outcomes (c' pathways). After accounting for effects described above, drivers with ADHD/Depression who were medicated had more crashes (β=.24, *p*=.01) and at-fault crashes/near-crashes (β=.37, *p*=.02), but not near-crashes (*p*=.07) when compared to non-medicated drivers. When medicated drivers with ADHD were compared to non-medicated drivers with ADHD, significant differences did not emerge in future crash (*p*=.11), near-crash (*p*=.17),

or at-fault crash/near-crash (p=.09) risk. Crash risk was associated with only drivers who stopped antidepressant medication throughout the course of the study (β=.61, p=.004). Significant differences did not emerge across any other crash-risk outcome (*all* p>.14) in models comparing antidepressant subgroups (*all* p>.30).

Discussion

The present study examined whether vulnerabilities in neurocognitive mechanisms of attention and inhibition, as measured by the CPT-II (Conners, 2000), are possible pathways through which ADHD symptoms impact future crash risk. The Conners CPT paradigm provides performance indicators of Disinhibition, Endogenous Orienting, Arousal Decrements, and Vigilance Decrements, which are considered foundational cognitive mechanisms for both basic and complex aspects of motor vehicle driving (Barkley & Cox, 2007; Posner & Petersen, 1990; Ranney, 1994). Through a dimension reduction approach using performance variables yielded by the CPT-II, the role of specific sub-components of attention (Endogenous Orienting, Arousal Decrements, Vigilance Decrements) and Inhibition were identified and examined (Riccio et al., 2002; Petersen & Posner, 2012). Further, the present study extended previous research on driving behavior in high incidence psychopathology through its longitudinal, prospective design and objective assessment of on-road future crash risk. Overall, ADHD symptoms were implicated both directly and indirectly, through underlying deficits in endogenous orienting, in portending future crashes, near-crashes, and at-fault crashes/near-crashes.

Consistent with previous research, ADHD symptoms at study entry prospectively predicted crashes, near-crashes, and at-fault crashes over the course of 1 to 2 years

(Aduen et al., *Under Review*; Cox, Madaan, & Cox, 2011; Vaa, 2014), continuing to position ADHD as a risk factor for adverse driving outcomes. ADHD symptoms of inattention, organization, and impulsivity were significantly related to CPT-II derived factors of Disinhibition, Endogenous Orienting, and Arousal Decrements, but not Vigilance Decrements, which provides evidence that behavioral sequelae of ADHD are associated with poorer neurocognitive performance (Barkley, 1991; Epstein et al., 2003; Weaver et al., 2009). Importantly, findings elucidate how specific cognitive endophenotypes relate to core ADHD symptoms (Doyle et al., 2005; Gau & Shang, 2010). Further, current results provided evidence for different components of attention subserving separate aspects of crash risk.

The CPT-II derived Endogenous Orienting construct portended future crashes and culpability for driving errors that led to crashes/near-crashes, while decrements in vigilance predicted near-crashes. Returning to Posner and Petersen's (1990) model of attention, endogenous orienting refers to selectively focusing (e.g., top-down processing) on visual input and, as such, also implicitly involves a trait level of high alertness. The derived CPT-II Endogenous Orienting factor captured this construct through omission errors and response time consistency throughout the duration of the task. Therefore, one potential explanation is that orienting is critical to detecting immediate changes in the driving environment. Deficits in this component of attention would make it more difficult for drivers to detect danger or maneuver successfully in response to high-risk road situations (Brouwer, 2002).

Conversely, decrements in vigilance or sustained attention, referred to by Posner and Petersen (1990) as maintaining a state of alertness across a prolonged span of time,

were associated with near-crash risk. The derived CPT-II Vigilance Decrements variables captured changes in reaction time and response accuracy over time. Managing imminent driving situations is heavily dependent on physiological state of alertness (Collet et al., 2005; Mehler et al., 2009). It is possible that individuals with weaknesses in vigilance become less alert to changing driving conditions after prolonged periods of time, but in the context of sufficient phasic alertness are able to reorient and respond (e.g., braking, accelerating, turning wheel abruptly) quickly enough to avoid the imminent crash. Critical driving situations are associated with a physiological response that increases arousal (Collet et al., 2005), thus, this elicited change in physiological state may provide a window for drivers to successfully maneuver or prevent an imminent crash.

