Acta Scientiarum

http://periodicos.uem.br/ojs/acta
ISSN on-line: 1807-8648
Doi: 10.4025/actascihealthsci.v40i1.33469

CIÊNCIAS DA SAÚDE / HEALTH SCIENCES

Cardiac autonomic profile in cervical spinal cord injury subjects practitioners of the physical exercise

Edgar William Martins[1], Roberto Magalhães[1], Moacir Marocolo[2] and Alex Souto Maior[1*]

*[1]Programa de Pós-Graduação em Ciências da Reabilitação, Universidade Augusto Motta, Av. Paris, 84, 21041-020, Bonsucesso, Rio de Janeiro, Rio de Janeiro, Brazil. [2]Departamento de Fisiologia, Instituto de Ciências Biológicas, Universidade Federal de Juiz de Fora, Juiz de Fora, Minas Gerais, Brazil. *Author for correspondence. E-mail: alex.bioengenharia@gmail.com*

ABSTRACT. The aim was investigate the time-course of cardiac autonomic response in men with incomplete cervical spinal cord injury (SCI) practitioners or not of physical exercise. Twenty men were separated into three groups: control group without SCI (CON; 28.3 ± 4.5 yrs; 178.4 ± 6.5 cm; 82.1 ± 6.8 kg; n=8), regularly engaged in strength training and low aerobic training; exercise group with cervical SCI (EG, 32.3 ± 4.5 yrs, 175.1 ± 5.3 cm, 73.6 ± 9.6 Kg; n=8) that practiced wheelchair rugby and sedentary group with cervical SCI (SG, 30.8 ± 5.3 yrs, 173.4 ± 10.1 cm, 69.7 ± 7.1 Kg; n=4) who did not practice physical exercise. Heart rate variability variables were calculated from ECG, in rest. CON showed high values compared to EG and SG of: standard deviation of R-R intervals (SDNN), proportion of adjacent R-R intervals differing by more than 50 ms, number of interval differences of successive NN intervals greater than 50 ms, root mean square of successive differences and the high-frequency spectral power. SDNN was significantly lower in EG compared to CON. changes in cardiac autonomic function could be noted in subjects with cervical SCI regularly engaged in an exercise program.

Keywords: autonomic nervous system, wheelchair exercise, spinal cord injury.

Perfil autonômico cardíaco de sujeitos tetraplégicos praticantes de atividade física

RESUMO. O objetivo do presente estudo foi investigar o perfil da modulação autonômica cardíaca em homens com lesão medular cervical incompleta (LMC) praticante de exercícios físicos. Vinte homens foram divididos em três grupos: grupo controle sem LMC (CON; 28,3 ± 4,5 anos; 178,4 ± 6,5 cm; 82,1 ± 6,8 kg; n = 8), envolvidos regularmente em treinamento de força e treinamento aeróbico de baixa intensidade; grupo exercício com LMC (GE, 32,3 ± 4,5 anos, 175,1 ± 5,3 cm, 73,6 ± 9,6 kg; n = 8) praticantes de rugby em cadeira de rodas; grupo sedentário com LMC (GS, 30,8 ± 5,3 anos, 173,4 ± 10,1 cm, 69,7 ± 7,1 kg; n = 4) não praticantes de exercícios físicos. As variáveis de domínio do tempo e frequência da variabilidade da frequência cardíaca foram calculadas a partir dos intervalos RR registradas em repouso. CON apresentaram NN50 (número de diferenças dos intervalos NN consecutivos superiores a 50 ms), pNN50 (percentual de intervalo RR normal que difere mais que 50 ms de seu adjacente), rMSSD (raiz quadrada da soma das diferenças sucessivas entre intervalos RR normais adjacentes ao quadrado) e o componente de alta frequência (HF) significativamente mais elevado quando comparados ao GE e GS. Por outro lado, o desvio-padrão dos intervalos R-R (SDNN) foi significativamente menor no GE quando comparado ao CON. Um programa de exercícios físicos regular pode contribuir com significativas mudanças na modulação autonômica cardíaca de indivíduos com LMC.

Palavras-chave: sistema nervoso autônomo, exercícios em cadeira de rodas, lesão medular cervical.

Introduction

A spinal cord injury (SCI) usually occurs with damage to any part of the spinal cord and/or nerves where displaced bone fragments, disc material, or ligaments bruise, which compromises spinal cord tissue (Nooijen et al., 2015; Saunders, Clarke, Tate, Forchheimer, & Krause, 2015). Thus, this traumatic event can exacerbate the physical and physiologic debilities in the musculoskeletal, cardiovascular, gastrointestinal, pulmonary and integumentary systems leading to shake substantial financial burden on health care systems (Saunders et al., 2015). Two types of SCI could be described: complete, which contributes to loss of function below the level of the injury, and incomplete, that result in some feeling below the point of injury (Harkey, White, Tibbs, & Haines, 2003). Data from 2010 showed that higher frequency of SCI are related to incomplete tetraplegia (45%), followed by incomplete paraplegia (21%), complete paraplegia (20%), and complete tetraplegia (14%) (Center, 2015). The average age at the time of injury is comprehended between 20 to 40 years, and the male/female ratio is 4:1, respectively (Biering-Sorensen, Bickenbach, El Masry, Officer, & von Groote, 2011; Krug, Sharma, & Lozano, 2000).

