Autonomic cardiovascular response during and after a graded exercise test in concussed athletes and healthy controls

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Abstract

Objective: Dysfunction of the autonomic cardiovascular system after a concussion is known to cause exercise intolerance due to symptoms exacerbation. The aim of this study was to compare athletes with symptoms of a sport-related concussion and healthy controls with regard to their heart rate during a graded exercise test and their heart rate recovery during the 5 min cool-down after the graded exercise test.

Methods: Sport-related concussion patients (N = 61; 31% female) and controls (N = 16; 50% female) participated in a graded exercise test on a cycle ergometer followed by 5 min active cool-down. Based on the results of graded exercise tests they were divided into four groups: (1) patients who reached the symptom threshold and had to stop the graded exercise test (symptom threshold; N = 39; 33.3% female), (2) patients with symptoms who finished the graded exercise test (S; N = 16; 25% female), (3) patients without symptoms (NS; N = 6; 33.3% female), (4) controls (N = 16; 50% female).

Main outcome measures: Heart rate, severity of headache and dizziness during graded exercise test, heart rate recovery (median (heart rate recoveries/maximal heart rate) ± median absolute deviation (MAD)) 30, 60 and 300 s after the start of cool-down.

Results: Heart rate recovery at 30 s was significantly slower in symptom (0.95 ± 0.01) compared to all other groups (p < 0.002; symptom threshold: 0.92 ± 0.02, NS: 0.91 ± 0.02, controls: 0.93 ± 0.02). Heart rate recovery at 60 s was significantly slower in symptom (0.90 ± 0.02) compared to the symptom threshold and controls (p < 0.041; 0.86 ± 0.03, 0.85 ± 0.04). Heart rate recovery at 300 s was significantly slower in symptom threshold (0.72 ± 0.05) compared to controls (p = 0.003; 0.66 ± 0.02).

Conclusions: Heart rate measurements in athletes with symptoms of sport-related concussion should be continued during cool-down after the graded exercise test, as dysfunction of the autonomic cardiovascular system might manifest also during cool-down.

Keywords
Sport-related concussion, mild traumatic brain injury, exercise intolerance, autonomic dysfunction, heart rate recovery

Date received: 15 December 2020; accepted: 20 August 2021

Introduction

Sport-related concussion (SRC) is classified as mild traumatic brain injury. Harmon et al.1 defined concussion as a ‘traumatically induced transient disturbance of brain function that involves a complex pathophysiologic process’. The incidence of SRCs varies according to specific types of sports. A recent meta-analysis on head injuries in team contact sports revealed the highest concussion incidence in rugby match play.2

The fifth consensus statement on concussion in sport recommends physical rest of 24 to 48 h before considering initiating the return-to-sport.1 SRC athletes should undergo a stepwise reintroduction to light aerobic training if they do not report symptoms increase during normal daily activity.3

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In some cases, SRC athletes may report symptoms, such as headache or dizziness, whenever the heart rate (HR) is increasing, denoted as exercise intolerance. Currently, the mechanism is not clearly understood, but it has been hypothesized that it is most likely due to a cardiovascular autonomic dysfunction, which leads to an impairment of the cerebral blood flow. The aggravation of pre-existing symptoms during HR increases leads to exhaustion and limits SRC athletes to train with the required intensity.

The altered autonomic nervous function of the cardiovascular system can also result in an exaggerated sympathetic and lower parasympathetic activity, resulting in an increased HR at rest (HRrest) compared to healthy controls. This specific autonomic dysfunction can be detected with graded exercise tests (GETs), for example, the Buffalo concussion bike test or the treadmill test. The test on the bike allows the investigation of the cardiovascular system limiting the stimulation of the cervical and vestibular system and vestibulo-oculomotor reflex as the bike is stationary. This test consists of a continuous increase of load until volitional exhaustion or until a symptom threshold (ST) is reached. The reaching of the ST indicates the presence of an autonomic dysfunction. However, no further guidelines are given in the case of symptoms increasing immediately after the physical effort. Symptoms development immediately after physical effort or exhaustion is crucial, for example in ice hockey, where players perform for 45 s followed by a 2 to 5 min recovery time on the bench. To our knowledge, no study has previously investigated the HR recovery (HRR) during the first 5 min after reaching the maximal HR (HRmax) through a GET.

