TITLE: Effects of an Aerobic Exercise Program on Driving Performance in Adults with Cardiovascular Disease

RUNNING HEAD: Exercise and Driving Performance in Cardiac Patients

AUTHORS: Jeffrey Gaudet MSc[1], Saïd Mekari MSc[2], Mathieu Bélanger PhD[3,4,5], Michel Johnson PhD[6]

[1] Graduate student, Faculty of Medicine and Health Sciences, Université de Sherbrooke
18 avenue Antonine-Maillet Moncton, New Brunswick Canada E1A 3E9
Jeffrey.gaudet@umoncton.ca

[2] Lecturer, School of Kinesiology, Acadia University
15 University Avenue Wolfville, Nova Scotia Canada B4P 2R6
Said.mekary@acadiau.ca

[3] Associate Professor, Department of Family Medicine, Université de Sherbrooke
18 avenue Antonine-Maillet Moncton, New Brunswick Canada E1A 3E9
Mathieu.f.belanger@usherbrooke.ca

[4] Director of Research, Centre de formation médical du Nouveau-Brunswick
18 avenue Antonine-Maillet Moncton, New Brunswick Canada E1A 3E9

[5] Epidemiologist, Vitalité Health Network
330 Université Avenue Moncton, New Brunswick Canada E1C 2Z3

[6] Professor, School of Kinesiology and Recreation, Université de Moncton
18 avenue Antonine-Maillet Moncton, New Brunswick Canada E1A 3E9
Michel.johnson@umoncton.ca

CORRESPONDING AUTHOR: Mathieu Bélanger
Centre de formation médicale du Nouveau-Brunswick
18 rue Antonine Maillet
Pavillon J.-Raymond-Frenette
Moncton, NB, Canada, E1A 3E9
Telephone: 1-506-863-2221
Fax: 1-506-863-2284
Mathieu.f.belanger@usherbrooke.ca

CONFLICT OF INTEREST: None declared.

SOURCE OF FUNDING: This study was supported by the New Brunswick Health Research Foundation.

ABSTRACT

OBJECTIVE: Cardiovascular disease has been linked to decreases in driving performance and an increased crash risk. Regular exercise has been linked with improved driving performance among healthy adults. The aim of the current study was to investigate the relationship between a 12 week cardiac rehabilitation program and driving performance among individuals with cardiovascular disease. METHODS: Twenty-five individuals, including 12 cardiac adults and 13 healthy adults, took part in this study. Simulated driving performance was assessed with a standardized demerit-based scoring system at 0 and 12 weeks. Cardiac participants completed a 12 week cardiac rehabilitation program between evaluations. RESULTS: At baseline, cardiac participants had a higher number of demerit points than healthy adults (120.9 ± 38.1 vs. 94.7 ± 28.3, $p = 0.04$). At follow-up, there was an improvement in both groups' driving evaluations, but the improvement was greater among the cardiac group such that there was no longer a difference in driving performance between both groups (94.6 ± 30 vs. 86.9 ± 34.8, $p = 0.51$). CONCLUSIONS: Participation in an aerobic exercise-based cardiac rehabilitation program appears to lead to improvements in simulated driving performances of individuals with cardiovascular disease.

KEYWORDS

Cardiovascular Disease, Automobile Driving, Rehabilitation, Aerobic Exercise

INTRODUCTION

Over 28 million individuals suffer from cardiovascular disease (CVD) in North America (Dai and Bancej, 2009; Roger et al., 2011) and its prevalence reaches approximately 20% at the age of 65 (Prevalence of coronary heart disease--United States, 2006-2010., 2011). Along with physical decline, CVD can also alter cognitive functions (Almeida et al. 2008; Pressler 2002). Several physiological changes that occur as a result of CVD have been shown to contribute to cognitive impairment, including low cardiac output, endothelial function, poor cardiovascular fitness, and reduced cerebral blood flow (Dai et al., 2008; Gunstad et al., 2005; Jefferson et al., 2007; Moser et al., 2004). Associations between CVD and cognitive impairment have been reported in normal cognitive aging (Breteler et al., 1994; Singh-Manoux et al., 2003) and with non-amnesic mild cognitive impairment, which represents a decline in attention and executive control functions rather than a loss in memory functions, as observed in more typical amnesic cognitive decline (Roberts et al., 2010). Decreases in non-amnesic cognitive functions may negatively impact complex cognitive tasks (Alosco et al., 2012, 2014; McLennan et al., n.d.; Wadley et al., 2008), such as automobile driving, which is recognised as an important activity of daily living (American Occupational Therapy Association, 2009). Although a recent study conducted in a province using a medical fitness to drive screening program found no increase in crash risk associated with CVD (Dow et al., 2013), other research has linked CVD to increases in crash risk ranging from 30 to 75% (Charlton et al., 2004; Dobbs, 2005; Vaa, 2005). Further, on road (Ahlgren et al., 2003) and simulator-based (Gaudet et al., 2013) evaluations have shown poorer driving performance among cardiac populations than among healthy adults. Yet, individuals with CVD remain active drivers after their cardiac event (Ahlgren et al., 2002)

