Long-Term Influence of Concussion on Cardiac-Autonomic Function in Adolescent Hockey Players

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Context: Concussion may negatively influence cardiovascular function and the autonomic nervous system, defined by alteration in heart rate variability (HRV). Differences in HRV most commonly emerge during a physical challenge, such as the final steps of the return-to-sport progression.

Objective: To assess the effect of concussion history on aspects of cardio-autonomic function during recovery from a bout of submaximal exercise in adolescent male hockey athletes.

Design: Case-control study.

Setting: Research laboratory.

Patients or Other Participants: Thirty-three male athletes participating in Midget-AAA hockey were divided into those with (n = 15; age = 16 ± 1 years, height = 1.78 ± 0.06 m, mass = 73.9 ± 7.4 kg, 10.5 ± 1.6 years of sport experience, 25.2 ± 18.3 months since last injury) or without (n = 18; age = 16 ± 1 years, height = 1.78 ± 0.05 m, mass = 74.8 ± 7.6 kg, 10.6 ± 1.9 years of sport experience) a concussion history. Those with a concussion history were binned on total count: 1 concussion or 2 or more concussions.

Intervention(s): All athletes underwent 5 minutes of resting HRV assessment, followed by 20 minutes of aerobic exercise at 60% to 70% of their maximal target heart rate and a 9-minute, postexercise HRV assessment.

Main Outcome Measure(s): Heart rate variability measures of mean NN interval, root mean square of successive differences, and standard deviation of NN interval (SDNN).

Results: Group demographic characteristics were not different. When the control and concussed groups were compared, group and time main effects for heart rate recovery, root mean square of successive differences, and SDNN (P values < .01), and an interaction effect for SDNN (P < .05) were demonstrated. Recovery trends for each group indicated that a history of 2 or more concussions may negatively affect cardio-autonomic recovery postexercise.

Conclusions: Our findings suggest that those with more than 1 previous concussion may be associated with a greater risk for long-term dysautonomia. Future use of HRV may provide clinicians with objective guidelines for concussion-management and safe return-to-participation protocols.

Key Words: dysautonomia, heart rate variability, mild traumatic brain injury

Key Points

- Athletes with a concussion history displayed suppressed cardiac autonomic recovery after moderate aerobic exercise compared with the nonconcussed control group.
- Players with multiple previous concussions exhibited an increased time to physiological recovery postexercise versus athletes with 1 or no concussions.
- Ongoing alterations to the autonomic system that persist beyond clinical recovery suggest that concussion is not a transient injury and may have consequences beyond cognitive function.

Concussion is defined as the onset of transient symptoms after a direct or indirect blow to the head. Common symptoms include headache, dizziness, anterograde or retrograde amnesia or both, nausea, and sensitivity to light and sound; yet changes in behavior, balance, cognitive function, and circadian rhythm may also ensue. Researchers have demonstrated that circadian disturbances may result in altered homeostatic pathways related to the bidirectional feedback loop between the cardiac system and the brain. The neuronal imbalances in the amygdala, insula, and hypothalamus may initiate arrhythmias, suggesting the influence of the insular and medial prefrontal cortices on modulation of heart rhythm. Due to the vagal innervation of the heart’s sinoatrial node, investigators hypothesized that cerebral functional disturbances may alter normal cardio-autonomic function for months or even years postconcussion.

To provide insight into the disturbances of the cardio-autonomic system, the authors of a previous study evaluated the variability of beat-to-beat changes in heart rate known as heart rate variability (HRV). Heart rate variability results from efferent sympathetic and parasympathetic activity of the autonomic nervous system (ANS) as well as afferent activity from the heart’s mechanosensitive and chemosensory neurons in its intrinsic nervous system. In otherwise healthy individuals (eg, those free of...
subclinical or clinically relevant conditions), HRV is dynamic and readily capable of responding to internal and external environmental stimuli. Within athletic populations, increases in HRV occur as an adaptation to improvements in aerobic conditioning as a result of chronic training. Conversely, decreases in HRV are associated with reduced capacity and neuronal transmission.

