Investigating the autonomic nervous system and cognitive functions as potential mediators of an association between cardiovascular disease and driving performance

Jeffrey Gaudet, M.Sc. ©, Mathieu Bélanger, Ph.D., Hélène Corriveau, pht, Ph.D., Said Mekary, Ph.D.©, Dean Hay, Ph.D., Michel Johnson, Ph.D.

Research was conducted at the Université de Moncton, CEPS Louis-J. Robichaud, 18 avenue Antonine-Maillet, Moncton, N-B, Canada

Corresponding author: Michel J. Johnson
Université de Moncton, CEPS Louis-J. Robichaud
18 avenue Antonine-Maillet, Moncton, N-B, Canada, E1A-3E9
Phone: (506)858-4811
Fax: (506)858-4308
michel.johnson@umoncton.ca

Abstract

Cardiovascular disease (CVD) impacts the autonomic nervous system and cognitive functions related to activities of daily living, including driving an automobile. Although CVD has been linked to unsafe driving, mechanisms underlying this relationship remain elusive. The aim of this study was to examine the role of cognitive functions and the autonomic nervous system as potential mediators of driving performance. Nineteen individuals having recently suffered a cardiac event and sixteen individuals with no history of CVD completed a simulated drive using a STISIM simulator to assess driving performance. Heart rate was recorded throughout testing using a Polar RS800CX heart rate monitor and measures of executive, orienting and alerting functions were obtained through the Attention Network Test. We used the Baron and Kenny analysis method to assess potential mediating effects of the relationship between CVD and driving performance. Executive function was the only potential mediator investigated to be associated with driving ($p < 0.01$) and CVD ($p < 0.05$), however, it did not appear to play a mediating role ($p = 0.28$). These results suggest that individuals with CVD exhibit decrements in complex cognitive tasks such as driving and that further research is needed to better understand the mechanisms underlying this relationship.

Keywords: Cardiovascular disease, Automobile Driving, Executive Function, Autonomic Nervous System, Driving Simulator, Visual Attention, Mediation Analysis

1. Introduction

Cardiovascular disease (CVD) is one of the most prevalent diseases in North America (Roger et al., 2011; Tracking Heart Disease and Stroke in Canada, 2009). Between the United States and Canada, a conservative estimate suggests that over 28 million individuals suffer from CVD (Public Health Agency of Canada, 2009; Roger et al., 2011). Approximately 20% of North Americans over the age of 65 declare having been diagnosed with CVD (Fang et al., 2011; Public Health Agency of Canada, 2009). Cardiac patients are often afflicted by an impairment of their autonomic nervous system (ANS), which is characterized either by an increase in sympathetic function, a decrease in parasympathetic function, or both (Thayer et al., 2010). Impaired ANS function has been linked to several types of CVDs, including coronary artery disease, ischemic heart disease, and heart failure (Musialik-Lydka et al., 2003; Rothschild et al., 1988; Schroeder et al., 2003; Wennerblom et al., 2000).

The ANS plays important regulatory roles during both physiological and psychological stresses. Activation of the ANS has been reported to occur during cognitive testing involving abilities such as attention, memory and executive function (Hansen et al., 2003; Moses et al., 2007; Mukherjee et al., 2011; Redondo et Del Valle-Inclan, 1992). A link between cognitive function and the ANS is also strongly supported by neuroimaging studies which have shown an activation of the prefrontal cortex during both periods of increased cognitive function and ANS stimulation (Chambers et al., 2006; Chikazoe et al., 2007; Garavan et al., 1999; Gianaros et al., 2004; Konishi et al., 1999; Lane et al., 2001; Lane et al., 2009; Thayer et al., 2009). Other studies also demonstrated that baseline activity of the ANS is associated to cognitive performance (Hansen et al., 2003; Porges et al., 1992; Thayer et al., 2009). Higher parasympathetic activity at rest has been

associated with better performance on memory, conflict resolution, general intelligence, attention and executive function tasks (Hansen et al., 2003; Jennings et al., 2002; Melis et van Boxtel, 2001; Vincent et al., 1996). In contrast, lower levels of resting parasympathetic function have been related to poorer attention and executive function tasks during both stressful and non-stressful situations (Hansen et al., 2009).

CVD has been documented to have adverse outcomes on the brain such as white matter lesions, losses in gray matter volume, and decrease in cerebral blood flow (Almeida et al., 2008; Bisschops et al., 2004; de Leeuw et al., 2001; Longstreth et al., 1996). Individuals with CVD have also been shown to exhibit decrements in cognitive functions such as attention, executive function, memory and verbal learning (Moser et al., 1999; Okonkwo et al., 2010; Silbert et al., 2007; Singh-Manoux et al., 2003; Vogels et al., 2007). Although the cognitive decrements observed among cardiac patients would not typically be sufficient to lead to a diagnosis of dementia or mild cognitive impairment, even subtle decreases in cognitive function may negatively impact complex cognitive tasks (Wadley et al., 2008), such as automobile driving.