Physical exercise is recommended for prevention and management of CVD (Fletcher et al., 2001). In addition to being associated with improvements in cardiovascular fitness (Ades, 2001; Kavanagh et al., 2002; Leon et al., 2005), data suggest that participation in an exercise-centered cardiac rehabilitation (CR) may also relate to improvements in cognition performance (Gunstad et al., 2005; Stanek et al., 2011). Although physical exercise has been linked to improvements in abilities associated with driving performance in healthy adults (Filipe Marmeleira et al., 2011;

Marmeleira et al., 2009; Marottoli et al., 2007), it was never explored whether physical exercise-related enhancements in driving performance could be perceived among persons with CVD. The aim of the present study was to investigate the possible relationship between a 12 week CR program and changes in simulator-tested driving performance in adults with CVD. We hypothesized that CR would lead to an improvement in driving performance.

METHODS

Participants

Thirty-four individuals (18 cardiac adults, and 16 healthy adults) were recruited and provided written informed consent for this study as approved by the Université de Sherbrooke, Université de Moncton, and Vitality Health Network Research Ethics Boards. None of the participants had a history of neurological or psychiatric disorder, stroke, epilepsy or drug / alcohol problems. 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 and have clearance from their physician to resume driving. Cardiac participants were recruited from a local CR program, and through advertisement. Healthy adults with no history of CVD were recruited to serve as a comparison group.

Participants' sociodemographic information, including age, education, presence of diabetes or hypertension, and driving experience were obtained through baseline self-report questionnaires. Education was categorised as: 1) never completed secondary education, 2) completed secondary education and 3) completed post-secondary education.

Study Design

Participants completed a simulated driving evaluation at baseline and again approximately 12 weeks later. Between baseline and follow-up evaluations, individuals in the cardiac group completed 12 weeks of CR, whereas individuals of the healthy group were not provided with any intervention. Changes in measurements observed among the healthy participants therefore provide an estimate of improvements in driving performance that could be expected from repeated exposure to the simulated driving task.

Cardiac Rehabilitation

The CR program was based on the recommendations of the American Heart Association (Leon et al., 2005; Pollock et al., 2000). Specifically, the 12-week comprehensive electrocardiogram monitored exercise and education program included two exercise sessions per week, and an education session bi-weekly. A customized exercise plan was developed for each cardiac participant based on their condition and needs. Individual sessions generally consisted of warm-up, 30-45 minutes of exercise using a variety of aerobic modalities including treadmills, stationary cycles, arm ergocycles, NuStep, elliptical trainers, and rowers, followed by cool down and stretching (see table 1 for an example of a typical exercise session). Exercise intensity was prescribed following the Karvonen method, with heart rate typically ranging between 75 to 85% of heart rate reserve. Education classes were given by health professionals of various fields and were designed to promote positive lifestyle changes, increase understanding of heart conditions, and reduce the risk of future cardiac events. Driving skills related information was not included in any of the education classes.

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 that has been used successfully in other studies (Bédard et al., 2008, 2010; Gaudet et al., 2013; Weaver et al., 2009). 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). Adequate intra- and inter-rater reliability (intraclass correlation coefficients >0.55 for 13 of 15 comparisons) and a correlation of 0.74 (p=0.035) between demerit points obtained from simulator (similar to the one used in this study) and on road evaluations support the use of a simulator in conjunction with an evaluation grid typical for on-road testing as was done in this study (Bédard et al., 2010).