Current concussion management ominously lacks objective assessments of injury pathophysiology, including measurements of HRV to gauge dysfunction and recovery trends. This is a critical shortcoming, as cardio-autonomic dysfunction may lead to long-term impairment after concussion (such as prolonged posttraumatic amnesia), hospital admissions, and a decreased likelihood of successful return to vigorous exercise. Indeed, at the onset of exercise, heart rate and cardiac output are elevated due to central signal commands from the vagus nerve. As exercise is prolonged or intensifies, sympathetic activation rises to increase heart rate and vasoconstriction to visceral organs in order to promote increased blood flow to skeletal tissues. Parasympathetic activation dominates the early stages of exercise recovery to permit cardio-deceleration in heart rate, stroke volume, and myocardial contractility, followed by sympathetic withdrawal, in which HRV gradually reemerges. In the postacute stage after concussion, athletes present with persistent changes in autonomic function as compared with a healthy cohort. Therefore, HRV alterations due to exercise should be measured during the acute and postacute phases of injury as well as several months postinjury to determine whether pathophysiological alternations persist.

Despite mounting evidence for acute cardio-autonomic dysfunction after concussion, limited information is available on how long HRV may be impaired and what role, if any, concussion history has in sport performance outcomes. Therefore, the purpose of our study was to assess the effect of concussion history on measures of cardio-autonomic function during recovery from a bout of submaximal exercise in adolescent male hockey athletes. Based on findings suggesting that mild physical exertion resulted in the reemergence of cardio-autonomic function among asymptomatic athletes, we hypothesized that asymptomatic athletes with a concussion history would demonstrate impaired HRV during recovery from a bout of submaximal exercise as compared with athletes who did not have a concussion history.

METHODS

Participants

Data were collected as part of an ongoing Quebec Hockey Program aimed at understanding the short and long-term consequences of concussion in youth hockey players. As part of their preseason evaluation, a subset of Midget-AAA (15 to 18 years old) hockey players completed an HRV protocol pre-exercise and postexercise. An institutional review board waiver of consent or assent was granted by the University of South Carolina to evaluate deidentified data. After screening for inclusion and exclusion criteria, we obtained demographic and deidentified medical histories for each participant. Athletes with a history of neurologic disease, psychiatric illness, non-sport-related brain injury, learning disability, attention-deficit/hyperactivity disorder, or any other condition that could influence cardio-autonomic functioning were excluded from the study. Furthermore, recruits were screened for all medication use, including those substances that could affect human performance and cognition as well as cardio-autonomic functioning. Because our goal was to evaluate the long-term influence of concussion on cardio-autonomic function, athletes with a history of concussion within the last 6 months and those still experiencing symptoms were excluded. Thus, only data from athletes who were more than 6 months postconcussion, asymptomatic, and free of neurologic and neuropsychiatric conditions were analyzed.

Once screened, individuals were divided into 2 groups (control, concussion history). All concussion diagnoses were confirmed by medical records and a resident neuropsychologist. Consistent with the National Institutes of Health Concussion Common Data Elements, control participants were asked, “Following a blow to the head, neck, or body, have you ever experienced any of the following symptoms?” Participants who reported undiagnosed concussions (ie, indicating any symptom after an impact) were excluded from the control group. After screening, 18 athletes were placed in the healthy control group (control) and 15 athletes were placed in the concussion group (CHx). We conducted exploratory analyses to determine if a cumulative effect existed by stratifying the CHx group based on those with a history of a single concussion (CHx1) and those with a history of 2 or more concussions (CHx2), all of whom were asymptomatic at the time of testing.

Procedures

To minimize any effects of diurnal variation on cardio-autonomic function, all participants were asked to void their bladders before testing at approximately the same time of day (ie, late morning). Furthermore, they were instructed to adhere to their normal eating habits and abstain from consuming any caffeinated beverages on the day of testing. All test procedures took place in a quiet room with regulated ambient temperature and stable humidity.