The major incidence of SCI is related to cervical trauma (59% of cases), which shows higher prevalence from vehicle crashes (38%), falls (30%), violence (14%), sports/recreation-related injuries (9%), medical/surgical (5%), and other causes (4%) (Center, 2015; Yang et al., 2013). A document published by the World Health Organization shows that global SCI incidence is about 40-80 new cases per million, which corresponds to 250,000 to 500,000 new cases per year around the world (Biering-Sorensen et al., 2011).

Subjects with cervical SCI are a high-risk group, with the highest reported mortality rate in spinal trauma when compared to thoracic or lumbar spine injuries (Yang et al., 2013). Cervical SCI promote a loss, either temporary or permanent, in the response sensory/motor, bladder/bowel function, and cardiac autonomic function (Grossman et al., 2012; Santos et al., 2012). Cardiac autonomic dysfunction is a frequent complication of SCI, especially after a cervical SCI, and result in increased morbidity and mortality (Garshick et al., 2005; Yang et al., 2013). This type of traumatic lesion maintains vagal afferent and efferent pathways intact while the spinal sympathetic system loses supraspinal autonomic control, when injuries occurred above of the thoracic spinal cord segments (T1–T4) (Sisto et al., 2012; Weaver, Fleming, Mathias, & Krassioukov, 2012). The interruption of cardiac sympathetic innervation promotes bradycardia and reduces myocardial contractility. These events contribute to autonomic dysfunction leading to ventricular arrhythmias and cardiac arrest (Chung et al., 2011; Ravensbergen, Walsh, Krassioukov, & Claydon, 2012).

Impairment of the autonomic cardiac regulation has been associated to increased incidence of cardiac arrhythmias and the analysis of heart rate variability (HRV) has been used as a tool for noninvasive assessment of cardiac autonomic balance in physiological and pathological conditions (Adebayo et al., 2015; Barth et al., 2015; Maior et al., 2013; Marocolo et al., 2013). HRV analysis may provide a noninvasive method for estimating the sympatho-vagal balance (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996; Marocolo et al., 2013; Thayer, Yamamoto, & Brosschot, 2010) and independent prognostic information about ventricular arrhythmia (Adebayo et al., 2015; Rodrigues, Tran, Guest, Middleton, & Craig, 2015).

Regarding to physical exercise, rugby wheelchair practitioners with complete cervical SCI had better performance during aerobic capacity tests of , due to possibly partial preservation of spinal sympathetic circuits (West, Romer, & Krassioukov, 2013). In this way, the sympathetic nerves decentralization on the exercise response is severe in tetraplegic subjects by impairs the HR increasing at the onset of exercise and the rapid deceleration after exercise (Takahashi et al., 2007). Considering the importance of autonomic function and few studies with SCI found described in the literature, the purpose of this study was to investigated the time-course of cardiac autonomic responses in sedentary and in trained menwith or without incomplete cervical SCI.

Material and methods

Subjects

Twenty men were recruited and separated into three groups: Control with intact spinal cord (CON, 28.3 ± 4.5 years; 178.4 ± 6.5 cm; 82.1 ± 6.8 kg; 27.2 ± 2.5 kg $m^{-2,}$ n = 8) , exercise group with cervical SCI (EG, 32.3 ± 4.5 years, 175.1 ± 5.3 cm, 73.6 ± 9.6 Kg; 23.8 ± 3.6 kg m^{-2}, n = 8) and sedentary group with SCI (SG, 30.8 ± 5.3 years, 173.4 ± 10.1 cm, 69.7 ± 7.1 Kg; 23.5 ± 2.9 kg m^{-2}, n = 4) who did not practice any type of physical exercise Subjects in the control group were regularly engaged in strength training of 3 days $week^{-1}$ and low aerobic training of 1 day $week^{-1}$ with a total volume of 210 minutes per week. CON subjects practiced a whole-body resistance exercise program during 60 min. day^{-1} with intensity between 60 and 70% of one maximum repetition (1RM) and rest interval inter-sets was 120 seconds. Furthermore, aerobic exercise was practiced during 30 minutes with intensity between 60 and 70% $VO_{2max.}$

The exercise group trained wheelchair rugby 2 days a week (60 min. day^{-1}), with a total volume of 120 minutes per week. All subjects practiced resistance exercise to upper body and trunk with resistance bands, wrist weights and medicine balls. However, specific training to wheelchair rugby consisted of basic fundamentals, defense, offense, or areas that need refinement. All subjects of the EG and SG group had incomplete cervical spinal cord injury (C5 - C7) with an average duration of more than 12 months. The level and completeness of SCI were determined by a complete neurological examination conducted as per the American Spinal Injury Association (ASIA) in all subjects with cervical SCI.

All experimental procedures were carried out in accordance with the Declaration of Helsinki and were approved by the local ethical committee. All subjects gave written informed consent before data collection and were considered healthy on the basis of history, physical examination and normal resting electrocardiogram. The following additional exclusion criteria were adopted: (a) use of drugs that could affect cardiorespiratory responses, (b) no smoking (c) systemic hypertension (≥ 140/90 mmHg) induced by the concentration of urinary volume, (d) metabolic disease, (e) urinary tract infection. No clinical problems occurred during the study.