Participants completed a driving course on the simulator following pre-recorded auditory directions. The evaluator evaluated the drive while seated at a workstation behind participants. Participants were given explanations on the basic operational functions of the driving simulator, and provided a 5 minute practice drive on a standardised course for acclimatization before completing a 20 minute test drive on a different standardised course as used in other studies. 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 in previous studies (Johnson et al., 2011; Weaver et al., 2009)). In addition to attenuating feasibility and safety concerns, the simulator also improves comparability of conditions for all participants.

Data Analysis

Mann-Whitney tests were used to compare the mean values of driving performance during the pre and post condition in both groups and Wilcoxon signed rank tests were used to compare within group differences in pre and post conditions. Unadjusted and adjusted linear regression models were used to compare pre-post change in driving performance between groups. Adjusted models accounted for between group differences in sex, education, age, hypertension and diabetes. These factors are known to be associated with cognitive function (Duron and Hanon, 2008; Grady, 2012; Jefferson et al., 2011; Reijmer et al., 2010) and driving (Lyman et al., 2002; Marshall, 2008; McGwin et al., 2000). We intended to recruit a minimum of 16 participants per group based on estimates that it would provide 80% power of detecting a within group change of ≥20% (standard deviation 20) (Marottoli et al., 2007) in driving performance with the potential for type 1 error set at 5%.

RESULTS

Of the 34 participants recruited, 25 were retained for the analyses. Among the cardiac participants, one had a worsening of his CVD which affected his ability to continue to participate in the study, 2 were unable to complete the driving test because of simulator sickness symptoms and 3 were lost to follow-up. 3 healthy participants were also lost to follow-up. Comparison of baseline scores between those who completed both series of data collection and those who withdrew after baseline indicated no meaningful clinical or statistical between group differences. There were also no meaningful differences between participants in the cardiac group and control group in terms of their age, education and sex distribution, or their driving experience (Table 1). Consistent with the definition of groups, the prevalence of hypertension was higher among cardiacs. Cardiovascular events of participants in the cardiac group included myocardial infarction [9 (75 %)], percutaneous coronary intervention [11 (92 %)], coronary artery by-pass graft [1 (8 %)], and angina [1 (8 %)].

(Insert Table 1)

At baseline, the participants in the cardiac group had a statistically significantly higher number of demerit points than those in the healthy adults group during their simulator-based driving evaluation (120.9 ± 38.1 vs. 94.7 ± 28.3, $p = 0.04$). Following the 12 weeks of study, there was an improvement in both groups' driving performance as assessed with the driving simulator ($p < 0.01$ for both groups). However, the improvement was greater among the cardiac group (β coefficient for between group difference in improvement = -20.4; 95% confidence interval = -

38.7 to -2.1; $p<0.05$) such that there were no differences between driving performances of both groups at the end of follow-up (94.6 ± 30 vs. 86.9 ± 34.8, $p = 0.51$). The between group difference in improvement continued to be statistically significant after adjustments for potential confounding variables ($p < 0.05$).

(Insert figure 1)

DISCUSSION

In this study, we found that individuals with CVD had lower simulator-assessed driving performances than apparently healthy adults, but that this difference disappeared following participation of CVD participants in a 12 week CR program. The exercise-related improvement in simulated driving performance appears to be independent of the improvement attributable to the repeated exposure to the driving simulator. This is the first study to directly assess the impact of an exercise program on driving performance in persons with CVD. Although based on a small sample, our results, which show a 22% reduction in driving simulator assessed demerit points following an exercise program, are consistent with other research which reported that healthy older adults over the age of 70 improved their driving performance by 37% following a 12-week exercise program including strength, flexibility, and coordination exercises (Marottoli et al., 2007). In other studies among older adults, training protocols combining physical and cognitive training led to driving related ability improvements, as quantified by on-road (Marmeleira et al. 2011) and simulator based (Marmeleira et al., 2009) speed of behavior tasks. The improvements in driving scores among participants in the CR training in our study occurred despite the absence of any emphasis on cognitive or physical tasks specific to driving as included in these other studies.