Exploratory analyses examining differences in neurocognitive performance between drivers with ADHD, Depression, and no known psychopathology revealed that drivers with high incidence psychopathology generally showed more deficits in endogenous orienting, suggesting a trans-diagnostic impairment in inattention (Nolen-Hoeksema & Watkins, 2011; Snyder, Miyake, & Hankin, 2015). Findings support the notion that overlap in this specific component of attention for both individuals with ADHD and Depression can represent considerable functional impact on tasks such as driving (Biederman et al., 2007; Wickens, Smart, & Mann, 2014).

Further, drivers with ADHD were more likely than Healthy Control drivers to experience future crashes, and showed more deficits in inhibition and arousal. Conversely, drivers with Depression were at heightened risk for near-crashes and showed unique impairment in vigilance decrements, compared to both drivers with ADHD and no known psychopathology. These findings suggesting increased risk for adverse driving

outcomes across high incidence psychopathology are consistent with past studies (Aduen et al., 2015; Vaa, 2014). Differential patterns of performance on derived CPT-II factors indicate that despite having trans-diagnostic deficits in endogenous orienting attention, ADHD and Depression also have disorder-specific impairments in sub-components of attention and other aspects of cognition (Bulmash et al., 2006; Fuermaier et al., 2015; Groom et al., 2015). Although indirect effects did not reach significance in the present study when comparing clinical groups, future studies are warranted to examine how disorder-specific cognitive impairments may have unique implications for functional driving outcomes.

Final exploratory analyses investigating medication effects revealed differences between medicated and non-medicated drivers with ADHD/Depression on markers of neurocognitive functioning and crash risk. Medicated drivers with Depression showed better inhibitory control than un-medicated drivers. Most notably, drivers with ADHD/Depression who reported being on medication either at study entry or exit experienced more future crashes and at-fault crashes compared to non-medicated drivers. This finding is unexpected given that previous studies have shown a reduction in crash risk associated with active treatment (Barkley & Cox, 2007; Cox et al., 2004). Because ADHD medication has well-documented benefits for motor vehicle driving, current results may reflect inconsistent adherence, interactions between unmedicated symptom severity and treatment status, and/or driving events that occur when medication is not metabolically active (Barkley & Cox, 2007; Cox, Madaan, & Cox, 2011). It must also be considered that the literature has been mixed regarding the effect of antidepressants on driving risk, with some studies finding cognitive side effects (e.g., attention, psychomotor

impairment) that may impact driving ability (Sansone & Sansone, 2009; Wingen et al., 2006). Alternatively, the trend toward increased crash risk in medicated drivers may also reflect effects of unmeasured factors such as severity and when treatment began within the driving monitoring period.

Of primary interest was the extent to which ADHD behavioral symptoms predicted future driving risk through their association with cognitive constructs of attention and disinhibition. Endogenous orienting was consistently implicated as the cognitive mechanism through which ADHD symptoms exerted their effect on crashes, near-crashes, and crash/near-crash culpability, while disinhibition, arousal decrements, and vigilance decrements failed to reach significance. That orienting –the capacity to attend to and select exogenous stimuli from the environment –mediated the relations between ADHD symptoms and all prospective markers of crash risk highlights the foundational nature of this cognitive mechanism to driving behavior (Michon, 1985; Barkley, 2004). The consistency of this finding in predicting not only future crashes, but also near-crashes and fault, suggests that deficits in top-down processing aspects of attention may be a primary contributor to crash risk. These findings are consistent with simulator studies that have shown that attention lapses or off-road glances often precede adverse driving outcomes, predict more driving errors, and interfere with successful avoidance of crashes (Barkley & Cox, 2007; Cox et al., 2004; Jerome, Habinski, & Segal, 2006). Implications for deficits in orienting attention are vast given that it is considered integral to operational aspects of driving performance and may be exacerbated in more complex driving scenarios involving increased passenger, road, and traffic demands (Barkley, 2004). Vulnerabilities in orienting also increase the potential for increased

distractibility to secondary tasks (Reimer et al., 2006; 2007; 2010), which becomes particularly problematic given increased use of cellular telephones and in-vehicle technology while driving (El Farouki et al., 2014; Kingery et al., 2015; Narad, Garner, & Brassell, 2013; Reimer et al., 2010).