Driving is a highly complex task that relies on a variety of cognitive functions such as attention, executive function, working memory, processing speed and reaction time in a large variety of conditions (Anstey et al., 2005). Although no mechanism has been identified, collision statistics have demonstrated that CVD is associated with an increased crash risk ranging from 30 to 75% (Charlton et al., 2004; Dobbs, 2005; Vaa, 2003). To our knowledge, only one study has directly looked at driving in a cardiac population and their results suggest that changes in cognitive function may play a role in reduced driving performance after cardiac surgery (Ahlgren et al., 2003).

Because of its integrated role in cognitive function and its impairment in various forms of CVD, the ANS may also be part of the causal pathway between CVD and driving performance. In this context, the aims of the present study were to examine the relationship between CVD, ANS function, cognitive function, and driving; and more specifically to verify if the relationship between CVD and driving is mediated by the ANS or cognitive function. We hypothesized that 1) individuals with CVD would perform poorer on driving than individuals with no history of CVD, and 2) the relationship between CVD and driving would be influenced by cognitive function and the ANS.

2. Material and methods

2.1 Participants and design

Cardiac patients were recruited from a local cardiac rehabilitation program, and through advertisement. Healthy individuals with no history of CVD were also recruited to serve as a comparison group. To be enrolled in the study, participants had to be over 50 years old, possess a valid driver's license and drive regularly (at least once a week). Additionally, participants in the cardiac group had to have suffered a cardiac event including myocardial infarction, coronary artery by-pass graft, percutaneous coronary intervention, or angina in the past 6 months. Exclusion criteria for both groups included a pacemaker implant, history of manifest stroke, epilepsy, and neurological diseases (e.g. Dementia, Alzheimer's disease, Parkinson's disease, and Schizophrenia). All participants provided informed written consent for this study as approved by the Université de Sherbrooke, Université de Moncton and Vitality Health Network Research Ethics Boards.

2.2 Variables and instruments

2.2.1 Heart rate variability

Evaluation of heart rate variability (HRV) was used to quantify autonomic nervous system activity (Tsuji et al., 1996). The sensitivity of HRV to changes in physical and psychological stress makes it a popular non-invasive method of quantifying the ANS among clinicians and researchers (Freeman, 2006; McArdle et al., 2007). Specifically, R-wave intervals (time between consecutive heart beats) were recorded using a Polar RS800CX heart rate monitor (Polar Electro OY, Kempele, Finland). Validity of the Polar monitors to record RR intervals has been confirmed against 12-lead (Porto et Junqueira, 2009), 5-lead (Weippert et al., 2010), 3-lead (Kingsley et al., 2005), and 2-lead (Gamelin et al., 2006) electrocardiographs (correlations ranging from 0.88 to 0.99). Heart rate data was continuously recorded throughout the study procedures at a sampling frequency of 1000Hz, providing a temporal resolution of 1 ms for each R-R period. LabChart 7 (ADInstruments, Toronto, Canada) was used to inspect the data, ensure correct R-wave identification and eliminate erroneous markers. We removed artifacts (<5ms or >2000ms) from the data and treated all other signals as normal intervals since a review of the R-R waves and the Poincaré plot revealed consistent rhythms. ~~Ectopic beats, as classified by the default LabChart setting as an R-R interval <600ms or >1000ms, were treated as normal intervals for this study.~~ Standard deviations of R-R intervals (SDNN) and the root mean square of successive differences (RMSSD) were then derived from time domain analysis in accordance with current recommendations from the European Task Force (Malik et al., 1996). Using the fast Fourier Transformation (FFT), the power spectrum for frequency domain HRV analysis was divided into three bands: very low frequency (VLF 0.0033–0.04Hz), low frequency (LF 0.04–0.15Hz) and high frequency (HF 0.15–0.40Hz) (Malik et al.,

1996). Only SDNN, RMSSD, LF, HF in absolute and normalised (LFnu, HFnu) units and LF:HF ratio were used for statistical analysis.

2.2.2 Attention

Three components of the human attention model were evaluated: alerting, orienting and executive function. The Attention Network Test (ANT) (Fan et al., 2002) provides measures for these three components within a single task administered with a computer screen and the arrow buttons of a standard keyboard. The ANT is a good predictor of simulated driving performance ($r^2 = 0.564$) and it is strongly associated with the Useful Field of View (UFOV) test ($r = 0.828$), a gold standard of neuropsychological driving tests (Weaver et al., 2009). ANT data were collected using a java program downloaded from Lakehead University's Center for Research on Safe Driving website (http://crsd.lakeheadu.ca/crsd-ant/). This shorter version of the ANT (CRSD-ANT) takes approximately 10 minutes to complete, compared to 30 minutes for the original version of ANT. The construction of the CRSD-ANT is identical to the original ANT (Fan et al., 2002; Weaver et al., 2009), except for a lower number of trials (1 block of 30 practice trials and 2 blocks of 62 trials). A comparison of the CRSD-ANT and the original ANT indicates correlations ranging from 0.88 and 0.91 for the various measures included in the ANT (Weaver et al., 2012, data not yet published).

