

Official Title:	Epigenetic and Cytokine Biomarkers During Recovery From Sports-Related Concussion
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Study Protocol

Objectives: Aim #1: Determine how salivary biomarker expression changes throughout recovery in adolescents after SRC. Aim #2: Determine the effect of prescribed aerobic exercise intervention on salivary biomarkers salivary miRNA expression in concussed adolescents

Design: 4 arm randomized control trial

Methods

This pilot randomized control trial was approved by the IRB at the University at Buffalo (#STUDY00005734). Power analysis was done using a simulation model and pilot data to determine sample size. Estimated power was calculated at a 0.05 significance level.

Potential participants are selected from incoming patients to the UBMD Concussion Management Clinic at Farber Hall at the University at Buffalo South Campus in Buffalo, NY, or other local affiliated UBMD locations (Orchard Park, Harlem Road, and Summit Clinic). For a patient to be eligible for the study, a sports medicine physician confirmed the diagnosis of an acute concussion within ten days of injury. Standard concussion diagnosis is based on history, a concussion symptom questionnaire, and a concussion-specific physical examination. If the participant meets eligibility criteria and was willing to participate, informed consent/assent will be obtained.

Inclusion and Exclusion Criteria

Inclusion Criteria: (1) 13–18 years old, (2) diagnosed with SRC within ten days of injury, (3) participates in an organized sport at least three days a week for the past six months.

Experimental Procedure

After informed consent/assent was obtained, the following assessments were completed in the order they appear in this document unless otherwise noted. Table 1 presents the overview of the flow of the procedures conducted with each participant.

Table 1. Schedule of Research Assessments

Initial Visit						
Consent (Assent)	BCPE/ PCSS*	Saliva Collection	Questionnaires	Oral Hygiene Simple	Buffalo Concussion Treadmill Test	Group Allocation
Intervention						
At home exercise intervention (14 days)						
Zoom Meetings with research assistants						
Follow- up (Day 7 and 14)						
BCPE/ PCSS		Saliva Collection	Questionnaires	Oral Hygiene Simple	Buffalo Concussion Treadmill Test	

*BCPE (Buffalo Concussion Physical Exam) and PCSS (Post-Concussion Symptom Scale) were completed before consent/ assent for concussed participants as a part of a standard concussion examination to confirm concussion diagnosis before recruitment.

Intervention

Participants are assigned to high and low-volume aerobic exercise groups. Exercise target training HRs were adjusted to 90% of the HRt identified on the graded exercise testing. The high-volume group is asked to exercise aerobically at 90% of their HRt for 30 minutes, five days a week. The low-volume group is asked to exercise aerobically at 90% of their HRt for 20 minutes, three days a week.

Statistical Analysis

Collected data will be compiled in Excel for analysis. All categorical demographic variables will be compared using χ^2 and t -tests as applicable on SPSS. Cluster analysis will be performed to assess the amount of exercise that participants completed. Independent t -tests will be conducted to assess sex differences in exercise completion after cluster analysis. Mixed model regressions will be composed in SPSS to assess the change in salivary BDNF over recovery time and between concussed participants and controls. Additionally, an RMANOVA will be completed to assess potential associations between BDNF expression and concussion history. Subsequent mixed models will include the expression of one miRNA as the dependent variable. To retain as much power as possible, only significant covariates will be included.