Although mechanisms underlying the relationship between exercise training and driving performance have not been studied, it is possible that the relationship observed is mediated by cognitive improvements. Exercise related improvements in cognitive functions were reported concurrently with driving related improvements by Marmeleira et al. (2009). In addition, it appears that participation in CR is associated with improvement in psychomotor speed, complex attention and executive function (Carles et al., 2007; Gunstad et al., 2005; Stanek et al., 2011), which are all cognitive abilities with documented links to driving performance and safety among older adults (Anstey et al., 2005). It is also possible that the relationship between exercise and driving performance stems from improvements in cardiovascular fitness. Although we did not have a measure of cardiovascular fitness, a large body of work has documented the positive effects of physical exercise on several indices of cardiovascular fitness such as heart function, vascular health, oxygen consumption capacity, cerebral blood flow (Bassett and Howley, 2000; Farinatti and Soares, 2009; González-Alonso et al., 2004; Subudhi et al., 2007). Better cardiovascular fitness has been associated with better cognitive functions relevant to driving in both healthy older adults (Angevaren et al., 2008; Colcombe et al., 2004) and adults with CVD (Gunstad et al., 2005). For a better understanding of the underlying mechanisms, future studies should include appropriate and sensitive measures of cognitive function and physical fitness.

The current study has some limitations, and caution should be taken in generalizing the findings. Evaluations were conducted using a driving simulator which may not provide a true measure of driving ability. However, although the perceptual and sensory feel of the simulator may not be completely realistic, the driving course as well as the evaluation grid used 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). Participants were not screened for visual acuity and function, despite vision being highly involved in the task of driving (Anstey et al., 2005; Audet et al., 2007). However, motor vehicle branches have established strict regulations regarding central and peripheral visual acuity (Canadian Medical Association, 2006) and each participant possessed a valid driver's license, drove regularly and was instructed to wear appropriate eyewear for driving. We note the heterogeneity of cardiac conditions and the inclusion of individuals with a history of diabetes and hypertension as another potential limitation. Despite common potential mechanisms such as impaired cognitive functioning, some etiologies may impact driving through other independent pathways like hypoglycemia and peripheral neuropathy (Inkster and Frier, 2013). The current study was not able to evaluate potential underlying mechanisms. It is a possibility that improvements in driving performance were the result of repeated exposure to the same simulator route, a short practice drive for acclimatization, regression to the mean or natural improvement among cardiac patients. Although our design enables accounting for the effect of time and training in the simulator, our findings need to be replicated in a larger controlled study including a group of cardiac individuals not participating in CR in order to account for the limitations listed. This was not feasible in our setting given eligible CVD participants wanted to take part in CR.

Although the mechanism remains to be understood, results from this study suggest that participation in a CR program can lead to improvements in simulator-assessed driving performance. This implies that the higher crash risk associated with CVD could be, at least partly, alleviated by participation in CR program. Although our results need to be confirmed, they suggest that participation in a CR should be encouraged among individuals with CVD for benefits that extend beyond cardiovascular fitness and which can have a positive influence on general public safety.

ACKNOWLEDGMENTS

The authors would like to thank Monique Dufour-Doiron and the Cardiac Wellness rehabilitation center for their assistance in recruiting participants.

REFERENCES

Ades PA (2001) Cardiac rehabilitation and secondary prevention of coronary heart disease. *The New England journal of medicine*, 345(12), 892–902, Available from: http://www.ncbi.nlm.nih.gov/pubmed/11565523 (accessed 8 December 2014).

Ahlgren E, Rutberg H and Aren C (2002) Patients with Coronary Artery Disease Are Active Car Drivers Both Before and Soon After Heart Surgery. *Traffic Injury Prevention*, Taylor & Francis Group, 3(3), 205–208, Available from: http://www.tandfonline.com/doi/abs/10.1080/15389580213649# (accessed 23 April 2015).

Ahlgren E, Lundqvist A, Nordlund A, et al. (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), 334–40, Available from: http://www.ncbi.nlm.nih.gov/pubmed/12614803 (accessed 8 December 2014).

Almeida OP, Garrido GJ, Beer C, et al. (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, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18715304 (accessed 8 December 2014).

Alosco ML, Spitznagel MB, Cohen R, et al. (2012) Cognitive impairment is independently associated with reduced instrumental activities of daily living in persons with heart failure. *The Journal of cardiovascular nursing*, 27(1), 44–50, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3175008&tool=pmcentrez&rendertype=abstract.

Alosco ML, Brickman AM, Spitznagel MB, et al. (2014) Reduced Gray Matter Volume Is Associated With Poorer Instrumental Activities of Daily Living Performance in Heart Failure. *The Journal of cardiovascular nursing*, Available from: http://www.ncbi.nlm.nih.gov/pubmed/25419946.