2.2.3 Driving simulation

The same certified driving evaluator assessed driving performance for all participants. This was done during a simulated drive using the Manitoba Road Test form, a standardized demerit-based scoring system based on the Province of Manitoba evaluation procedure (Bédard et al., 2008). Demerit points were assessed for infractions falling in five general categories

(starting/stopping/backing, signal violations/right of way/inattention, moving on roadway, passing/speed, and turning). Either 5 or 10 demerits were assessed for each infraction, depending on severity. Total score was obtained by calculating the sum of infractions observed by the evaluator (higher score corresponding to lower performance). Supporting the use of a simulator in conjunction with an evaluation grid typical for on-road testing, Bédard et al. (2010) demonstrated a strong correlation between demerit points obtained from simulator (similar to the one used in this study) and on road evaluations (r=.74, p=.035). Participants completed a driving course on the simulator following pre-recorded auditory directions, while the evaluator was seated behind them at a workstation evaluating the drive. Simulated drives were done on a fixed base driving simulator (STISIM Drive® Model 100) consisting of steering wheel with horn, foot pedals (brake and accelerator), and signal indicators, with the driver's view presented across a 20 inch monitor. Typical dashboard instruments, including speedometer and tachometer, were presented on the monitor screen. The monitor was positioned approximately 80 cm in front of the driver's seat. The monitor provided a 45 degree field-of-view at any one time. A rear-view mirror was displayed in the central upper portion of the monitor, and side-view mirrors were displayed on the lower outer portions of the monitor. The simulated courses were designed using STISIM Drive™ software (Systems Technology, Inc., California, USA). A 3.1 km orientation drive was used to familiarise participants with the simulator. The 5 minute course included highway and residential sections, as well as external environmental cues such as traffic signs and signals. The 12.2 km, or approximately 20 minute, test drive was a reproduction of a standard road test route for obtaining a driver's licence (identical to the route utilised previously by Johnson et al (2011) and Weaver et al. (2009)). In addition to attenuating feasibility and safety concerns, the simulator also improves comparability of conditions for all participants.

2.3 Data analysis

We used the four steps of the Baron and Kenny (1986) method to assess the mediating effects of HRV and ANT on the relationship between CVD and driving performance. The procedure was repeated for each potential mediator (single mediation analysis). In the first step, we used a regression model to examine the association between CVD (yes or no) and driving performance. The second step included a regression looking at the association between CVD and the potential mediators (HRV and ANT derived variables) (Cerin et al., 2006). In step three, we used regression models to describe associations between the potential mediators (HRV and ANT) and driving performance. For the final step, we proceeded with a regression model investigating the contribution of CVD in explaining variation in driving performance when accounting for potential mediators. In this sequential series of regressions, we proceeded to step four, when statistically significant relationships were observed in the first three steps. With this approach, a partial mediation effect is supported when the regression coefficient for the mediator remains significant, and a full mediation effect is supported if the independent variable (CVD) is no longer significant. For each model, we calculated unadjusted and adjusted parameter estimates. Age, sex, education, diabetes, and hypertension are known to be associated with cognitive function (age, education, diabetes, and hypertension) (Duron et Hanon, 2008; Grady, 2012; Jefferson et al., 2011; Reijmer et al., 2010), ANS function (age, sex, diabetes, and hypertension) (Moodithaya et Avadhany, 2012; Schroeder et al., 2003; Zhang et al., 2011) and driving (age, diabetes and hypertension) (Lyman et al., 2002; Marshall, 2008; McGwin et al., 2000). In partly adjusted models, we included age, sex and education as covariates and we additionally included diabetes and hypertension in the fully

adjusted models in order to control for possible confounding influences. Data were analysed with the SAS statistical package version 9.1 (SAS Institute Inc, Cary, NC, USA).

3. Results

Nineteen participants with cardiovascular disease and sixteen participants with no history of cardiovascular disease were enrolled in this study. Two cardiac participants were unable to complete the driving test due to simulator sickness symptoms, and uncontrollable technical problems resulted in the loss of HRV data of four cardiac and one control participants, leaving 33 and 30 participants for the driving performance and HRV related analyses, respectively. All participants in the cardiac group had some form of cardiovascular event in the last six months, including myocardial infarction [13 (68 %)], PCI [14 (74 %)], CABG [3 (16 %)], and angina [3 (16 %)]. There were no meaningful differences between participants in the cardiac and control group in terms of their age, sex distribution, driving experience, and the various measures of resting HRV and ANT (Table 1). On average, participants in the control group had higher levels of education than participants in the cardiac group. The prevalence of hypertension was marginally higher among the cardiac participants. The cardiac group also had a higher average number of demerit points, which was indicative of poorer driving performances, when compared to the control group.

(Insert table 1)

3.1 Assessment of Mediators of the Relationship between CVD and Driving Performance

STEP 1: The between group difference in driving performance was statistically significant, including after adjustments for potential confounding variables (Table 2). STEP 2: There were no

significant difference in components of ANT or HRV between participants in the cardiac and control groups in unadjusted models. However, models adjusted for age, sex, education, hypertension, and diabetes suggested that participants in the cardiac group had poorer executive function than participants in the control group. Statistical adjustments did not lead to between group differences for the other components of the ANT and all components of HRV. STEP 3: The executive function score was significantly positively related to driving performance in the adjusted and unadjusted models (table 3). Executive function was the only component of ANT or HRV to have a statistically significant relationship with driving. STEP 4: For the final step of the mediation analysis, only executive function was investigated as a potential mediator of the relationship between cardiovascular disease and driving performance. In this final model, executive function did not contribute to explaining variance in driving performance (Table 4).