Before testing, participants were outfitted with a Zephyr BioHarness (Medtronic Zephyr, Boulder, CO) strap, complete with Zephyr BioModule sensor (Medtronic Zephyr) to collect electrocardiographic (ECG) and respiratory data. Electrocardiographs were collected with a sampling frequency of 250 Hz. All participants underwent a seated, eyes-open resting ECG assessment for 5 minutes. Then each person performed a bout of aerobic activity on a cycle ergometer (Lode, Groningen, Netherlands) that consisted of a 5-minute incremental warmup, followed by 20 minutes of steady-state aerobic exercise at approximately 60% to 70% of his age-predicted (220-age) maximum heart rate. Participants cycled at approximately 60 revolutions/minute while the load (W) was adjusted to maintain target heart rate (beats/min; controls = 128.2 ± 2.5 beats/min, CHx = 129.7 ± 2.8 beats/min). After the 20-minute steady-state aerobic exercise, participants completed a 2-minute active cool down (unloaded cycling) followed by a seated, 10-minute, eyes-open ECG assessment. Because the respiratory rate may influence HRV measurements, participants were guided by a metronome (rate of 6 breaths/min) to breathe in for 5 seconds, followed by 5 seconds of
Table 1. Participants' Demographic Characteristics a

| Characteristic | Control | Total | 1 Concussion | ≥2 Concussions |
|---------------|---------|-------|-------------|---------------|
| n             | 18      | 16    | 11          | 5             |
| Age, y        | 16 ± 1  | 16 ± 1| 16 ± 1      | 16 ± 1        |
| Height, m     | 1.78 ± 0.05 | 1.79 ± 0.06 | 1.81 ± 0.05 | 1.75 ± 0.08   |
| Mass, kg      | 74.4 ± 7.6 | 74.6 ± 7.6 | 76.5 ± 7.4  | 70.5 ± 7.1    |
| Body mass index, kg/m² | 23.4 ± 2.2 | 23.6 ± 2.6  | 23.4 ± 2.1  | 23.1 ± 1.2    |
| Time since last concussion, mo | Not applicable | 25.1 ± 17.6 | 27.4 ± 20.5 | 20.0 ± 8.4    |

a Data are presented as group mean ± SD. Demographics and pre-exercise heart rate, root mean square of successive NN interval difference, and SDNN interval were matched for control participants and participants reporting a concussion history. Athletes with a concussion history were further stratified into those with a single concussion versus 2 or more concussions. Demographic characteristics between groups were not different (all P values > .05).

Additional information:

expiration. Respiratory rate was maintained across groups before and after the intervention. Total testing time was approximately 1 hour.

Raw ECG data were processed with Kubios HRV (version 2.0; Biosignal Analysis and Imaging Group, Kuopio, Finland). The R-R intervals were quantified as the mean value of NN intervals (NN/HR) and to identify any artifact caused by movement. Ectopic beats and artifact caused by movement were removed via the Kubios algorithm for artifact removal. Once the ectopic beats were removed, a 10% Hanning window was applied to each ECG collected (eg, rest and postexercise). Rest and postexercise ECGs were then segmented into 2-minute blocks to evaluate participants’ recovery. Two-minute data-collection windows have been shown to be accurate for computing the root mean square of successive NN interval differences (RMSSD) and the standard deviation of NN intervals (SDNN). From these data, time-domain parameters of HRV were computed for each epoch, including the mean value of NN intervals (NN/HR), SDNN, and RMSSD.12

Statistical analyses were conducted using IBM SPSS (version 25; IBM Corp, Armonk, NY), and the figures were created using GraphPad Prism (version 8.0 for Windows; GraphPad Software, San Diego, CA). An a priori level of significance was set at P ≤ .05.