ECG recording and Heart Rate Variability (HRV) analysis

ECG was continuously recorded (sampling rate of 1 kHz with 12-bit resolution) using a 12-lead ECG monitor system (CONTEC, model 8000D). All data were stored and analyzed off-line. Heart rate and the R-R time series were extracted from 10-min ECG tracings (V5 lead), recorded at rest after 15 minutes in the sitting position, using an R-R detection algorithm (MATLAB 7.0, The MathWorks, Inc, Natick, MA, USA). ECG recording occurred under spontaneous voluntary ventilation at rest (all groups showed an average breathing rate of about 12 breaths per min). The ECG tracing was manually inspected and edited for any ectopic beats. Both the ectopic and the post-extra-systolic beats were deleted and replaced by interpolated adjacent R-R interval values (Maior et al., 2013; Marocolo et al., 2013).

The following time domain of HRV variables were analyzed: R-R (mean of all normal R-R intervals) during the 10-min. recording; SDNN (standard deviation of successive normal R-R intervals); NN50 (number of interval differences of successive NN intervals greater than 50 ms); pNN50 (percentage of normal R-R intervals greater than 50 ms) and RMSSD (root mean square of the mean squared differences of successive R-R intervals) (Chung et al., 2011; Nooijen et al., 2015; Saunders et al., 2015).

For frequency-domain analysis, R-R intervals time series were re-sampled to equal intervals by spline cubic interpolation method at 2 Hz, and mean value and linear trend were removed. Fast Fourier transformation was used for calculating the power spectrum (Welch's periodogram was employed to assess the 1024-point spectra with a Hanning window and 50% overlap). Spectral power was obtained by integrating the power spectrum density function in the very low-frequency (VLF: 0.0033 and 0.04 Hz.), the low-frequency (LF: 0.04–0.15 Hz), and the high-frequency (HF: 0.15–0.40 Hz) bands. The spectral power was also computed in normalized units for the HF [HFnu = HF/ (total power - VLF) X 100] and LF [LFnu = LF/(total power - VLF) X 100], and the autonomic balance evaluated by the LF/HF (Chung et al., 2011; Saunders et al., 2015).

Statistical analysis

Data are presented as the means ± standard deviation. The data were initially analyzed using the Shapiro–Wilk normality test and the homoscedasticity test (Bartlett criterion). All variables presented normal distribution and homoscedasticity. Comparisons within groups were performed with a one-way ANOVA for repeated measures followed by Tukey's post hoc tests. Additionally, to determine the magnitude of the findings, effect size (ES) statistics were calculated for inter-groups (Control vs. EG Vs. SG) responses for rest and post-effort. The ES was calculated to determine the meaningfulness of the difference using the $f2$ for ANOVA. The magnitude of the ES was classified as small (< 0.1), medium (0.1–0.49) or large (> 0.5) (Cohen, 1988). The significance level was 0.05 and the software used for data analysis was GraphPad® (Prism 6.0, San Diego, CA, USA).

Results

Figure 1 shows the values mean of RR interval and total power in the three groups. The RR interval of control group was significantly (p=0.01) longer when compared to EG (Δ%= 18.7%) and SG (Δ%= 19.2%) (Figure 1A). In contrast, no significant changes were observed in ECG parameters inter-groups (p > 0.05) as shown in Figure 1B. But, comparison of effect size statistics of total power between control group Vs. EG and SG groups showed large values (>0.5).

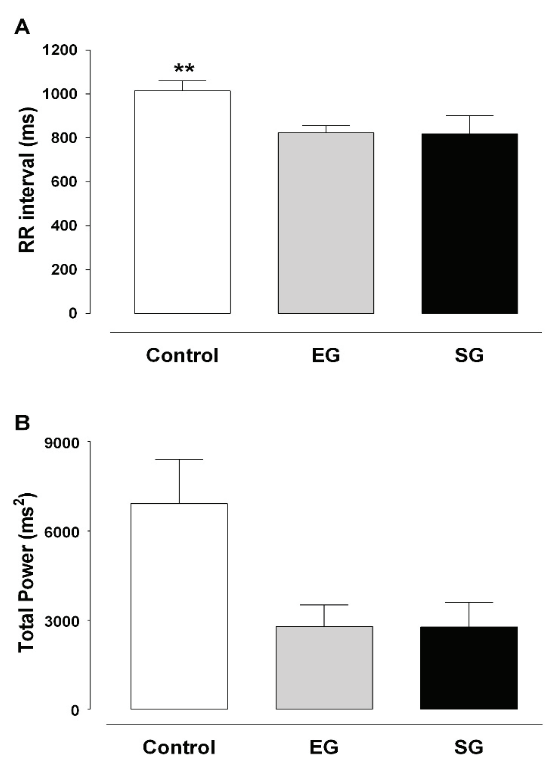

Figure 1. R-R intervals (A) and Total Power (B) at rest to control group (n = 8), exercise group with cervical SCI (EG; n= 8) and sedentary group with cervical SCI (SG; n=8). Values are expressed as mean ± standard deviation. **p < 0.01 versus EG and SG.

Figure 2 shows LF normalized, LF, HF normalized, and HF for the three groups at rest. Although none significant differences have been found inter-groups was observed a tendency to reduce the LF normalized by effect size statistics medium (0.43) values of SG when compared to EG (Figure 2A). On the other hand, LF component also no showed significant differences, but was observed a medium (0.48) and large (>0.51) effect size statistics values to EG and SG, respectively, in relation to control group (Figure 2B). However, HF normalized (EG – Δ%= 59.4%; SG - Δ%= 75%) and HF component (EG - Δ%= 84.1%; SG - Δ%= 78.9%) showed reduction significant in EG and SG when compared to control group (Figure 2C and D). LF-HF ratio no showed differences significant inter-groups (Control = 1.60 ± 1.05 %; EG = 4.39 ± 3.43%; SG = 3.52 ± 1.9%; p > 0.05), but effect size statistics for both groups with SCI (EG and SG) presented medium (0.48) to large (>0.5) values in relation to control group.