(Insert table 2)

(Insert table 3)

(Insert table 4)

4. Discussion

This is the first study to compare the driving performance of cardiac and healthy individuals using a simulated driving task. Our results suggest that individuals with CVD perform worse than their healthy counterparts during a simulated driving task which is consistent with observational studies (Charlton et al., 2004; Dobbs, 2005, Vaa, 2003). Our results nevertheless contrast with a study which noted a deterioration of driving abilities following CABG and PCI during on-road testing, but not during the simulated driving evaluation (Ahlgen et al., 2003). This discrepancy may be attributable to the method used to evaluate simulator driving in this previous study, which

consisted of looking at measures generated by the simulator such as speed, lateral position, reaction time and time to collision. In contrast, our evaluation is consistent with on-road driving evaluation parameters, which may be more sensitive to driving performance in this clinical population while using a simulator.

In this study, executive function was the only cognitive component to be related to driving performance. This is consistent with the driving literature, which suggests that executive function is one of the more strongly correlated cognitive functions to driving (Anstey et al., 2005; Asimakopulos et al., 2011; Ranney, 1994). Executive function has been associated with driving outcome in several populations including young drivers, older adults, individuals with early-stage cognitive decline, multiple sclerosis, stroke, Alzheimer's disease, Parkinson's and dementia (Anstey et al., 2011; Barkley et al., 2002; Daigneault et al., 2002; Lafont et al., 2010; Lincoln et Radford, 2008; Mantyla et al., 2009; Marshall et al., 2007; Ranchet et al., 2011; Whelihan et al., 2005). Our observation of poorer executive efficiency among participants with CVD is also consistent with reports of cognitive decrements associated with a variety of cardiovascular related risk factors (ex: smoking, hypertension, obesity, etc.) and diseases (ex: coronary artery disease, ischemic heart disease, heart failure, etc.) (Waldstein et Wendell, 2010).

Despite being associated with CVD and driving performance, our analyses suggest that executive function does not play a mediating role in the relationship between CVD and driving. Among the potential explanations for this result, we note first, the possibility that executive function is a confounding factor, being correlated with both the independent and dependent variables while not playing an intermittent role. In this instance, executive function would not be considered a

mechanism in the causal pathway between CVD and driving performance. Second, it is possible that the measure used to assess executive function did not adequately assess the construct of interest as it relates to driving. In this study, executive function was measured as a sub-component of the ANT. The ANT is a repetitive non incremental cognitive task which may be of considerably lower cognitive difficulty than the task of driving. Without appropriate task difficulty, it may be possible for cardiac participants to perform similarly to their healthy counterparts. It is documented that populations susceptible to cognitive decrements can still perform to similar levels as healthy individuals on easy cognitive tasks (Archibald et Fisk, 2000; Carlesimo et al., 1994; Earles et al., 2004). However, when faced with more challenging cognitive tasks, individuals with cognitive decrements generally perform poorer than cognitively healthy individuals (Castel et al., 2009; de Frias et al., 2007; Ewen et al., 2012). We noted relatively small increases in heart rate activity during the ANT, suggesting that the task required little mental effort in comparison with the driving task. It is therefore possible that the ANT test was not challenging enough to sufficiently discriminate between the executive functioning of cardiac and healthy individuals. A third potential explanation for the absence of a mediation effect often relates to limited statistical power. However, an examination of confidence intervals around the parameter estimates suggests that this potential explanation does not apply for this study (not close to being significant).

Limitations of this study include that our cardiac group consisted of a heterogeneous sample of older adults with differing types of CVD, thus limiting our ability to identify factors mediating the relationship between specific CVD and driving. This nevertheless improves the generalizability of our results given our sample had more chances of being representative of the population of older adults with CVD. The small sample size in this study may have ~~also~~ limited our ability to detect

mediating factors; however, the beta coefficients were close to null value suggesting that the factors would have remained non-significant even with a larger sample size. Another limitation is that using a driving simulator may not provide a true measure of driving ability. However, although the perceptual and sensory feel of the simulator mayare not be completely realistic, the driving course as well as the evaluation grid usedutilized in this study allowed us to look at driving performance within the tactical and operational levels that are critical to everyday driving (i.e. following the speed limit, stopping, yielding to the right of way, etc.) Moreover, the simulator we used is associated with levels of presence measures that are similar to those observed with higher end simulators (Johnson et al., 2011). We note the inclusion of individuals with a history of diabetes and hypertension as another potential limitation. Future studies should look to exclude these comorbidities since this would remove the necessity to adjust statistically. Finally, although the finding that executive function was related to driving performance is consistent with the literature, it is possible that this relationship was statistically significant as a result of the multiple tests computed.