Repeated-measures analyses of variance (ANOVAs) were performed to identify group differences (control versus CHx) for heart rate, RMSSD, and SDNN. To further analyze the influence of the number of prior injuries, we calculated additional ANOVAs to explore the cumulative effect (control versus CHx1 versus CHx2) of demographic characteristics and resting dependent data. Separate 2 (group) × 4 (time) repeated-measures ANOVAs (RMANOVAs) were performed to determine if differences were present for heart rate and time-domain HRV variables (RMSSD, SDNN) during the recovery period (1–3, 3–5, 5–7, and 7–9 minutes postexercise). We assessed separate 3 (cumulative effect) × 4 (time) RMANOVAs to determine if differences were present for RMSSD and SDNN during the same recovery periods. The nature of significant group or time main effects was addressed via Tukey post hoc tests.

The percentage of recovery relative to rest was calculated for the post 1- to 3- and 7- to 9-minute intervals (ie, [post-rest/pre-rest] × 100) for NN, RMSSD, and SDNN. Separate factorial ANOVAs were generated to identify the presence of group (control versus CHx) and cumulative effect (control versus CHx1 versus CHx2) differences on the percentage of recovery relative to rest for each variable. To explore the linearity between heart rate and time-domain HRV measures, linear regression analyses were performed and compared between groups. For those relationships in which linear significance was identified, we conducted separate F tests to determine if the respective slopes of the regression lines deviated significantly from 0. Using heart rate as the covariate, analyses of covariance (ANCOVAs) were then calculated to establish whether the respective slopes were different between groups.

RESULTS

The control and CHx groups were matched for demographic characteristics and pre-exercise heart rate, RMSSD, and SDNN. The control, CHx1, and CHx2 groups were also matched for demographics (Table 1) and pre-exercise heart rate (Figure 1). Despite matching, group main effects were present for pre-RMSSD and SDNN (P values < .05); post hoc tests revealed that CHx1 and CHx2 were different in RMSSD (eg, 49 ± 13 and 77 ± 17 milliseconds) and SDNN (eg, 66 ± 14 and 92 ± 197 milliseconds), respectively (Figure 1). Regarding the recovery of heart rate, RMSSD, and SDNN, a group main effect was demonstrated for NN/HR (P < .01), time main effects for NN/HR (P < .0001), RMSSD (P < .01), and SDNN (P < .01), as well as an interaction effect for SDNN (P < .05; Table 2).

To further explore the role of more than 1 concussion on cardio-autonomic function, separate 3 (cumulative effect) × 4 (time) RMANOVAs were performed. Group (P < .01) and time (P < .0001) main effects for NN/HR existed, but the interaction effect did not achieve significance. Tukey post hoc tests indicated the cumulative effect (CHx1 versus CHx2) of elevated NN/HR compared with the control group throughout recovery (P < .05; Figure 1). No group main effect was observed for RMSSD or SDNN, yet a significant time main effect was noted in each analysis (P < .01; Figure 1). Of the 2 time-domain aspects of HRV, only the SDNN had a significant interaction effect (P < .05; Figure 1). To assist in standardizing the recovery outcomes, we calculated the percentage of recovery relative...
to rest for the post 1- to 3- and 7- to 9-minute intervals for NN/HR, RMSSD, and SDNN. For each comparison, the omnibus model was significant for NN/HR (P < .05), RMSSD (P < .01), and SDNN (P < .01), indicating the groups differed in recovery factors relative to baseline.

Figure 1. Heart rate and time-domain parameters of heart rate variability during recovery from submaximal exercise by group. Triangles represent the control group; diamonds, those with a history of 1 concussion; and squares, those with a history of 2 or more concussions. Abbreviations: RMSSD, root mean squares of successive NN interval differences; SDNN, SDs of NN intervals.