Figure 3 shows at rest mean values of pNN50, NN50, SDNN and RMSSD for the three groups. In the time-domain analysis, pNN50, NN50 and the RMSSD were significantly reduced in the EG (pNN50 - Δ%= 82.3%; NN50 - Δ%= 89%; RMSSD - Δ%= 60.7%) and SG (pNN50 - Δ%= 67%; NN50 - Δ%= 82.9%; RMSSD - Δ%= 52.5%) when compared to control group (p=0.0001) (Figure 3A, B, and D). On the other hand, control group exhibited higher SDNN (Δ% = 29.5%) only in relation to EG (Figure 3C).

Discussion

This study presents an evaluation of the time-course of cardiac autonomic response achieved at rest in a small sample of men with and without incomplete cervical SCI. We showed that the time-course of deleterious effects over the heart function were able to detect early signals of cardiac autonomic dysfunction in men with incomplete cervical SCI when compared to male adults with intact spinal cord. The principal novel findings of this study are that subjects of the EG showed a significant decrease in the SDNN, at rest, when compared with control group. Furthermore, the magnitude of ES statistics between EG vs. SG presented moderate values in relation to LF normalized.

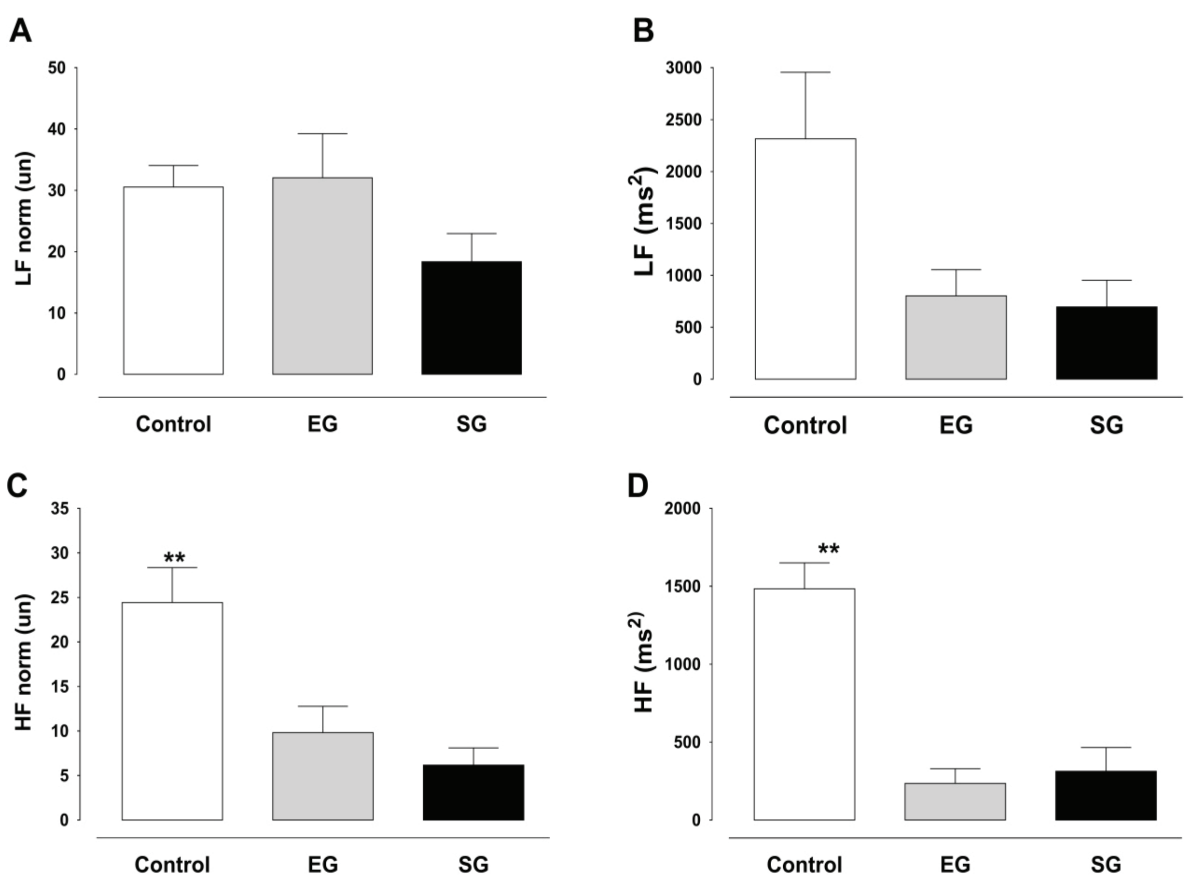

Figure 2. Frequency-domain heart rate variability indexes at rest. Values are expressed as mean ± standard deviation. * p < 0.0001 versus EG and SG.