Despite decrements in vigilance portending future near-crashes, deficits in traits of tonic and phasic alertness failed to explain the relation between ADHD symptoms and crash risk. It is possible that behavioral symptoms of inattention in ADHD, such as increased distractibility and difficulty engaging and disengaging attention, as they relate to driving errors are better understood through weaknesses in exogenous and endogenous orienting, as opposed to a general dampening of arousal (Dingus et al., 2016; Fuermaier et al., 2015; Huang-Pollock & Nigg, 2003). Further, disinhibition also failed to explain the relations between ADHD symptoms and future crash risk. Although the literature has been mixed in its conclusions regarding inhibition deficits in ADHD (Alderson et al., 2007; Lijffijt et al., 2005; Nigg, 2001), this finding was surprising given that self-report and neurocognitive measures of inhibition have been found to have moderate associations with increased motor vehicle accidents, traffic violations, and driving errors (Biederman et al., 2007; Bioulac et al., 2016; Groom et al., 2015).

In both of these cases, it is possible that findings may have been impacted by construct measurement. Prior studies have utilized several neuropsychological assessment measures to assess the construct of alerting (e.g., Test of Attentional Performance [TAP]; Conners Continuous Performance Task [CPT]) and inhibition (e.g., Stroop Color-Naming Test, Wisconsin Card Sorting Test [WCST]), which may have influenced and contributed to discrepant results (Bioulac et al., 2016). Moreover, with

one exception (Merkel et al., 2013), studies that have found significant associations between behavioral inhibition and driving errors have assessed driving through cross-sectional, simulator designs (Barkley et al., 2002; Bioulac et al., 2016; Groom et al., 2015; Jongen et al., 2011). The simulated driving framework analyzes pre-programmed driving scenarios and tasks, which makes it possible to parse out cognitive deficits that may lead to specific driving errors. However, despite being more sensitive to cognitive weaknesses and driving errors, results from simulator studies often do not align with analysis of on-road driving behavior (Fuermaier et al., 2015; Lundqvist et al., 2000). The current study's large sample and methodological refinements of assessing driving risk prospectively and objectively increase confidence and generalizability of conclusions regarding how cognitive deficits contribute to future crash risk.

Limitations

The present study sought to better understand the cognitive mechanisms that underlie prospective crash risk as a function of clinical status. In doing so, multiple components of neurocognition were examined as mechanisms through which ADHD symptoms predict increased future risk for criterion-based, objectively-measured crashes, near-crashes, and crash culpability. Despite the study's methodological refinements in understanding mechanisms underlying driving risk in ADHD, the following caveats must be considered when interpreting the results. Only one neurocognitive assessment measure, the CPT-II (Conners, 2000), was used to characterize inhibition and attention processes. Although a dimension reduction approach allowed for distinct cognitive mechanisms to be derived from this task, it is unknown how constructs would compare if multiple assessment measures were used to assess each neurocognitive component

(Miyake et al., 2000). Additionally, the CPT-II (Conners, 2000) test-retest reliability is variable for some performance scores, which could have weakened our factors. Further, although the present study found that the CPT-II measures several sub-components of attention – many corresponding with Posner and Petersen's (1990) three-network model – it is unclear how results from the present study will compare to other studies using measures based on this well-developed model of attention (Fan et al., 2002; Posner & Petersen, 1990; Weaver et al., 2009).

Although known risk factors for adverse driving outcomes were controlled, including demographic variables and miles driven, other factors that could have impacted test administration and performance were unavailable. Current analysis of medication effects was limited to only drivers with ADHD and Depression who reported medication at study entry and exit. These exploratory analyses were further limited by lack of examination of proximal risk factors for crashes, such as *in situ* driver behaviors, cell phones, substance use, medication formulation, and whether medication was active at the time of a crash. The naturalistic study design precluded clinical interviewing regarding perceived medication efficacy, emergent effects, or timing in relation to crashes, and thus informs protective effects of medication treatment-as-usual rather than optimal dosing. Lastly, we were unable to replicate previous CPT-II factor structures (Bytoft et al., 2017; Vertinski et al., 2014) and the use of exploratory methods may have weakened associations among our neurocognitive predictors and outcomes.