Figure 2. Truncated violin plots demonstrating the recovery trends for each group across 2 postaerobic exercise time intervals (post 1–3 minutes and post 7–9 minutes) for A, the root mean square of successive NN interval differences, B, the standard deviation of the NN interval, and C, heart rate. Groups are presented based on concussion history: none (control), 1 (CHx1), or multiple (CHx2). Each violin plot presents the group median (---) and interquartile range (-----). The truncation of each plot represents the minimum and maximum observation for each group. * P < .05. Abbreviations: HR, heart rate; RMSSD, root mean squares of successive NN interval differences; SDNN, SDs of NN intervals.
(Figure 2). Specifically, the CHx2 group was different from the CHx1 and control groups ($P < .05$ for each) at the post 1- to 3- and 7- to 9-minute intervals for NN/HR, RMSSD, and SDNN, suggesting that a history of multiple concussions may negatively affect cardio-autonomic recovery postexercise (Figure 2).

To determine the presence of linearity between the percentage of recovery in NN/HR and RMSSD and SDNN, separate simple regression analyses were conducted for each group. Both the control ($R^2 = 0.59$) and CHx1 ($R^2 = 0.66$) groups had significant linear relationships ($P < .01$) between NN/HR and RMSSD at the post 1- to 3-minute interval, but the CHx2 group ($R^2 = 0.66$) only trended toward significance ($P = .09$). By the post 7- to 9-minute interval, the significant linear relationship in the control and CHx1 groups abated; however, significance was still present in the CHx2 group ($R^2 = 0.97$; $P < .01$). Similarly, the control ($R^2 = 0.23$) and CHx1 ($R^2 = 0.54$) groups had significant linear relationships ($P < .05$) between HR and SDNN at the post 1- to 3-minute interval, but the CHx2 group only trended toward significance ($R^2 = 0.74$; $P = .06$). For the post 7- to 9-minute interval, a significant linear relationship was observed in the control ($R^2 = 0.40$) and CHx2 ($R^2 = 0.80$) groups ($P < .01$). For all analyses and groups, the slope of the regression line deviated significantly from 0 ($P < .05$) in the relationship between HR and RMSSD and HR and SDNN.

**DISCUSSION**

We sought to determine the persistent effects of concussion on cardio-autonomic recovery in male adolescent hockey players by assessing HRV before and after a single bout of moderate aerobic exercise. Between the control and CHx groups, our results suggest that athletes with a concussion history displayed a longer time to return to baseline HRV measures postexercise. Furthermore, our exploratory analyses indicated these differences may increase if an athlete sustains multiple concussions. By using the postexercise 1- to 3- and 7- to 9-minute intervals to determine the percentage of recovery relative to rest, we noted that those with multiple prior concussions had a suppressed cardiac autonomic recovery after moderate aerobic exercise compared with healthy control individuals and those who reported only a single concussion. These findings are consistent with a series of works that demonstrated persisting subclinical alterations after concussion, including alterations in brain electrophysiology,14 gait,15 and postural sway.16 If or how these alterations manifest with age has not yet been elucidated.

Dysautonomia due to rhythmic fluctuations in parasympathetic (PNS) and sympathetic (SNS) nervous system activity at the sinoatrial node is directly associated with cardiovascular activity and was evident in a study that integrated aerobic fitness tests.17 During exercise, overall HRV is markedly reduced and regained throughout an individual’s recovery, typically with a larger increase in the first several minutes of recovery.18 In individuals with concussion, the mechanical changes associated with the neurometabolic variations negatively affected cerebral circulation,19 disturbing cerebral blood flow modulation20 and, thus, HRV. Alterations in cerebral blood flow are reportedly due to ANS impairments from uncoupling events of the central autonomic centers of the brain and arterial baroreceptors.21 Similarly, multiple researchers have observed acute and subacute alterations in HRV after concussion. La Fountaine et al22 measured HRV and heart rate complexity between participants with acute concussions and an age-matched control group before and after an isometric hand grip test. Heart rate complexity was different between the groups immediately after concussion but equalized at 2 weeks postinjury.22