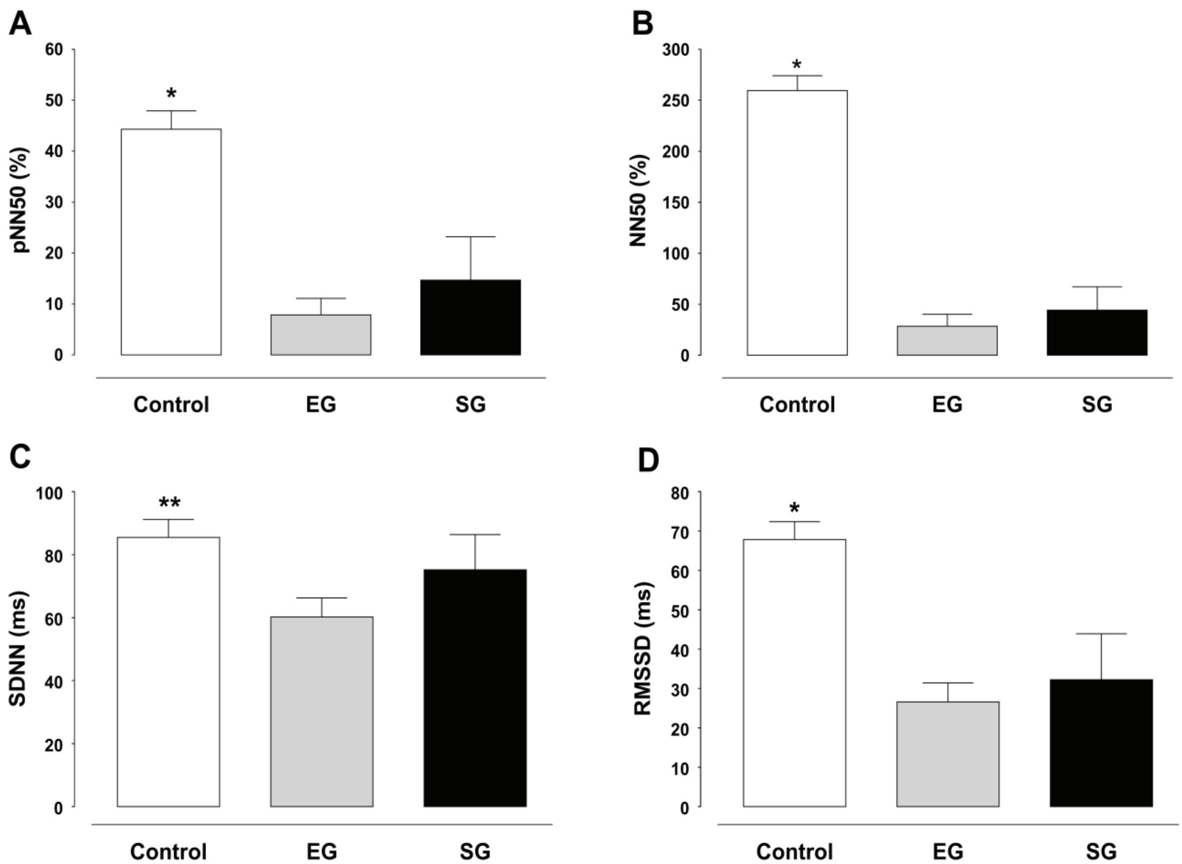

Figure 3. Time-domain heart rate variability indexes at rest. Values are expressed as mean ± standard deviation. * $p < 0.0001$ vs EG and SG; ** $p < 0.0001$ vs EG.

SDNN represent the global indicators of HRV, some studies suggest that SDNN lower than 70 ms, in subjects with intact spinal cord, is an excellent marker of increased risk of cardiac disease in patients with ischemic heart disease dysfunction and sudden death (Bigger et al., 1992; Fauchier, Babuty, Cosnay, & Fauchier, 1999). Other studies have associated the decrease of SDNN value (above 70 ms), after myocardial infarction, with almost 4 times more chance to die in the next 3 years (Buccelletti et al., 2009). This autonomic response can be associated with an autonomic dysfunction that reflects in a reduction of the variability of R-R intervals and in a lower SDNN.

In relation spinal cord injury, subjects with chronic complete cervical SCI showed significant decrease of SDNN when compared to incomplete cervical SCI (Demirel, Yilmaz, Korkut, Atilgan, & Akkaya, 1999; Leaf, Bahl, & Adkins, 1993). However, during acute phase of the incomplete cervical SCI was observed rise of SDNN possibly to recovery of autonomic function and remodeling of damaged axons after trauma (Malmqvist et al., 2015; Raineteau & Schwab, 2001). Possibly an autonomic adjustment occurs chronic phase of the injury with the practice of physical activity can a remodeling occur?. Our data showed lower values of SDNN (60.2 ± 14.8 ms) in chronic incomplete cervical SCI when compared to control group (85.4 ± 16.1 ms), thus speculating that parasympathetic activity is also decreased in patients with tetraplegia associated to sympathetic withdrawal by cervical spinal cord injury. Consequently, this response may be a mechanism for maintained autonomic homeostasis (Wang et al., 2000), but the degree of preserved sympathetic function in tetraplegic athletes may suggest a predisposition to engage in high-performance sports or loss during exercise (Currie, West, Hubli, Gee, & Krassioukov, 2015). In this context, the type of spinal cord injury can be determinant to performance during physical activity.