5. Conclusions

In summary, this study further supports the hypothesis that CVD is associated with poorer simulator-assessed driving performance. It also suggests that CVD is associated with poorer executive function. However, we could not identify mediators of the relationship between CVD and driving performance through this study. Given the high prevalence of CVD, including among drivers, more research is necessary to develop a better understanding of the mechanisms underlying the relationship between CVD and poorer driving performance.

Acknowledgments

The authors would like to thank Monique Dufour-Doiron and the Coeur en Santé cardiopulmonary rehabilitation center for their assistance in recruiting participants. This study was supported in part by the New-Brunswick Health Research Foundation and the Réseau de recherche en sécurité routière.

References

Ahlgren, E., Lundqvist, A., Nordlund, A., Aren, C., & Rutberg, H. (2003). Neurocognitive impairment and driving performance after coronary artery bypass surgery. *European Journal of Cardio-Thoracic Surgery : Official Journal of the European Association for Cardio-Thoracic Surgery, 23*(3), 334-340.

Almeida, O. P., Garrido, G. J., Beer, C., Lautenschlager, N. T., Arnolda, L., Lenzo, N. P., . . . Flicker, L. (2008). Coronary heart disease is associated with regional grey matter volume loss: Implications for cognitive function and behaviour. *Internal Medicine Journal, 38*(7), 599-606.

Anstey, K. J., & Wood, J. (2011). Chronological age and age-related cognitive deficits are associated with an increase in multiple types of driving errors in late life. *Neuropsychology, 25*(5), 613-621.

Anstey, K. J., Wood, J., Lord, S., & Walker, J. G. (2005). Cognitive, sensory and physical factors enabling driving safety in older adults. *Clinical Psychology Review, 25*(1), 45-65.

Archibald, C. J., & Fisk, J. D. (2000). Information processing efficiency in patients with multiple sclerosis. *Journal of Clinical and Experimental Neuropsychology, 22*(5), 686-701.

Asimakopulos, J., Boychuck, Z., Sondergaard, D., Poulin, V., Ménard, I. and Korner-Bitensky, N. (2011), Assessing executive function in relation to fitness to drive: A review of tools and their ability to predict safe driving. *Australian Occupational Therapy Journal*, 1-47.

Barkley, R. A., Murphy, K. R., Dupaul, G. I., & Bush, T. (2002). Driving in young adults with attention deficit hyperactivity disorder: Knowledge, performance, adverse outcomes, and the role of executive functioning. *Journal of the International Neuropsychological Society : JINS, 8*(5), 655-672.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*(6), 1173-1182.

Bedard, M., Porter, M. M., Marshall, S., Isherwood, I., Riendeau, J., Weaver, B., . . . Miller-Polgar, J. (2008). The combination of two training approaches to improve older adults' driving safety. *Traffic Injury Prevention, 9*(1), 70-76.

Bedard, M. B., Parkkari, M., Weaver, B., Riendeau, J., & Dahlquist, M. (2010). Assessment of driving performance using a simulator protocol: Validity and reproducibility. *The American Journal of Occupational Therapy.: Official Publication of the American Occupational Therapy Association, 64*(2), 336-340.

Bisschops, R. H., van der Graaf, Y., Mali, W. P., van der Grond, J., & SMART study group. (2004). High total cerebral blood flow is associated with a decrease of white matter lesions. *Journal of Neurology, 251*(12), 1481-1485.

Carlesimo, G. A., Fadda, L., Lorusso, S., & Caltagirone, C. (1994). Verbal and spatial memory spans in alzheimer's and multi-infarct dementia. *Acta Neurologica Scandinavica, 89*(2), 132-138.

Castel, A. D., Balota, D. A., & McCabe, D. P. (2009). Memory efficiency and the strategic control of attention at encoding: Impairments of value-directed remembering in alzheimer's disease. *Neuropsychology, 23*(3), 297-306.

Cerin, E., Taylor, L. M., Leslie, E., & Owen, N. (2006). Small-scale randomized controlled trials need more powerful methods of mediational analysis than the baron-kenny method. *Journal of Clinical Epidemiology, 59*(5), 457-464.

Chambers, C. D., Bellgrove, M. A., Stokes, M. G., Henderson, T. R., Garavan, H., Robertson, I. H., . . . Mattingley, J. B. (2006). Executive "brake failure" following deactivation of human frontal lobe. *Journal of Cognitive Neuroscience, 18*(3), 444-455.

Charlton J, Koppel S, O'Hare M, Andrea D, Smith G, Khodr B, Langford J, Odell M, Fildes B. (2004) Influence of Chronic Illness on Crash Involvement of Motor Vehicle Drivers, Report No. 213, Monash University Accident Research Centre, Clayton, Australia.

