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Chronic Exertional Symptoms Post-Concussion in the Military Population:

The Role of Heart Rate Variability and Graded Exercise Treatment

Introduction

Since 2001, over 325,000 SM's have sustained a traumatic brain injury with over 80% of those being mTBI¹, making it a prominent issue in military healthcare. While most sports concussions usually resolve with rest and gradual return to activity, up to 35% of military-related concussions result in chronic physical, sensory, emotional, and affective symptoms that make it unsafe for them to perform full active duty responsibilities². While the Zurich sports concussion guidelines prescribe cognitive and physical rest until all symptoms resolve³, specific parameters for type and duration of rest have not been established, and the majority of current evidence actually demonstrates negative physiologic and cognitive effects of rest beyond a few days after mTBI⁴. Thus, research has begun to investigate the effectiveness, safety, optimal parameters, and reasoning for gradual exercise progression following concussion.

Heart Rate Variability Post-Concussion

Autonomic nervous system (ANS) dysfunction has repeatedly been theorized to be associated with chronic mTBI symptoms since many of the processes the ANS is responsible for regulating remain impaired in patients with chronic mTBI^{3,5}. The ANS functions to continuously regulate heart rate in response to blood pressure oscillations, respiration rate, thermoregulation, and circadian rhythm⁶. These autonomic modulations result in slight differences in time periods between consecutive heart beats, termed

heart rate variability (HRV).⁷ Reduced HRV indicates impaired efficiency of autonomic modulation, and analysis of HRV has been shown in multiple studies to be a feasible, reliable and accurate measure of ANS functioning⁷. Reduced HRV and impaired cerebral autoregulation has also been demonstrated in patients during the post-acute/chronic stages of mTBI^{8,9,10}. Thus, HRV may be a viable target for intervention to improve symptoms of chronic concussion, but research in this area is only in the very initial stages.

Interestingly, several studies of athletes in the acute stage of concussion show that HRV differs significantly between those with mTBI and matched controls only during response to exercise, and not at rest^{11,12}. Similarly, a recent cross-sectional study of university level athletes in the chronic stage of concussion exhibited significantly reduced HRV in comparison to matched controls during exertion but not at rest¹³. The reduced HRV after concussion may play into the body's inability to properly auto-regulate constant cerebral perfusion pressure and cerebral blood flow in response to the increased systemic arterial pressure that occurs with exertion¹⁴, explaining this phenomenon and why symptoms of concussion, such as headache and dizziness, tend to be aggravated with exertional activity. This evidence further indicates the possibility of the continued influence of ANS dysfunction on chronic concussion symptoms with exertional activity.

Research regarding HRV in specifically the military population following mTBI is lacking, but early pilot studies indicate that pain, post-traumatic stress symptoms, and mTBI may together reduce HRV in SM's. Importantly, this evidence also indicates that HRV in this population may be modified by intervention that increases respiratory

activity, such as aerobic exercise^{15,16}. Thus, overall evidence points to a convincing role of ANS dysfunction in continuance of chronic concussion symptoms that affect exertional abilities, but further research targeting populations in the chronic stages of concussion and military populations is warranted. Additionally, analysis of HRV via a polar or seems to be a relatively easy, inexpensive, and quick technique to reliably and accurately assess ANS functioning in this population, and has good potential to be utilized to monitor patient progress and help guide return to duty decisions.

Graded Exercise Treatment

Considering the need for athletes, SM's and other individuals post-concussion to return to regular activity without symptom limitation, and that rest beyond the first few days after concussion may have more negative than beneficial effects⁴, establishment of an effective and safe exercise rehabilitation program for those with chronic concussion symptoms and exertional complaints has become a focus in the most leading-edge research. Additionally, exercise has been shown to increase the respiratory activity that may be necessary to increase HRV and improve cerebral blood flow¹⁷, further justifying its potential benefits of exercise training. Thus far, initial stages of research have shown a significant association between chronic exertional symptoms and abnormal cerebral blood flow on fMRI¹⁸, as well as suggested that damaged communication between autonomic brain centers and baroreceptors of the heart may play a role in the impaired autoregulation and HRV that leads to persistent exertional symptoms¹⁹.

The Zurich Consensus Statement provides non-specific recommendations for athletes to begin with light activity and progress to sport specific activity once symptom-

free at rest³. However, these recommendations are very broad and non-specific, and there is no recommendation or consensus on safe effective treatment if symptoms do not resolve. Leddy and Willer have established what seems to be the most specific protocol for a gradually progressive sub-symptom threshold exercise treatment for this population²⁰, which has demonstrated decreased exertional chronic concussion symptoms in athletes in several initial studies^{18,20}. This protocol utilizes the Buffalo Concussion Treadmill Test (BCTT) to provide a baseline and assess patient progress. The individual walks on a treadmill at gradually increasing incline until concussion symptoms are aggravated. The individual then begins exercising at 80% of that heart rate for 20 minutes multiple times a week and is re-evaluated every 2 weeks with the BCTT to set a new heart rate goal for exercise until the patient can complete the full 20 minute BCTT without symptom exacerbation.²⁰

On average, current studies of submaximal exercise treatments have demonstrated decreased number and severity of exertional symptoms, increased exercise tolerance, and improved ability to return to prior level of activity in athletes and community populations in comparison to continued rest⁴. It is important to note that combination of graded submaximal training may be more beneficial when incorporated into a comprehensive therapy plan⁴. Also, only initial stages of research have been completed to address exercise treatment for chronic post-concussion symptoms. Thus, the existing evidence is of relatively low quality, lacking randomization, large sample sizes, and specific comparison to other forms of treatment. Thus, further higher level research with larger sample sizes and randomization is necessary.