The aim of this study is to investigate the HR during the GET and the HRR in the 5 min after reaching the HRmax as this aspect may impact the way SRC athletes should return to sport.

**Methods**

This case series study compared athletes referred to the Swiss Concussion Center due to an SRC and healthy controls with regard to HR, severity of headache and dizziness during GET, and HRR after the GET. The study protocol was in accordance with the 2013 Declaration of Helsinki for research involving human subjects and was approved by the local ethics committee (BASEC-nr-2017-01208).

**Participants**

Male and female athletes who were referred to Swiss Concussion Center and fulfilled the following inclusion criteria: (1) recreational up to elite level, (2) aged 18 years or older (3) suffering from an SRC were examined and evaluated for eligibility for study participation by two senior neurologists (N.F. or A.P.) before being scheduled for a GET on the cycle ergometer. Healthy, age-matched recreational and competitive athletes with no history of SRC were recruited from the general population as a control group. Exclusion criteria were: (1) symptom severity score ≥7 on a numeric rating scale (NRS; 0–10, with 0 = no symptoms and 10 = severe symptoms) prior to the start of the GET, (2) exercise inability due to comorbidities, such as orthopaedic injury and heart disease.

**Graded exercise test**

Participants performed a GET on a cycle ergometer (Ergometer 8000-med-t, Proxomed, Germany) using a modified version of the Buffalo concussion bike test. First, participants rested supine for 5 min. They were then asked to perform a 5-min warm-up on the cycle ergometer at a constant resistance adjusted according to the subject’s body weight with a constant cadence of 60 to 65 repetitions per minute (r/min). After the warm-up, while participants continued cycling at 60 r/min, resistance was increased each minute according to the individual body weight until volitional exhaustion or until the severity of headache and/or dizziness increased ≥3 of 10 NRS points in comparison with pre-exercise symptom level, that is, ‘ST’. A 5-min cool-down period with the same resistance and cadence used during warm-up terminated the GET.

HR was recorded continuously during the GET using an HR sensor (1 Hz, Polar H7 HR Monitor, Finland). The severity of headache and/or dizziness was asked every 2 min during the whole test procedure.

**Data grouping**

Patients were divided into three subgroups according to the change in symptom severity during the GET (Figure 1A). Group NS: patients who did not experience any symptoms during the whole test and stopped GET at voluntary exhaustion (Figure 1B). Group S: patients who experienced symptoms below ST during the GET and stopped GET at voluntary exhaustion (Figure 1C). Group ST: patients who had to stop GET due to symptom increase ≥3 scores on the NRS from pre-exercise value (Figure 1D). Subjects of the control group did not experience any symptoms at any time during the GET (Figure 1B).

**Data processing**

HR was calculated as a mean value over 5 min for the rest (HRrest) and the warm-up (HRwarm-up) period. During the GET, only the HRmax was used for the data analysis. HRR at 30, 60 and 300 s (HRR30s, HRR60s, and HRR300s) during cool-down was calculated as the ratio between HR at the three time points and HRmax. These three values were chosen to observe the influence of parasympathetic activation (HRR30s and HRR60s) as well as parasympathetic and
sympathetic activation (HRR300s). Furthermore, HRR30s is the only parameter not dependent on exercise intensity. The difference of symptom severity at rest and HRmax, as well as between HRmax and end of cool-down was used for statistical analysis.

**Statistical analysis**

The continuous variables were compared using one-way analysis of variance (ANOVA) or non-parametrical Kruskal–Wallis test. The latter was used when data normality was not confirmed by the Lilliefors test. Specifically, demographics variables – age and weight – were compared between SRC athletes and control group, and between the three patient groups (NS vs. S vs. ST) using a one-way ANOVA, while proportions – gender, number of elite/recreational athletes – were compared using a chi-square test. The number of concussions, time since the most recent concussion, exercise duration and HR variables (HRrest, HRwarm-up, HRmax, HRR30s, HRR60s and HRR300s) were compared between groups using the Kruskal–Wallis test. For post-hoc multiple comparisons, Tukey’s honest significant difference procedure was performed to retrain the family-wise error rate. The differences of dizziness and headache severity between rest to HRmax, and end of cool-down were compared between the S and ST group using rank-sum test. A p-value of <0.05 (after correction in multiple comparisons) was considered statistically significant. All analyses were performed in MATLAB (MatLab 8.2; The MathWorks, Inc., USA).