Chikazoe, J., Konishi, S., Asari, T., Jimura, K., & Miyashita, Y. (2007). Activation of right inferior frontal gyrus during response inhibition across response modalities. *Journal of Cognitive Neuroscience, 19*(1), 69-80. doi:10.1162/jocn.2007.19.1.69

Daigneault, G., Joly, P., & Frigon, J. Y. (2002). Executive functions in the evaluation of accident risk of older drivers. *Journal of Clinical and Experimental Neuropsychology, 24*(2), 221-238.

de Frias, C. M., Dixon, R. A., Fisher, N., & Camicioli, R. (2007). Intraindividual variability in neurocognitive speed: A comparison of parkinson's disease and normal older adults. *Neuropsychologia, 45*(11), 2499-2507.

de Leeuw, F. E., de Groot, J. C., Achten, E., Oudkerk, M., Ramos, L. M., Heijboer, R., . . . Breteler, M. M. (2001). Prevalence of cerebral white matter lesions in elderly people: A population based magnetic resonance imaging study. the rotterdam scan study. *Journal of Neurology, Neurosurgery, and Psychiatry, 70*(1), 9-14.

Dobbs, B. M. (2005). *Medical conditions and driving: A review of the scientific literature (1960-2000).* (Technical Report No. DOT HS 809 690). Washington, DC: U.S. Department of Transportation, National Highway Traffic Safety Administration.

Duron, E. & Hanon, O. (2008). Hypertension, cognitive decline and dementia. *Archives of Cardiovascular Disease, 101*(3), 181-189.

Earles, J. L., Kersten, A. W., Berlin Mas, B., & Miccio, D. M. (2004). Aging and memory for self-performed tasks: Effects of task difficulty and time pressure. *The Journals of Gerontology.Series B, Psychological Sciences and Social Sciences, 59*(6), P285-93.

Ewen, J. B., Moher, J. S., Lakshmanan, B. M., Ryan, M., Xavier, P., Crone, N. E., . . . Mahone, E. M. (2012). Multiple task interference is greater in children with ADHD. *Developmental Neuropsychology, 37*(2), 119-133.

Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience, 14*(3), 340-347.

Fang, J., Shaw, K., & Keenan, N. (2011). Prevalence of coronary heart disease --- united states, 2006--2010. *Morbidity and Mortality Weekly Report, 60*(40), 1377-1381.

Freeman, R. (2006). Assessment of cardiovascular autonomic function. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 117*(4), 716-730.

Gamelin, F. X., Berthoin, S., & Bosquet, L. (2006). Validity of the polar S810 heart rate monitor to measure R-R intervals at rest. *Medicine and Science in Sports and Exercise, 38*(5), 887-893.

Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America, 96*(14), 8301-8306.

Gianaros, P. J., Van Der Veen, F. M., & Jennings, J. R. (2004). Regional cerebral blood flow correlates with heart period and high-frequency heart period variability during working-memory tasks: Implications for the cortical and subcortical regulation of cardiac autonomic activity. *Psychophysiology, 41*(4), 521-530.

Grady, C. (2012). The cognitive neuroscience of ageing. *Nature reviews. Neuroscience 13*(7), 491-505.

Hansen, A. L., Johnsen, B. H., & Thayer, J. F. (2003). Vagal influence on working memory and attention. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 48*(3), 263-274.

Hansen, A. L., Johnsen, B. H., & Thayer, J. F. (2009). Relationship between heart rate variability and cognitive function during threat of shock. *Anxiety, Stress, and Coping, 22*(1), 77-89.

Heart rate variability: Standards of measurement, physiological interpretation and clinical use. task force of the european society of cardiology and the north american society of pacing and electrophysiology. (1996). *Circulation, 93*(5), 1043-1065.

Mis en forme : Anglais (Canada)

Jefferson, A. L., Gibbons, L. E., Rentz, D. M., Carvalho, J. O., Manly, J., Bennett, D. A., & Jones, R. N. (2011). A life course model of cognitive activities, socioeconomic status, education, reading ability, and cognition. *Journal of the American Geriatrics Society, 59*(8), 1403-1411.

Johnson, M. J., Chahal, T., Stinchcombe, A., Mullen, N., Weaver, B., & Bedard, M. (2011). Physiological responses to simulated and on-road driving. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology,*

Kingsley, M., Lewis, M. J., & Marson, R. E. (2005). Comparison of polar 810s and an ambulatory ECG system for RR interval measurement during progressive exercise. *International Journal of Sports Medicine, 26*(1), 39-44.

Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., & Miyashita, Y. (1999). Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI. *Brain : A Journal of Neurology, 122 (Pt 5)*(Pt 5), 981-991.

Lafont, S., Marin-Lamellet, C., Paire-Ficout, L., Thomas-Anterion, C., Laurent, B., & Fabrigoule, C. (2010). The wechsler digit symbol substitution test as the best indicator of the risk of impaired driving in alzheimer disease and normal aging. *Dementia and Geriatric Cognitive Disorders, 29*(2), 154-163.

Lane, R.D., Reiman, E.M., Ahern, G.L., Thayer, A. (2001). Activity in medial prefrontal cortex correlates with vagal component of heart rate variability during emotion. *Brain Cogn, 47*, 97-100.

Lane, R. D., McRae, K., Reiman, E. M., Chen, K., Ahern, G. L., & Thayer, J. F. (2009). Neural correlates of heart rate variability during emotion. *NeuroImage, 44*(1), 213-222.