American Occupational Therapy Association (2009) Talking Points. Available from: http://www.aota.org/Older-Driver/Professionals/Awareness/Talking-Points.aspx.

Angevaren M, Aufdemkampe G, Verhaar HJJ, et al. (2008) Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *The Cochrane database of systematic reviews*, (3), CD005381, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18646126 (accessed 22 November 2014).

Anstey KJ, Wood J, Lord S, et al. (2005) Cognitive, sensory and physical factors enabling driving safety in older adults. *Clinical psychology review*, 25(1), 45–65, Available from: http://www.ncbi.nlm.nih.gov/pubmed/15596080 (accessed 7 December 2014).

Audet T, Arcand M, Godbout C, et al. (2007) Conduite automobile. In: Arcand M and Hébert R (eds), *Précis pratique de gériatrie*, Québec: Edisem, pp. 1099–1112.

Bassett DR and Howley ET (2000) Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Medicine and science in sports and exercise*, 32(1), 70–84, Available from: http://www.ncbi.nlm.nih.gov/pubmed/10647532 (accessed 8 December 2014).

Bédard M, Porter MM, Marshall S, et al. (2008) The combination of two training approaches to improve older adults' driving safety. *Traffic injury prevention*, 9(1), 70–6, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18338298 (accessed 8 December 2014).

Bédard MB, Parkkari M, Weaver B, et al. (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), 336–40, Available from: http://www.ncbi.nlm.nih.gov/pubmed/20437921 (accessed 29 April 2015).

Breteler MM, Claus JJ, Grobbee DE, et al. (1994) Cardiovascular disease and distribution of cognitive function in elderly people: the Rotterdam Study. *BMJ (Clinical research ed.)*, 308(6944), 1604–8, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2540432&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Canadian Medical Association (2006) *Driver's Guide: Determining Medical Fitness to Operate Motor Vehicles*. Ottawa, Canada.

Carles S, Curnier D, Pathak A, et al. (2007) Effects of short-term exercise and exercise training on cognitive function among patients with cardiac disease. *Journal of cardiopulmonary rehabilitation and prevention*, 27(6), 395–9, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18197075 (accessed 12 December 2014).

Charlton J, Koppel S, O'Hare M, et al. (2004) *Influence of chronic illness on crash involvement* *of motor vehicle drivers*. Available from: http://trid.trb.org/view.aspx?id=1158150 (accessed 8 December 2014).

Colcombe SJ, Kramer AF, Erickson KI, et al. (2004) Cardiovascular fitness, cortical plasticity, and aging. *Proceedings of the National Academy of Sciences of the United States of America*, 101(9), 3316–21, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=373255&tool=pmcentrez&rendertype=abstract (accessed 6 September 2014).

Dai S and Bancej C (2009) Tracking heart disease and stroke in Canada 2009. *Chronic* ..., Available from: http://scholar.google.ca/scholar?hl=en&q=Tracking+heart+disease+and+stroke+in+Canada.+2009&btnG=&as_sdt=1,5&as_sdtp=#0 (accessed 8 December 2014).

Dai W, Lopez OL, Carmichael OT, et al. (2008) Abnormal regional cerebral blood flow in cognitively normal elderly subjects with hypertension. *Stroke; a journal of cerebral circulation*, 39(2), 349–54, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2701215&tool=pmcentrez&rendertype=abstract (accessed 23 October 2015).

Dobbs B (2005) *Medical conditions and driving: A review of the scientific literature (1960-2000)*. Washington, DC.

Dow J, Gaudet M and Turmel E (2013) Crash rates of quebec drivers with medical conditions. *Annals of advances in automotive medicine / Annual Scientific Conference ... Association for the Advancement of Automotive Medicine. Association for the Advancement of Automotive Medicine. Scientific Conference*, 57, 57–66, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3861823&tool=pmcentrez&rendertype=abstract (accessed 12 June 2015).

Duron E and Hanon O (2008) Hypertension, cognitive decline and dementia. *Archives of cardiovascular diseases*, 101(3), 181–9, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18477946 (accessed 8 December 2014).

Farinatti PT V and Soares PPS (2009) Cardiac output and oxygen uptake relationship during physical effort in men and women over 60 years old. *European journal of applied physiology*, 107(6), 625–31, Available from: http://www.ncbi.nlm.nih.gov/pubmed/19711096 (accessed 8 December 2014).