Although these results provide insight into the effect of HRV during the acute and subacute phases after concussion, we did not explore the effect of high-intensity physical activity on HRV. Leddy and Willer23 developed the Buffalo Concussion Treadmill Test (BCTT) to reestablish physiological recovery postconclusion, including improved autonomic function and cerebral blood flow regulation, for use after the acute phase ($>3$ days). According to their protocol, the test may establish the degree of physiological recovery to better predict an individual’s prognosis and assist in the differential diagnosis of nonspecific concussive symptoms.21 Based on their findings,23 currently recommended clinical practice is to engage athletes in moderate exercise to best gauge their physiological recovery.
Although our study was not designed to examine the specific underlying neurologic biology after concussion, we believe those with a history of concussion may be susceptible to long-term or even permanent alterations in ANS neurotransmission. Particularly in hockey players, subsequent repetitive head impacts may exacerbate previous concussive pathophysiology, resulting in potentially permanent cardio-autonomic alterations. Recent researchers\cite{23} discovered the frontal cortex’s ability to modulate vagal tone and specifically influence the ANS divisions—the PNS and SNS. Activation of the SNS causes an increase in heart rate due to the innervation of postganglionic sympathetic fibers on the atria, ventricles, and coronary arteries.\cite{24} Previous investigators\cite{25} used functional near-infrared spectroscopy and resting-state magnetic resonance imaging to identify reductions in connectivity of the frontal lobe as a result of concussion. These findings suggested that reduced frontal cortex connectivity may have a direct relationship with dysautonomia.\cite{26}

Additionally, Thayer and Lane\cite{27} demonstrated hemispheric differences in neurocardiac activation, specifically in the right prefrontal cortex. To further evaluate cardio-autonomic influence on the brain, Williamson et al\cite{28} determined that disruption of white matter tracts may result in decreased signaling from the prefrontal cortex to the brain stem after traumatic brain injury results in a loss of inhibitory control of the ANS. Therefore, the damage to white matter tracts from a concussion may have a negative long-term effect on the integral networks that modulate cardio-autonomic function.

Though we exclusively investigated long-term dysautonomia due to concussion history as reflected in recovery trends during postaerobic exercise, sympathovagal balance is a multifaceted concept related to congenital, physiological, and neuropsychological factors. However, even external influences such as circadian rhythm and environmental stimuli have been reported to negatively influence the validity of HRV assessments.\cite{29} Our findings are also limited by the reliance on a single-sex population. Because explicit HRV differences between males and females exist, our outcomes cannot be generalized to a female population.\cite{30} Future authors who pursue larger, mixed-sex studies will help provide a more comprehensive understanding of cardio-autonomic functioning in both males and females, especially with respect to the cumulative effect of concussion. It should also be noted that HRV tends to lessen with sedentary habits and increase with aerobic capacity, thus making it problematic to determine the true source of differences. However, as all measures were taken at the beginning of the season, we believe the participants were of approximately equal fitness during the 20-minute intervention (controls: 128.2 ± 2.5 beats/min, CHx: 129.7 ± 2.8 beats/min) or at least that fitness levels were randomly distributed between the groups.

CONCLUSIONS

Overall, we investigated the relationship of the long-term effects of cardio-autonomic dysfunction and concussion history. Our results showed that those with a concussion history had decreased HRV versus those without prior concussions. Furthermore, the hockey athletes in our cohort demonstrated increased time to physiological recovery after moderate aerobic exercise compared with both the CHx1 group and healthy control individuals. In sum, athletes with extensive concussion histories warrant continued monitoring by sports medicine clinicians due to their potentially elevated risk of long-term dysautonomia. In addition, the CHx2 athletes displayed greater physiological dysfunction after moderate aerobic exercise than both the CHx1 and control groups. Future use of HRV assessments in concussion management may eventually provide clinicians with objective metrics of persisting pathophysiology, which could inform clinical decision making after multiple concussions in athletic populations.

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