Lincoln, N. B., & Radford, K. A. (2008). Cognitive abilities as predictors of safety to drive in people with multiple sclerosis. *Multiple Sclerosis (Houndmills, Basingstoke, England), 14*(1), 123-128.

Longstreth, W. T.,Jr, Manolio, T. A., Arnold, A., Burke, G. L., Bryan, N., Jungreis, C. A., . . . Fried, L. (1996). Clinical correlates of white matter findings on cranial magnetic resonance imaging of 3301 elderly people. the cardiovascular health study. *Stroke; a Journal of Cerebral Circulation, 27*(8), 1274-1282.

Lyman, S., Ferguson, S. A., Braver, E. R., & Williams, A. F. (2002). Older driver involvements in police reported crashes and fatal crashes: Trends and projections. *Injury Prevention : Journal of the International Society for Child and Adolescent Injury Prevention, 8*(2), 116-120.

Malik, M., Bigger, J. T., Camm, A. J., Kleiger, R. E., Malliani, A., Moss, A. J., & Schwartz, P. J. (1996). Heart rate variability. standards of measurement, physiological interpretation, and

clinical use. Task force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *European Heart Journal, 17*(3), 354-381.

Mantyla, T., Karlsson, M. J., & Marklund, M. (2009). Executive control functions in simulated driving. *Applied Neuropsychology, 16*(1), 11-18.

Marshall, S. C., Molnar, F., Man-Son-Hing, M., Blair, R., Brosseau, L., Finestone, H. M., . . . Wilson, K. G. (2007). Predictors of driving ability following stroke: A systematic review. *Topics in Stroke Rehabilitation, 14*(1), 98-114.

Marshall, S. C. (2008). The role of reduced fitness to drive due to medical impairments in explaining crashes involving older drivers. *Traffic Injury Prevention, 9*(4), 291-298.

McArdle, W. D., Katch, F. I., & Katch, V. L. (2007). *Exercise physiology: Energy, nutrition & human performance (6th ed.)*. United States of America: Lippincott Williams & Wilkins.

McGwin, G.,Jr, Sims, R. V., Pulley, L., & Roseman, J. M. (2000). Relations among chronic medical conditions, medications, and automobile crashes in the elderly: A population-based case-control study. *American Journal of Epidemiology, 152*(5), 424-431.

Melis, C., & van Boxtel, A. (2001). Differences in autonomic physiological responses between good and poor inductive reasoners. *Biological Psychology, 58*(2), 121-146.

Moodithaya, S., & Avadhany, S. T. (2012). Gender differences in age-related changes in cardiac autonomic nervous function. *Journal of Aging Research, 2012*, 679345.

Moser, D. J., Cohen, R. A., Clark, M. M., Aloia, M. S., Tate, B. A., Stefanik, S., . . . Tilkemeier, P. L. (1999). Neuropsychological functioning among cardiac rehabilitation patients. *Journal of Cardiopulmonary Rehabilitation, 19*(2), 91-97.

Moses, Z. B., Luecken, L. J., & Eason, J. C. (2007). Measuring task-related changes in heart rate variability. *Conference Proceedings : ...Annual International Conference of the IEEE Engineering in Medicine and Biology Society.IEEE Engineering in Medicine and Biology Society.Conference, 2007*, 644-647.

Mukherjee, S., Yadav, R., Yung, I., Zajdel, D. P., & Oken, B. S. (2011). Sensitivity to mental effort and test-retest reliability of heart rate variability measures in healthy seniors. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 122*(10), 2059-2066.

Musialik-Lydka, A., Sredniawa, B., & Pasyk, S. (2003). Heart rate variability in heart failure. *Kardiologia Polska, 58*(1), 10-16.

Okonkwo, O. C., Cohen, R. A., Gunstad, J., Tremont, G., Alosco, M. L., & Poppas, A. (2010). Longitudinal trajectories of cognitive decline among older adults with cardiovascular disease. *Cerebrovascular Diseases (Basel, Switzerland), 30*(4), 362-373.

Porges, S. W. (1992). Vagal tone: A physiologic marker of stress vulnerability. *Pediatrics, 90*(3 Pt 2), 498-504.

Porto, L. G., & Junqueira, L. F.,Jr. (2009). Comparison of time-domain short-term heart interval variability analysis using a wrist-worn heart rate monitor and the conventional electrocardiogram. *Pacing and Clinical Electrophysiology : PACE, 32*(1), 43-51.

Ranchet, M., Paire-Ficout, L., Marin-Lamellet, C., Laurent, B., & Broussolle, E. (2011). Impaired updating ability in drivers with parkinson's disease. *Journal of Neurology, Neurosurgery, and Psychiatry, 82*(2), 218-223.

Ranney, T. A. (1994). Models of driving behavior: A review of their evolution. *Accident; Analysis and Prevention, 26*(6), 733-750.

Redondo, M., & Del Valle-Inclan, F. (1992). Decrements in heart rate variability during memory search. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 13*(1), 29-35.