On the other hand, decrease of RMSSD, pNN50, and NN50 in cervical SCI is mainly by parasympathetic activity influence where directly related with lower RR interval. Based on the parasympathetic influence, the RMSSD index has better statistical properties for assessing parasympathetic activity than NN50 and pNN50 (Malmqvist et al., 2015; Rodrigues et al., 2015). The

RMSSD has been used as a better index of cardiac parasympathetic control since it is uncontaminated by sympathetically mediated HRV (Berntson, Lozano, & Chen, 2005).

The LF power not showed significant difference inter-groups, whereas the magnitude of the effect size seems to be influenced by practice of physical activity when LF power values were normalized (LF_{un}). The normalization of values in frequency domain contributed to minimize the effect of changes in total power of LF and HF values ("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), and could be a relevant factor to significantly reduced HF values between SCI and the control group. The LF power component is an index that reflects fluctuations mediated by both cardiac vagal and sympathetic nerves (Perini & Veicsteinas, 2003). On the other hand, some studies suggest that the sympathetic activity contributes to LF value approximately 15% more than the vagal activity (Eckberg, 1997; Malik, 1998; Montano et al., 2009; Piccirillo et al., 2009). However, the increases in sympathetic activity induced by nitroprusside contributes to a significant correlation between sympathetic nerve activity and LF_{un}, consequently, the LF component of HRV have been utilized as an index of cardiac sympathetic control (Reyes del Paso, Langewitz, Mulder, van Roon, & Duschek, 2013; Saul et al., 1991). This increase of the sympathetic activity mediated by LF_{un} seems influence to elevate the LF/HF ratio induced-exercise in subjects with cervical SCI. Results of the study of Takahashi et al. (2007) no showed significant difference inter groups (tetraplegic Vs. intact spinal cord) but observed a tendency exaggerated in LF power values in athletes tetraplegic during rest. Perhaps the destruction of descending sympathetic pathways was incomplete in some subjects with cervical SCI. A physiological view of increase LF_{un} would be related to autonomic dysfunction. However, this response in subjects with cervical spinal cord injury may be associated to adjustment of the cardiac autonomic system from remodeling of damaged axons after trauma induced-exercise. Thus, West et al. (2013) suggest that partial preservation of sympathetic autonomic control and response of the cardiovascular system to exercise may be a determinant for adjustment of the cardiac autonomic profile in practitioners of physical exercise with cervical SCI.

Limitations of the present study showed a small number of patients. However, it was not possible to include more patients in the EG and SG groups since this study prospectively included consecutive patients admitted with a cervical SCI, so the inherent nature of the study makes this potential bias inevitable. Further investigation could give information about how the heart adapts to physical exercises in a situation of damage to sympathetic innervation and which patients are especially vulnerable to the cardiac instability resulting of the cervical SCI. Furthermore, it would be important to verify the contribution of training equipment (i.e. graduated compression stockings or blood flow restriction) in the profile of cardiac autonomic control of subjects with cervical SCI.

Conclusion

We concluded that changes in cardiac autonomic system can be observed with practice of physical exercise in subjects with cervical SCI. This response was observed with decrease of SDNN and a tendency exaggerated in LFnu values, suggesting adjustment of the cardiac autonomic system from remodeling of damaged axons induced-exercise. This enhanced sympathetic activity with practice of physical exercise can contribute to minimize risk of cardiac arrhythmias and sudden cardiac death in subjects with cervical SCI.

References

Adebayo, R. A., Ikwu, A. N., Balogun, M. O., Akintomide, A. O., Ajayi, O. E., Adeyeye, V. O., ... Oketona, O. A. (2015). Heart rate variability and arrhythmic patterns of 24-hour Holter electrocardiography among Nigerians with cardiovascular diseases. *Vascular health and risk management*, *11*(2), 353-359. doi: 10.2147/VHRM. S81106.

Barth, Z., Nomeland Witczak, B., Schwartz, T., Gjesdal, K., Flato, B., Koller, A., … Sjaastad, I. (2015). In juvenile dermatomyositis, heart rate variability is reduced, and associated with both cardiac dysfunction and markers of inflammation: a cross-sectional study median 13.5 years after symptom onset. *Rheumatology*, *55*(3), 535-543. doi: 10.1093/rheumatology/kev376

Berntson, G. G., Lozano, D. L., & Chen, Y. J. (2005). Filter properties of root mean square successive difference (RMSSD) for heart rate. *Psychophysiology*, *42*(2), 246-252. doi: 10.1111/j.1469-8986.2005.00277.x

Biering-Sorensen, F., Bickenbach, J. E., El Masry, W. S., Officer, A., & von Groote, P. M. (2011). ISCoS-WHO collaboration. International Perspectives of Spinal Cord Injury (IPSCI) report. *Spinal cord*, *49*(6), 679-683. doi: 10.1038/sc.2011.12.

Bigger, J. T., Jr., Fleiss, J. L., Steinman, R. C., Rolnitzky, L. M., Kleiger, R. E., & Rottman, J. N. (1992). Correlations among time and frequency domain measures of heart period variability two weeks after acute myocardial infarction. *The American journal of cardiology*, *69*(9), 891-898. doi: 10.1016/0002-9149(92)90788-Z

Buccelletti, E., Gilardi, E., Scaini, E., Galiuto, L., Persiani, R., Biondi, A., … Silveri, N. G. (2009). Heart rate variability and myocardial infarction: systematic literature review and metanalysis. *European review for medical and pharmacological sciences*, *13*(4), 299-307.