Clinical and Research Implications

Overall, present results provide evidence that inattention, specifically endogenous orienting attention, mediates relations between ADHD symptoms and future risk for

crashes, near-crashes, and crash/near-crash culpability. Importantly, a 14-minute visual-motor attention and inhibition task was found to not only be predictive of adverse driving outcomes 1 to 2 years later following initial assessment, but also highlighted a mechanism through which ADHD symptoms portend higher risk for poor driving outcomes of ranging severity (e.g., near crashes, crashes). This creates an important opportunity for clinicians to assess, intervene, and make recommendations based on the specific findings of this task as it relates to driving. Future studies are warranted to examine *in-situ* driving behaviors to better characterize the inattentive errors that lead to increased crashes (e.g., eyes of road, looking at objects outside/inside the car, adjusting in-vehicle devices, using technology). Determining whether similar behaviors precede crashes across ADHD severity levels will be helpful for developing transdiagnostic and disorder-specific interventions to reduce adverse driving outcomes. Identifying inattention as a key mechanism through which risk is transmitted has significant public health implications for designing effective preventative intervention methods (e.g., driver training, technology-enhanced accommodations, vehicle adaptations). Implementation of these interventions has the potential to reduce the social, financial, health, and legal outcomes associated with motor vehicle collisions for drivers with high incidence disabilities such as ADHD.

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Table 1. Driver Demographic Data by Diagnostic Grouping

	Overall Sample (N=3,226)		ADHD (N=274)		Depression (N=249)		Healthy Control (N=1,806)		Clinical Subgroup Chi-square
	M	SD	M	SD	M	SD	M	SD	
Miles Driven	9527.9	7315.8	9874.2	7346.9	9716.6	6846.1	9390.9	7510.0	p=.53, *ns*
Days Monitored	440.49	210.65	423.39	202.68	442.17	210.34	439.85	213.36	p=.46, *ns*
BAQS ADHD Score	3.20	2.18	7.43	2.57	3.39	1.63	1.86	1.01	p<.0005
Percent involved in									
No crashes	70.3%		58.8%		64.7%		72.8%		p<.001
Single crash	19.9%		23.4%		21.7%		19.1%		
Multiple crashes	9.8%		17.9%		13.7%		8.1%		
No near-crashes	61.7%		52.2%		52.2%		64.4%		p<.001
Single near-crash	21.7%		25.5%		24.5%		20.8%		
Multi. near-crashes	16.6%		22.3%		23.3%		14.8%		
Age Group	N	%	N	%	N	%	N	%	p<.005
16-17	258	8.0	40	14.7	13	5.2	126	7.0	
18-20	520	16.1	71	26.0	39	15.7	248	13.8	
21-25	597	18.5	77	28.2	53	21.3	280	15.5	
26-35	327	10.1	25	9.2	25	10.0	192	10.6	
36-50	349	10.8	25	9.2	38	15.3	198	11.0	
51-65	383	11.9	11	4.0	37	14.9	234	13.0	
66-75	345	10.7	12	4.4	28	11.2	213	11.8	
75+	442	13.7	12	4.4	16	6.4	312	17.3	
Not reported	5	0.2	1	0.004	0	0.0	3	0.002	
Gender									p<.005
Male	1537	47.6	131	48.3	75	30.4	900	50.3	
Female	1661	51.5	140	51.7	172	69.6	890	49.7	
Missing	28	0.9	3	0.01	2	0.001	16	0.001	
Education									p<.005
Some high school	271	8.4	39	14.3	14	5.7	126	7.0	
H.S. graduate	1241	38.5	118	43.2	100	40.5	660	36.8	
College degree +	1692	52.4	116	42.5	133	53.8	1006	56.1	
Not reported	22	0.7	1	0.003	2	0.001	14	0.008	
Marital Status									p<.005
Not Married	1989	61.7	211	77.9	162	65.3	1054	58.9	
Married	1207	37.4	60	22.1	86	34.7	734	41.1	
Not reported	30	0.9	3	0.01	1	0.004	18	0.001	
Annual Income									p=.04
Under $29K	556	17.2	60	21.9	52	20.9	282	15.6	
$30K to $39K	378	11.7	26	9.5	27	10.8	233	12.9	
$50K to $69K	537	16.6	36	13.1	39	15.7	297	16.4	
$70K to $99K	551	17.1	36	13.1	44	17.7	316	17.5	
$100K to $149K	462	14.3	37	13.5	36	14.5	258	14.3	
$150K or higher	219	6.8	28	10.2	14	5.6	133	7.4	
Not reported	523	16.2	51	18.6	37	14.9	287	15.9	