**Results**

Sixty-one SRC athletes and 16 healthy controls participated in the study (Table 1). Patients and controls were similar regarding baseline characteristics but not for the level of sport and for the duration of exercise (Table 1).

The majority of patients (N = 39, 63.9%) reached the ST. Voluntary exhaustion without any symptoms (NS) was observed in the minority of the concussed patients (N = 6). The statistical comparisons revealed no difference between the three patient groups, and between patients and control except for the weight (patients vs. controls; see Table 1 for details). The three patient subgroups were similar with regard to age, weight, number of previous concussions and days since the most recent concussion.
HR responses

No significant difference in the median HR_{rest} (Figure 2A) and HR_{warm-up} (Figure 2B) was found between groups. In contrast, median HR_{max} was significantly different between groups (p < 0.001; Figure 2C). Post-hoc multiple comparisons revealed that ST had a significantly lower median HR_{max} than S, NS and controls (see Figure 2 for p-values).

During cool-down, HRR30s, HRR60s and HRR300s differed significantly (p < 0.001, p = 0.004 and p = 0.003, respectively) between groups (Figure 3). Post-hoc multiple comparisons revealed that HRR30s of S was significantly higher compared to NS, ST and controls (Figure 3A), while HRR60s of S was significantly higher compared to ST and controls (Figure 3B). In contrast, HRR300s of ST was significantly higher only compared to controls (Figure 3C).

Symptoms

At the end of the GET (Figure 4A and B), the severity of dizziness and headache had increased in the S group (8 of 16 and 8 of 16, respectively) and in the ST group (25 of 39 and 35 of 39, respectively) compared to the pre-activity level. The increase was higher in ST than the S group for headache (p < 0.001), but not for dizziness (p = 0.188).

At the end of cool-down (Figure 4C and D) no significant change of dizziness severity was observed in both groups (S 9 of 16; ST 21 of 39) compared to the end of GET. In contrast, 21 of 39 ST patients (54%) reported a decrease in headache, while in the group S group four of 16 patients (25%) reported an increase and two of 16 patients (13%) a decrease in headache. The difference in headache severity between S and ST groups was significant (p = 0.001).

Discussion

This study provides preliminary evidence for the influence of an autonomic dysfunction on the ST during the GET on a cycling ergometer, and the HRR in the initial 5 min after reaching the HR_{max} in SRC patients. The four main findings were: (1) a slower HRR30s in S compared to the other groups; (2) a slower recovery of HRR60s in S compared to the ST and control; (3) a significantly slower HRR300s in ST compared to control; (4) differences in changes of dizziness and headache during the cool-down.

HR evolution

Our analysis of HR added an important aspect to the Buffalo concussion bike test. Indeed, our results concerning the HRR during the cool-down pointed out the importance of including the recovery part in test measurements and analysis apart from the period of gradual load increase. HR measurement and analysis during cool-down may help to identify patients with an autonomic dysfunction who
would otherwise be missed, since autonomic dysfunction was exclusively assessed by patients who could not tolerate physical effort. Despite a lower $HR_{\text{max}}$ in ST compared to all other groups (consistent with previous studies), slower HRR30s and HRR60s were found in S compared to the other groups. This finding confirms the importance of HR assessment during and after the incremental test.

