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Do post concussion-like symptom responses change following exercise or sports participation in a non-concussed cohort?

Author Information

Arun Prasad Balasundaram^{1,5}

Josie Athens²

Anthony G. Schneiders³

Paul McCrory⁴

S John Sullivan⁵

^{1,5}Department of Health Sciences, Institute of Health and Society, University of Oslo, Oslo, Norway

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²Department of Preventive and Social Medicine, Dunedin School of Medicine, University of Otago, Dunedin, New Zealand

³School of Human, Health & Social Sciences, Central Queensland University, Branyan, Australia

⁴The Florey Institute of Neuroscience and Mental Health – Melbourne Brain Centre, University of Melbourne, Heidelberg, Victoria, Australia

⁵Center for Health, Activity and Rehabilitation Research, School of Physiotherapy, University of Otago, Dunedin, New Zealand

Corresponding Author: Arun Prasad Balasundaram

Department of Health Sciences, Institute of Health and Society, University of Oslo, 0373, Oslo, Norway

Phone: + 47 22845397, Email address: a.p.balasundaram@medisin.uio.no

Running Head: Exercise and Post concussion-like symptoms

Abstract

The purpose of this study were; 1) To determine the reliable change in post concussion-like symptoms reported following self-selected exercise or sports activities. 2) To explore the potential influence of gender and exercise parameters on post concussion-like symptoms reported by a non-concussed cohort following exercise/training.

A pre-post observational design was used. A convenience sample of students aged 18-30 years who visited a university recreation centre to engage in their chosen exercise activity, and a purposeful sample of men's and women's rugby union players engaged in their regular training sessions. All participants reported their symptoms using the SCAT2 post-concussion symptom scale, and exercise variables such as type, duration, volume and intensity were collected pre and post-exercise. The reliable change index was used to determine the change in symptom scores

reported from pre-to-post-exercise/training. Multiple linear regression analysis was used to model the exercise variables to explain the impact on the reporting of symptoms.

A total of 260 participants (146 males and 114 females) completed their self-selected exercise activity or rugby union training. Approximately two-thirds of all participants did not demonstrate a change (increase or decrease) in total symptom score (201/260, 77.9%) and/or symptom severity score (212/260, 81.9%) from pre to post-exercise/training.

The symptom response following exercise or sports training did not change in the majority of participants. Clinicians need to be aware of these findings in order to make informed decisions on return-to-play following a concussive brain injury.

Key words: Sport-related concussion; Rugby Union; Training, Reliable Change Index; Return-to-Play; Real-World Context

Introduction

The clinical assessment following a concussion is usually conducted using a multifaceted approach (Echemendia et al., 2013). In addition to neuropsychological assessment and balance testing, self-reported symptoms are also used in the diagnosis of a concussion and for making clinical decisions on return-to-play (RTP). The practice of self-reported symptoms is a key aspect in the determination of when a concussed athlete is ready to begin a graduated RTP exercise protocol (McCrory et al., 2013). The stepwise progressive exercise protocol is symptom-based, where a player can proceed to the next level when they are asymptomatic at the current level for 24 hours following provocative exertion of the stepwise exercise protocol (McCrory et al., 2013). In the event of concussion symptoms occurring during exertion, it is suggested that the athlete do not progress and return to the previous level of exercise protocol at which the athlete was asymptomatic (McCrory et al., 2013). However, determining the asymptomatic status of an athlete is challenging, considering there is a lack of operational definition (Alla et al., 2012).

The Concussion in Sport (CIS) group's consensus guidelines also state that symptom assessments be conducted at least fifteen minutes following exercise/sports participation cessation due to the possible influence of the effects of exercise and/or fatigue (McCrory et al.,

2013). This recommendation is based on healthy individuals' response to high-intensity exercise where balance tasks were impaired for up to 15 minutes' post-exercise (Schneiders et al., 2010). However, there is limited evidence to support this time specification for assessment of symptoms following a concussion. To date, only a sole study (Alla et al., 2010) has specifically explored the impact of differing intensities (moderate & high) of exercise on the reporting of post concussion-like symptoms in non-concussed individuals. The authors demonstrated that fifteen minutes of exercise was sufficient to provoke post concussion-like symptoms in a non-concussed cohort (Alla et al., 2010). In addition to provoking symptoms, there was an increase in the severity of symptoms (SSS) after moderate-intensity exercise, and further increases were noted with high-intensity exercise. The authors also found that the post concussion-like symptoms, which increased immediately (post-test) following exercise returned to their baseline levels after a rest (recovery) period of five minutes. It must be noted that these results related to the intensity of exercise, duration of exercise and rest (recovery) period have been shown only in a controlled environment. Therefore, these results cannot necessarily be extrapolated to the real-world exercise context, where participants are generally exercising at self-driven intensities or as demanded by the level of engagement in their activity. Apart from these factors, it could be speculated that selected exercise parameters including type and volume of exercise (training load) would also have an influence on post concussion-like symptoms. Hence, these factors warrant further investigation considering that they could have a significant impact while conducting a graduated RTP protocol.