Note. *BAQS = Barkley Adult ADHD Quick Screen*.

Table 2. *Principal Component Analysis (PCA) Results for CPT-II; 4-Factor Solution, Varimax Rotation (N = 3,138)*

		Factor Loadings			
Description	Variable	Disinhibition	Orienting	Arousal Decrements	Vigilance Decrements
Incorrect responses to non-targets (i.e., letter X)	Commissions	**.92**	.17	-.04	.09
Discrimination between non-targets and targets (i.e., all other letters)	Detectability (D')	**.90**	.17	-.04	.06
Response speed for non-perseverative responses, in milliseconds	HRT	**-.77**	.40	.21	.04
Speed-versus-accuracy trade-off	Beta	**-.53**	.41	-.09	-.05
Within respondent response speed consistency	Variability	-.06	**.79**	.23	.18
Response speed consistency across duration of test	HRT SE	-.29	**.77**	.41	.11
Responses made in less than 100 milliseconds	Perseverations	.14	**.67**	-.10	.12
Missed targets (i.e., non-X's)	Omissions	.03	**.63**	-.11	-.22
Average reaction time at 1, 2, or 4 second ISIs	HRT ISI Change	-.03	.06	**.84**	-.03
Change in SE of reaction times at 1, 2, or 4 second ISIs	HSE ISI Change	-.06	-.01	**.84**	.06
Change in reaction time across duration of test	HRT Block Change	.04	.04	-.01	**.86**
Changes in response consistency across duration of test	HRT SE Block Change	.07	.04	.050	**.86**
	Eigenvalues	3.18	2.33	1.54	1.36
	% of variance	26.47	19.38	12.81	11.29

Note. Factor loadings ≥ .45 are bolded; HRT= Hit Reaction Time; SE= Standard Error; ISI= Interstimulus Interval.

Table 3. Partial Correlations (correcting for covariates including age, gender, education, marital status, time in study, miles driven)

		1	2	3	4	5	6	7	8	9	10
1	Disinhibition	1									
2	Endogenous Orienting	.061**	1								
3	Arousal Decrements	.015	-.012	1							
4	Vigilance Decrements	-.004	.000	.004	1						
5	Crash Count	.004	.043*	-.024	-.013	1					
6	Near-Crash Count	.008	.034	-.014	-.040*	.246**	1				
7	Fault Count	.004	.045*	-.014	-.025	.737**	.732**	1			
8	Crash Fault Count	.002	.038*	-.021	-.009	.958**	.231**	.748**	1		
9	Near-Crash Fault Count	.005	.034	-.004	-.029	.291**	.874**	.843**	.274**	1	
10	BAQS Score	.070**	.086**	.043*	-.014	.058**	.054**	.072**	.061**	.055**	1

*Note. *= p< .05, **= p<.001.*

Figure 1. ADHD Symptoms (BAQS Score) predictor and neurocognitive mediators of crashes, near-crashes, and at-fault crashes/near-crashes. Four neurocognitive mediators, (1) Disinhibition, (2) Endogenous Orienting, (3) Arousal Decrements, (4) Vigilance Decrements, were uncorrelated by design and tested simultaneously. All models controlled for age, gender, education, marital status, time in study, and miles driven. Significant pathways (*) shown in black font; non-significant (*ns*) pathways shown in grey font. Results are reported as β (SE). ER = Effect Ratio (shown only for significant indirect effects).