Filipe Marmeleira JF, Soares de Melo FM, Tlemcani M, et al. (2011) Exercise can improve speed of behavior in older drivers. *Journal of aging and physical activity*, 19(1), 48–61, Available from: http://www.ncbi.nlm.nih.gov/pubmed/21285475 (accessed 8 December

2014).

Fletcher GF, Balady GJ, Amsterdam EA, et al. (2001) Exercise standards for testing and training: a statement for healthcare professionals from the American Heart Association. *Circulation*, 104(14), 1694–740, Available from: http://www.ncbi.nlm.nih.gov/pubmed/11581152 (accessed 12 December 2014).

Gaudet J, Belanger MF, Corriveau H, et al. (2013) Investigating the autonomic nervous system and cognitive functions as potential mediators of an association between cardiovascular disease and driving performance. *Canadian journal of physiology and pharmacology*, Universite de Sherbrooke, Canada., 91(5), 346–352, Available from: http://ovidsp.ovid.com/ovidweb.cgi?T=JS&PAGE=reference&D=medl&NEWS=N&AN=23656301.

González-Alonso J, Dalsgaard MK, Osada T, et al. (2004) Brain and central haemodynamics and oxygenation during maximal exercise in humans. *The Journal of physiology*, 557(Pt 1), 331–42, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1665053&tool=pmcentrez&rendertype=abstract (accessed 30 October 2014).

Grady C (2012) The cognitive neuroscience of ageing. *Nature reviews. Neuroscience*, 13(7), 491–505, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3800175&tool=pmcentrez&rendertype=abstract (accessed 9 July 2014).

Gunstad J, Macgregor KL, Paul RH, et al. (2005) Cardiac rehabilitation improves cognitive performance in older adults with cardiovascular disease. *Journal of cardiopulmonary rehabilitation*, 25(3), 173–6, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3226758&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Inkster B and Frier BM (2013) Diabetes and driving. *Diabetes, obesity & metabolism*, 15(9), 775–83, Available from: http://www.ncbi.nlm.nih.gov/pubmed/23350766 (accessed 22 April 2015).

Jefferson AL, Poppas A, Paul RH, et al. (2007) Systemic hypoperfusion is associated with executive dysfunction in geriatric cardiac patients. *Neurobiology of aging*, 28(3), 477–83, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2741683&tool=pmcentrez&rendertype=abstract (accessed 23 October 2015).

Jefferson AL, Gibbons LE, Rentz DM, et al. (2011) A life course model of cognitive activities, socioeconomic status, education, reading ability, and cognition. *Journal of the American Geriatrics Society*, 59(8), 1403–11, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3222272&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Johnson MJ, Chahal T, Stinchcombe A, et al. (2011) Physiological responses to simulated and on-road driving. *International journal of psychophysiology : official journal of the International Organization of Psychophysiology*, 81(3), 203–8, Available from: http://www.ncbi.nlm.nih.gov/pubmed/21726587 (accessed 8 December 2014).

Kavanagh T, Mertens DJ, Hamm LF, et al. (2002) Prediction of long-term prognosis in 12 169 men referred for cardiac rehabilitation. *Circulation*, 106(6), 666–71, Available from: http://www.ncbi.nlm.nih.gov/pubmed/12163425 (accessed 8 December 2014).

Leon AS, Franklin BA, Costa F, et al. (2005) Cardiac rehabilitation and secondary prevention of coronary heart disease: an American Heart Association scientific statement from the Council on Clinical Cardiology (Subcommittee on Exercise, Cardiac Rehabilitation, and Prevention) and the Council on Nut. *Circulation*, 111(3), 369–76, Available from: http://www.ncbi.nlm.nih.gov/pubmed/15668354 (accessed 2 October 2014).

Lyman S, Ferguson SA, Braver ER, et al. (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), 116–20, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1730843&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Marmeleira JF, Godinho MB and Fernandes OM (2009) The effects of an exercise program on several abilities associated with driving performance in older adults. *Accident; analysis and prevention*, 41(1), 90–7, Available from: http://www.ncbi.nlm.nih.gov/pubmed/19114142 (accessed 8 December 2014).

Marottoli RA, Allore H, Araujo KLB, et al. (2007) A randomized trial of a physical conditioning program to enhance the driving performance of older persons. *Journal of general internal medicine*, 22(5), 590–7, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1852916&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Marshall SC (2008) The role of reduced fitness to drive due to medical impairments in explaining crashes involving older drivers. *Traffic injury prevention*, 9(4), 291–8, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18696384 (accessed 2 December

2014).