Generally, it has been accepted that these clinical effects of graded aerobic exercise training in athletic populations may be generalized to military patients due to similarly vigorous activity requirements. However, no studies in the military population have been performed to confirm this postulation. Considering the high incidence of military mTBI¹, the differing mechanism of injury in military-related concussions, and the tendency of military-related concussions to result in more chronic symptoms than sports-related², research specific to this population is also warranted. At this point, the state of evidence on this subject consistently suggests that controlled progressive aerobic exercise training at a sub-symptom level based on heart rate reached during treadmill testing may be both safe and effective in decreasing chronic exertional concussion symptom severity and decreasing activity limitations due to symptom exacerbation with exertion. However, due to the small quantity of relevant research, best clinical judgement and patient preferences should also be taken into account to make the most informed treatment decisions.

References

1. DoD worldwide numbers for TBI. Defense and Veterans Brain Injury Center Web site. <http://dvbic.dcoe.mil/dod-worldwidenumbers-tbi>. Published May 15, 2015. Accessed April 1, 2016.
2. Schneiderman AI, Braver ER, Kang HK. Understanding sequelae of injury mechanisms and mTBI incurred during the conflicts in Iraq and Afghanistan: persistent PCS and PTSD. *Am J Epidemiol*. 2008;167:1446-52.
3. McCrory P, Meeuwisse WH, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. *Br J Sports Med*. 2013;47(5):250-8.
4. Schneider KJ, Iverson GL, Emery CA, McCrory P, Herring SA, Meeuwisse WH. The effects of rest and treatment following sport-related concussion: a systematic review of the literature. *The British Journal of Sports Medicine*. 2013;47:304-307.
5. Ellemberg D, Henry LC, Macciocchi SN, Guskiewicz KM, Broglio SP. Advances in sport concussion assessment: from behavioral to brain imaging measures. *J Neurotrauma*. 2009;26:2365–2382.
6. Marques AH, Silverman MN, Sternberg EM. Evaluation of stress systems by applying noninvasive methodologies: measurements of neuroimmune biomarkers in the sweat, heart rate variability and salivary cortisol. *Neuroimmunomodulation*. 2010;17:205– 208.
7. 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. *Eur Heart J*. 1996;17:354–381.
8. Thayer JF, Ahs F, Fredrikson M, et al. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker for stress and health. *Neurosci Biobehav Rev*. 2012;36:747-56.
 9. Keren O, Yupatov S, Radai MM, Elad-Yarum R, Faraggi D, Abboud S, Ring H, Groswasser Z. Heart rate variability (HRV) of patients with traumatic brain injury (TBI) during the postinsult sub-acute period. *Brain Inj*. 2005;19:605–611.
 10. King ML, Lichtman SW, Seliger G, Ehert FA, Steinberg JS. Heart-rate variability in chronic traumatic brain injury. *Brain Inj*. 1997;11:445–453.
 11. Gall B, Parkhouse W, Goodman D. Heart rate variability of recently concussed athletes at rest and exercise. *Med Sci Sports Exerc*. 2004;36:1269–1274.
 12. La Fontaine MF, Heffernan KS, Gossett JD, Bauman WA, De Meersman RE. Transient suppression of heart rate complexity in concussed athletes. *Auton Neurosci*. 2009;148:101–103.
 13. Abaji JP, Curnier D, Moore RD, Elleberg D. Persisting effects of concussion on heart rate variability during physical exertion. *Journal of Neurotrauma*. 2015. doi:10.1089/neu.2015.3989.
 14. DeWitt DS, Prough DS. Traumatic cerebral vascular injury: the effects of concussive brain injury on the cerebral vasculature. *J Neurotrauma*. 2003;20:795–825.

15. Tan G, Fink B, Dao TK, et al. Associations among pain, PTSD, mTBI and heart rate variability in veterans of Operation Enduring and Iraqi Freedom: a pilot study. *Pain Med.* 2009;10:1237-45.
16. Tan G, Dao TBK, Farmer L, et al. Heart rate variability (HRV) and PTSD: a pilot study. *Appl Psychophysio Biofeedback.* 2011;36:27-35.
17. Brown RP, Gerbarg PL. Sudarshan Kriya. Yogic breathing in the treatment of stress, anxiety, and depression: part I-neurophysiologic model. *J Altern Complement Med.* 2005;11:189–201.
18. Leddy JJ, Cox JL, Baker JG, Wack DS, Pendergast DR, Zivadinov R, Willer B. Exercise treatment for postconcussion syndrome: a pilot study of changes in functional magnetic resonance imaging activation, physiology, and symptoms. *Journal of Head Trauma Rehabilitation.* 2013;28(4):241-249.
19. Goldstein B, Toweill D, Lai S, et al. Uncoupling of the autonomic and cardiovascular systems in acute brain injury. *Am J Physiol.* 1998; 275 (4 Pt 2): R1287-92.
20. Leddy JJ, Koslowski K, Donnelly JP, Pendergast DR, Epstein LH, Willer B. A preliminary study of subsymptom threshold exercise training for refractory post-concussion syndrome. *Clinical Journal of Sport Medicine.* 2010;20(1):21-27.