Reijmer, Y. D., van den Berg, E., Ruis, C., Kappelle, L. J., & Biessels, G. J. (2010). Cognitive dysfunction in patients with type 2 diabetes. *Diabetes/metabolism Research and Reviews, 26*(7), 507-519.

Roger, V. L., Go, A. S., Lloyd-Jones, D. M., Adams, R. J., Berry, J. D., Brown, T. M., . . . American Heart Association Statistics Committee and Stroke Statistics Subcommittee. (2011). Heart disease and stroke statistics--2011 update: A report from the american heart association. *Circulation, 123*(4), e18-e209.

Rothschild, M., Rothschild, A., & Pfeifer, M. (1988). Temporary decrease in cardiac parasympathetic tone after acute myocardial infarction. *The American Journal of Cardiology, 62*(9), 637-639.

Schroeder, E. B., Liao, D., Chambless, L. E., Prineas, R. J., Evans, G. W., & Heiss, G. (2003). Hypertension, blood pressure, and heart rate variability: The atherosclerosis risk in communities (ARIC) study. *Hypertension, 42*(6), 1106-1111.

Silbert, B. S., Scott, D. A., Evered, L. A., Lewis, M. S., & Maruff, P. T. (2007). Preexisting cognitive impairment in patients scheduled for elective coronary artery bypass graft surgery. *Anesthesia and Analgesia, 104*(5), 1023-8, tables of contents.

Singh-Manoux, A., Britton, A. R., & Marmot, M. (2003). Vascular disease and cognitive function: Evidence from the whitehall II study. *Journal of the American Geriatrics Society, 51*(10), 1445-1450.

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart rate variability, prefrontal neural function, and cognitive performance: The neurovisceral integration

perspective on self-regulation, adaptation, and health. *Annals of Behavioral Medicine : A Publication of the Society of Behavioral Medicine, 37*(2), 141-153.

Thayer, J. F., Yamamoto, S. S., & Brosschot, J. F. (2010). The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *International Journal of Cardiology, 141*(2), 122-131.

Tracking heart disease and stroke in canada. (2009). Canada: Public Health Agency of Canada. Retrieved from http://www.phac-aspc.gc.ca.proxy.cm.umoncton.ca/publicat/2009/cvd-avc/pdf/cvd-avs-2009-eng.pdf

Tsuji, H., Larson, M. G., Venditti, F. J.,Jr, Manders, E. S., Evans, J. C., Feldman, C. L., & Levy, D. (1996). Impact of reduced heart rate variability on risk for cardiac events. the framingham heart study. *Circulation, 94*(11), 2850-2855.

Vaa T. (2003) Impairment, Diseases, Age and Their Relative Risks of Accident Involvement: Results from Meta-Analysis, TØI Report 690 for the Institute of Transport Economics, Oslo, Norway.

Vincent, A., Craik, F. I., & Furedy, J. J. (1996). Relations among memory performance, mental workload and cardiovascular responses. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology, 23*(3), 181-198.

Vogels, R. L., Scheltens, P., Schroeder-Tanka, J. M., & Weinstein, H. C. (2007). Cognitive impairment in heart failure: A systematic review of the literature. *European Journal of Heart Failure : Journal of the Working Group on Heart Failure of the European Society of Cardiology, 9*(5), 440-449.

Wadley, V. G., Okonkwo, O., Crowe, M., & Ross-Meadows, L. A. (2008). Mild cognitive impairment and everyday function: Evidence of reduced speed in performing instrumental activities of daily living. *The American Journal of Geriatric Psychiatry : Official Journal of the American Association for Geriatric Psychiatry, 16*(5), 416-424.

Waldstein, S. R., & Wendell, C. R. (2010). Neurocognitive function and cardiovascular disease. *Journal of Alzheimer's Disease : JAD, 20*(3), 833-842.

Weaver, B., Bédard, M., McAuliffe, J., & Parkkari, M. (2009). Using the attention network test to predict driving test scores. *Accident Analysis & Prevention, 41*(1), 76-83.

Weippert, M., Kumar, M., Kreuzfeld, S., Arndt, D., Rieger, A., & Stoll, R. (2010). Comparison of three mobile devices for measuring R-R intervals and heart rate variability: Polar S810i, suunto t6 and an ambulatory ECG system. *European Journal of Applied Physiology, 109*(4), 779-786.

Wennerblom, B., Lurje, L., Tygesen, H., Vahisalo, R., & Hjalmarson, A. (2000). Patients with uncomplicated coronary artery disease have reduced heart rate variability mainly affecting vagal tone. *Heart (British Cardiac Society), 83*(3), 290-294.

Whelihan, W. M., DiCarlo, M. A., & Paul, R. H. (2005). The relationship of neuropsychological functioning to driving competence in older persons with early cognitive decline. *Archives of Clinical Neuropsychology : The Official Journal of the National Academy of Neuropsychologists, 20*(2), 217-228.

Zhang, J., Tu, W., Dai, J., Lv, Q., & Yang, X. (2011). Dysfunction of pre- and post-operative cardiac autonomic nervous system in elderly patients with diabetes mellitus. *Archives of Gerontology and Geriatrics*.

Mis en forme : Français (Canada)