During rest, HR is the result of a balance between excitatory sympathetic and inhibitory parasympathetic activity. When healthy subjects start to cycle, the central command leads to a parasympathetic withdrawal with simultaneous sympathetic activation causing a cascade of physiological events such as an increase in HR, myocardial contractibility force (stroke volume) and peripheral vasoconstriction. In addition, the operating point of the arterial baroreceptor reflex is shifted to a higher arterial blood pressure set point. Simultaneously, the central command and the muscle tetano-receptors (mechano-receptors) lead to a vagal (parasympathetic) inhibition as well, and a second-time metabo-receptors in the muscle lead to an increased sympathetic nerve activity until the maximal effort is reached. By exercise cessation in the absence of central command and muscle tetano-receptors (mechano-receptors) feedback, the arterial baroreceptors lead to cardiac parasympathetic reactivation (increase in vagal activity), which is the principal determinant of the immediate fall in HR (HRR30s and HRR60s). In the first 30 s after the end of the exercise, HRR does not depend on the exercise intensity reached. In contrast 5 min after, the HRR depends also on the sympathetic reactivation and is influenced by exercise intensity. According to our results, which showed a slower HRR30s and HRR60s in the S group, it may be that this group of patients suffer from a cardiovascular autonomic dysfunction related to an impairment of the parasympathetic reactivation resulting in an increase of the symptoms during the cool-down. After 5 min HRR was slower in the ST group, which may indicate autonomic dysfunction, relying mainly on sympathetic activation.

Due to the feasibility and safety of this test, physicians should consider using this protocol not only with athletes but also with the general population suffering from mild traumatic brain injury.

**Symptoms evolution**

A previous study showed that symptom severity after physical exertion only improves after 24 h, while no change has been observed after 5 and 30 min. To our knowledge there are no studies, which have investigated symptoms development during the first 5 min after physical exhaustion or ST, although it may reflect a cardiovascular autonomic dysfunction. In most patients of the S group who experienced slower HRR compared to the other groups, indeed, the severity of headache and dizziness did not decrease during the cool-down, remaining stable or even or increasing. Despite the lack of research in this area, our results

![Figure 3. Boxplots of HR recovery measured at 30 s (A), 60 s (B), and 300 s (C) after the graded exercise test in the different groups: patients with symptoms who finished the test (S); patients who reached the ST and had to stop the test (ST); patients without symptoms during the test (NS); control group. The $p$-values of post-hoc multiple comparisons are shown only when the Kruskal–Wallis test was found statistically significant ($p < 0.05$).](image-url)
suggest that autonomic dysfunction may have an influence even on the HRR. It is important to consider that the influence of other components on symptom evolution (such as cervicogenic, vestibular and/or oculomotor impairments) cannot be excluded at this stage, therefore additional studies are needed.

**Implications**

If a cardiovascular autonomic dysfunction is detected, the ST allows tailoring a training plan aimed to resolve this specific dysfunction. As previously shown, the patient is suggested to train constantly at 80% to 90% of his/her HR at the ST. This ST-adapted training allows the patient’s autonomic functions to improve without provocation of symptom exacerbation. No guidelines are given in the case of symptoms increasing right after the physical effort.

Considering these preliminary results showing not only an impairment on reaching the maximal physical effort but also on the HRR, new therapy methods such as interval training (IT) should be considered. IT, indeed, has been demonstrated to improve both central and peripheral components of VO₂max, while constant training, only the peripheral ones and mainly the oxygen extraction. For this reason, SRC athletes suffering from autonomic dysfunction may benefit from IT instead of constant training.

**Study limitations**

The sample size was relatively small, and therefore, no attempt was made to conduct subgroup analyses according to gender, sport and time since the most recent concussion. Since the GET was done as a part of our routine clinical practice, no restriction about medications, caffeine or sleep was done. Also, the fitness level of the study participants was not assessed. Since the majority of the patients’ group were elite athletes and none of the control, it is possible that the patients’ groups differed from the controls in fitness level. However, to the best of our knowledge, no study has shown an effect of fitness level on concussion.

![Figure 4](image-url)
symptoms or autonomic symptoms after mild traumatic brain injury. Another limitation is that HRR60s and HRR300s depend on the exercise intensity. For this reason would be interesting, to stop all the patients at the same exercise intensity (defined as a percent of the HR_{max} or a percent of the maximal power) and see how does it affect the results with respect to HHR60s and HRR300s.

**Conclusion**

In SRC patients, cardiovascular autonomic dysfunction could manifest not only as exercise intolerance but in impaired HRR after exercise as well, leading to an increase of headache and dizziness during cool-down. Our new findings highlight the importance of including the cool-down assessment in the diagnosis of cardiovascular autonomic dysfunction in SRC patients. Further research with additional measurements such as inclusion of blood pressure and HR variability during cool-down should be performed to better understand pathophysiological mechanisms.

**Acknowledgements**

The authors thank the participants of this study.

**Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Schulthess Foundation

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