McGwin G, Sims R V, Pulley L, et al. (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), 424–31, Available from: http://www.ncbi.nlm.nih.gov/pubmed/10981455 (accessed 8 December 2014).

McLennan SN, Mathias JL, Brennan LC, et al. (n.d.) Cognitive impairment predicts functional capacity in dementia-free patients with cardiovascular disease. *The Journal of cardiovascular nursing*, 25(5), 390–397, Available from: http://www.ncbi.nlm.nih.gov/pubmed/20714236.

Moser DJ, Hoth KF, Robinson RG, et al. (2004) Blood vessel function and cognition in elderly patients with atherosclerosis. *Stroke; a journal of cerebral circulation*, 35(11), e369–72, Available from: http://www.ncbi.nlm.nih.gov/pubmed/15472091 (accessed 23 October 2015).

Pollock ML, Franklin BA, Balady GJ, et al. (2000) AHA Science Advisory. Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription: An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, Am. *Circulation*, 101(7), 828–33, Available from: http://www.ncbi.nlm.nih.gov/pubmed/10683360 (accessed 8 December 2014).

Pressler SJ (n.d.) Cognitive functioning and chronic heart failure: a review of the literature (2002-July 2007). *The Journal of cardiovascular nursing*, 23(3), 239–249, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18437066.

Prevalence of coronary heart disease--United States, 2006-2010. (2011) *MMWR. Morbidity and mortality weekly report*, 60(40), 1377–81, Available from: http://www.ncbi.nlm.nih.gov/pubmed/21993341 (accessed 8 December 2014).

Reijmer YD, van den Berg E, Ruis C, et al. (2010) Cognitive dysfunction in patients with type 2 diabetes. *Diabetes/metabolism research and reviews*, 26(7), 507–19, Available from: http://www.ncbi.nlm.nih.gov/pubmed/20799243 (accessed 28 November 2014).

Roberts RO, Knopman DS, Geda YE, et al. (2010) Coronary heart disease is associated with non-amnestic mild cognitive impairment. *Neurobiology of aging*, 31(11), 1894–902, Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2888961&tool=pmcentrez&rendertype=abstract (accessed 8 December 2014).

Roger VL, Go AS, Lloyd-Jones DM, et al. (2011) Heart disease and stroke statistics--2011 update: a report from the American Heart Association. *Circulation*, 123(4), e18–e209, Available from: http://www.ncbi.nlm.nih.gov/pubmed/21160056 (accessed 9 July 2014).

Singh-Manoux A, Britton AR and Marmot M (2003) Vascular disease and cognitive function: evidence from the Whitehall II Study. *Journal of the American Geriatrics Society*, 51(10), 1445–50, Available from: http://www.ncbi.nlm.nih.gov/pubmed/14511166 (accessed 8 December 2014).

Stanek KM, Gunstad J, Spitznagel MB, et al. (2011) Improvements in cognitive function following cardiac rehabilitation for older adults with cardiovascular disease. *The International journal of neuroscience*, 121(2), 86–93, Available from: http://www.ncbi.nlm.nih.gov/pubmed/21062215 (accessed 8 December 2014).

Subudhi AW, Dimmen AC and Roach RC (2007) Effects of acute hypoxia on cerebral and muscle oxygenation during incremental exercise. *Journal of applied physiology (Bethesda, Md. : 1985)*, 103(1), 177–83, Available from: http://www.ncbi.nlm.nih.gov/pubmed/17431082 (accessed 4 December 2014).

Vaa T (2005) Impairments, diseases, age and their relative risks of accident involvement: Results from meta-analysis. Available from: https://www.toi.no/getfile.php/Publikasjoner/TØI rapporter/2003/690-2003/690-2003-el.pdf (accessed 8 December 2014).

Wadley VG, Okonkwo O, Crowe M, et al. (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), 416–24, Available from: http://www.ncbi.nlm.nih.gov/pubmed/18448852 (accessed 8 December 2014).

Weaver B, Bédard M, McAuliffe J, et al. (2009) Using the Attention Network Test to predict driving test scores. *Accident; analysis and prevention*, 41(1), 76–83, Available from: http://www.ncbi.nlm.nih.gov/pubmed/19114140 (accessed 3 December 2014).