Center, N. S. C. I. S. (2015). *Facts and Figures at a Glance*. Birmingham, AL: University of Alabama at Birmingham.

Chung, F. P., Hu, Y. F., Chao, T. F., Higa, S., Cheng, H., Lin, Y. J., ... Chen, S. A. (2011). The correlation between ventricular repolarization and clinical severity of spinal cord injuries. *Heart rhyth: the official journal of the Heart Rhythm Society*, *8*(6), 879-884. doi: 10.1016/j.hrthm.2011.01.034

Cohen, J. (1988). *Statistical power analysis for the behavioural sciences*. Hillsdale, NJ: Lawrence Erlbaum.

Currie, K. D., West, C. R., Hubli, M., Gee, C. M., & Krassioukov, A. V. (2015). Peak heart rates and sympathetic function in tetraplegic nonathletes and athletes. *Medicine and science in sports and exercise*, *47*(6), 1259-1264. doi: 10.1249/MSS.0000000000000514.

Demirel, G. D. S., Yilmaz, H., Akkaya, V., Atilgan, D., & Korkut, F. (1999). Cardiac Dysrhythmias and Autonomic Dysfunction in Chronic Spinal Cord Injury: A 24-Hour Holter Monitoring and Heart Rate Variability Study. *Neurorehabil Neural Repair*, *13*(4), 7. doi: 10.1177/154596839901300405

Eckberg, D. L. (1997). Sympathovagal balance: a critical appraisal. *Circulation*, *96*(9), 3224-3232. doi: 10.1161/01.CIR.96.9.3224

Fauchier, L., Babuty, D., Cosnay, P., & Fauchier, J. P. (1999). Prognostic value of heart rate variability for sudden death and major arrhythmic events in patients with idiopathic dilated cardiomyopathy. *Journal of the American College of Cardiology*, *33*(5), 1203-1207. doi: 10.1016/S0735-1097(99)00021-2

Garshick, E., Kelley, A., Cohen, S. A., Garrison, A., Tun, C. G., Gagnon, D., & Brown, R. (2005). A prospective assessment of mortality in chronic spinal cord injury. *Spinal cord*, *43*(7), 408-416. doi: 10.1038/sj.sc.3101729

Grossman, R. G., Frankowski, R. F., Burau, K. D., Toups, E. G., Crommett, J. W., Johnson, M. M., ... Harrop, J. S. (2012). Incidence and severity of acute complications after spinal cord injury. *Journal of neurosurgery. Spine*, *17*(1 Suppl), 119-128. doi: 10.3171/2012.5.AOSPINE12127.

Harkey, H. L., White, E. A. T., Tibbs, R. E., Jr., & Haines, D. E. (2003). A clinician's view of spinal cord injury. *Anatomical record. Part B, New anatomist*, *271*(1), 41-48. doi: 10.1002/ar.b.10012

Heart rate variability. (1996). 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. doi: 10.1093/oxfordjournals.eurheartj.a014868.

Heart rate variability. (1996). 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.. *Circulation*, *93*(5), 1043-1065. doi: 10.1161/01.CIR.93.5.1043.

Krug, E. G., Sharma, G. K., & Lozano, R. (2000). The global burden of injuries. *American journal of public health*, *90*(4), 523-526.

Leaf, D. A., Bahl, R. A., & Adkins, R. H. (1993). Risk of cardiac dysrhythmias in chronic spinal cord injury patients. *Paraplegia*, *31*(9), 571-575. doi: 10.1038/sc.1993.92

Maior, A. S., Carvalho, A. R., Marques-Neto, S. R., Menezes, P., Soares, P. P., & Nascimento, J. H. (2013). Cardiac autonomic dysfunction in anabolic steroid users. *Scandinavian journal of medicine & science in sports*, *23*(5), 548-555. doi: 10.1111/j.1600-0838.2011.01436.x

Malik, M. (1998). Sympathovagal balance: a critical appraisal. *Circulation*, *98*(23), 2643-2644. doi: 10.1161/01.CIR.98.23.2643

Malmqvist, L., Biering-Sorensen, T., Bartholdy, K., Krassioukov, A., Welling, K. L., Svendsen, J. H., ... Biering-Sorensen, F. (2015). Assessment of autonomic function after acute spinal cord injury using heart rate variability analyses. *Spinal cord*, *53*(1), 54-58. doi: 10.1038/sc.2014.195.

Marocolo, M, Maior, A.S., Katayama, P. L., da Mota, G. R., Barbosa Neto, O., Lauria, A. A., Santos, E. L. (2013). Anabolic steroid treatment induces cardiac autonomic dysfunction in rats: time-course of heart rate variability. *American Journal of Biomedical Engineering*, *3*(3), 9. doi: 10.5923/j.ajbe.20130303.02

Montano, N., Porta, A., Cogliati, C., Costantino, G., Tobaldini, E., Casali, K. R., & Iellamo, F. (2009). Heart rate variability explored in the frequency domain: a tool to investigate the link between heart and behavior. *Neuroscience and biobehavioral reviews*, *33*(2), 71-80. doi: 10.1016/j.neubiorev.2008.07.006.

Nooijen, C. F., Post, M. W., Spooren, A. L., Valent, L. J., Broeksteeg, R., Sluis, T. A., ... van den Berg-Emons, R. J. (2015). Exercise self-efficacy and the relation with physical behavior and physical capacity in wheelchair-dependent persons with subacute spinal cord injury. *Journal of neuroengineering and rehabilitation*, *12*(1), 103. doi: 10.1186/s12984-015-0099-0.

Perini, R., & Veicsteinas, A. (2003). Heart rate variability and autonomic activity at rest and during exercise in various physiological conditions. *European journal of applied physiology*, *90*(3-4), 317-325. doi:10.1007/s00421-003-0953-9

Piccirillo, G., Ogawa, M., Song, J., Chong, V. J., Joung, B., Han, S., ... Chen, P. S. (2009). Power spectral analysis of heart rate variability and autonomic nervous system activity measured directly in healthy dogs and dogs with tachycardia-induced heart failure. *Heart rhythm : the official journal of the Heart Rhythm*

Society, *6*(4), 546-552. doi: 10.1016/j.hrthm. 2009.01.006

Raineteau, O., & Schwab, M. E. (2001). Plasticity of motor systems after incomplete spinal cord injury. *Nature reviews. Neuroscience*, *2*(4), 263-273. doi: 10.1038/35067570

Ravensbergen, H. J., Walsh, M. L., Krassioukov, A. V., & Claydon, V. E. (2012). Electrocardiogram-based predictors for arrhythmia after spinal cord injury. *Clinical autonomic research : official journal of the Clinical Autonomic Research Society*, *22*(6), 265-273. doi: 10.1007/s10286-012-0166-6

Reyes del Paso, G. A., Langewitz, W., Mulder, L. J., van Roon, A., & Duschek, S. (2013). The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: a review with emphasis on a reanalysis of previous studies. *Psychophysiology*, *50*(5), 477-487. doi: 10.1111/psyp.12027.

Rodrigues, D., Tran, Y., Guest, R., Middleton, J., & Craig, A. (2015). Influence of neurological lesion level on heart rate variability and fatigue in adults with spinal cord injury. *Spinal cord*, *54*(4), 292-297. doi: 10.1038/sc.2015.174

Santos, E. A., Santos Filho, W. J., Possatti, L. L., Bittencourt, L. R., Fontoura, E. A., & Botelho, R. V. (2012). Clinical complications in patients with severe cervical spinal trauma: a ten-year prospective study. *Arquivos de neuro-psiquiatria*, *70*(7), 524-528. doi: 10.1590/S0004-282X2012000700010.

Saul, J. P., Berger, R. D., Albrecht, P., Stein, S. P., Chen, M. H., & Cohen, R. J. (1991). Transfer function analysis of the circulation: unique insights into cardiovascular regulation. *The American journal of physiology*, *261*(4 Pt 2), H1231-1245.

Saunders, L. L., Clarke, A., Tate, D. G., Forchheimer, M., & Krause, J. S. (2015). Lifetime prevalence of chronic health conditions among persons with spinal cord injury. *Archives of physical medicine and rehabilitation*, *96*(4), 673-679. **doi**: 10.1016/j.apmr.2014.11.019

Sisto, S. A., Lorenz, D. J., Hutchinson, K., Wenzel, L., Harkema, S. J., & Krassioukov, A. (2012). Cardiovascular status of individuals with incomplete spinal cord injury from 7 NeuroRecovery Network rehabilitation centers. *Archives of physical medicine and rehabilitation*, *93*(9), 1578-1587. doi: 10.1016/j.apmr. 2012.04.033.

Takahashi, M., Matsukawa, K., Nakamoto, T., Tsuchimochi, H., Sakaguchi, A., Kawaguchi, K., & Onari, K. (2007). Control of heart rate variability by cardiac parasympathetic nerve activity during voluntary static exercise in humans with tetraplegia. *Journal of applied physiology*, *103*(5), 1669-1677. doi: 10.1152/japplphysiol.00503.2007

Task Force of the European Society of Cardiology, the North American Society of Pacing and Electrophysiology. (1996). Heart rate variability: standards of measurement, physiological interpretantion and clinical use. *Circulation, 93*(5), 1043-1065.

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. doi: 10.1016/j.ijcard.2009.09.543.

Wang, Y. H., Huang, T. S., Lin, J. L., Hwang, J. J., Chan, H. L., Lai, J. S., & Tseng, Y. Z. (2000). Decreased autonomic nervous system activity as assessed by heart rate variability in patients with chronic tetraplegia. *Archives of physical medicine and rehabilitation*, *81*(9), 1181-1184. doi: 10.1053/apmr.2000.6300

Weaver, L. C., Fleming, J. C., Mathias, C. J., & Krassioukov, A. V. (2012). Disordered cardiovascular control after spinal cord injury. *Handbook of clinical neurology*, *109*(1), 213-233. doi: 10.1016/B978-0-444-52137-8.00013-9

West, C. R., Romer, L. M., & Krassioukov, A. (2013). Autonomic function and exercise performance in elite athletes with cervical spinal cord injury. *Medicine and science in sports and exercise*, *45*(2), 261-267. doi: 10.1249/MSS.0b013e31826f5099.

Yang, S., Ding, W., Yang, D., Gu, T., Zhang, F., Zhang, D., ... Song, Y. (2013). Epidemiology and risk factors of cervical spine injury during heating season in the patients with cervical trauma: a cross-sectional study. *PloS one*, *8*(11), e78358. doi: 10.1371/journal.pone. 0078358.

Received on September 9, 2016.
Accepted on May 11, 2017.