In addition to the exploration of these factors, there is also a need to investigate gender/sex differences as they relate to symptom reporting due to mixed findings in the current literature. Sex differences were not noted in the reporting of post concussion-like symptoms following an acute exercise programme under controlled conditions (Gaetz & Iverson, 2009). Meanwhile, several studies have shown that females report a greater number and severity of symptoms at rest (Covassin et al., 2006; Jinguji et al., 2012; Mrazik et al., 2013). Hence it is not clear whether females would report a greater number of symptoms following exercise, especially when monitored in a real-world environment. The aims of this study were to determine the reliable change in reporting of post concussion-like symptoms, and to investigate the effects of key exercise parameters and gender differences on symptom reporting following self-selected exercise activity or sports (rugby union) training in non-concussed individuals.

Materials and Methods

Participants were recruited as two cohorts from different sites, namely the Unipol Recreation Centre (URC) at the University of Otago and the Otago University Rugby Football Club (OURFC). All participants provided informed consent and the study was approved by the Human Ethics Committee of the University of Otago. These sites were situated in close proximity to each other and a separate strategy was followed while recruiting at each site. A research assistant (RA) intercepted potential participants entering the URC and invited them to participate in the study. The RA also administered a screening question to determine if they had sustained a concussion (medical diagnosis or other) in the previous three months (exclusion criteria). Following this, each participant moved to a designated location, where members ($n=4$) of the research team explained the project, obtained consent, and collected the data.

All participants completed a pre-exercise/training questionnaire, which consisted of the SCAT2 post-concussion symptom scale (McCrory et al., 2009), and other variables such as frequency of exercise/sports participated in a typical week and intensity of exercise measured with Borg's rate of perceived exertion (RPE) scale (Borg, 1998). The SCAT2 symptom scale consists of 22 items each rated on a 7-point Likert scale which enables calculation of the total symptom score (TSS) and symptom severity score (SSS). Most of the self-reported symptom scales/checklists have not been subjected to rigorous and robust psychometric evaluation (Alla et al., 2009). The authors (Alla et al., 2009) concluded that the scales/checklists in current use lack psychometric properties as they were 'evolved' rather than scientifically developed. However, it has been reported that there is some evidence of face validity and reliability for the individual components of SCAT2, but not for the whole SCAT2 tool (Valovich et al., 2012). Despite this evidence, they emphasized the need for the SCAT2 tool to undergo testing for measurement properties in order to detect any meaningful change. More recently, the psychometric properties of the individual components of SCAT3 tool were found to vary across domains (Chin et al., 2016). It must be noted that major changes have not been made to the SCAT3 instrument compared to the SCAT2 scale. This is particularly the case for the symptom component of SCAT2 tool.

The Borg's RPE scale is a 10-point category-ratio scale that has previously shown excellent psychometric properties (Noble et al., 1983). The participants engaged in a range of self-selected activities (workout) including individualized exercise programs (e.g. biking, treadmill running or

free weights) and/or group exercise classes (e.g. step-fit or cardio-core). There was no requirement for the participants to change any aspect of their planned exercise and/or post-exercise activities (e.g. showering/relaxing) due to the study. Following their workout, each participant returned to the same designated location in the URC in order to complete the post-exercise questionnaire. This questionnaire incorporated the SCAT2 post-concussion symptom scale, Borg's RPE scale and customised questions for the duration of exercise (e.g. today, how long did you do the exercise?), type of exercise (e.g. aerobics, weight training) and recovery period (e.g. today, how long since you stopped exercising?).

A second cohort was selected to provide insight into the symptom response of a more structured sport-based activity. Men's and women's rugby union teams ($n=3$) from the OURFC were recruited following a pre-practice information session conducted in the team's locker room. A brief description about the project was verbally presented by one of the members of the research team who invited expression of interest to participate, and answered any questions raised by the participants. Those players who volunteered also self-reported any incidence of a concussion in the previous three months that would exclude them from the study. Each participant completed the pre-exercise questionnaire described earlier before they moved on to the sports field (outdoor) to undergo their routine practice session (e.g. skill activity). At the completion of the training, all participants were asked to return to the locker room to complete the post-exercise questionnaire. The participants from both sites received a bottle of sports drink for their participation in the study.

All statistical analyses were performed using the R statistical software, version 3.0.2. The data obtained from both the sites were combined for all analyses. The reliable change index (RCI) formula (Iverson et al., 2003) was used to determine the change in symptoms from pre-to-post-exercise.

Reliable change index: $S_{diff} = \sqrt{(SEM_1)^2 + (SEM_2)^2}$

Where, S_{diff} = standard error of difference, SEM_1 and SEM_2 = standard error of measurement of pre and post-exercise symptoms respectively.

Following the calculation of S_{diff} value for the post concussion-like symptoms, an 80% confidence interval value was calculated by multiplying the S_{diff} value by 1.282. This value of

1.282 is the z-score associated with the 80% confidence interval (Schmidt et al., 2012). The value obtained was rounded to the nearest whole number to provide an 80% confidence interval predictive cut-off score (CIPCS). The difference in post concussion-like symptom scores from pre-to post-exercise for each participant was examined and compared with the 80% CIPCS. Using this information, each participant was categorised as having either 'declined', 'improved' or 'not improved'. A reliable decline (increase) or improvement (decrease) was considered to have occurred when the difference in symptoms from pre-to post-exercise exceeded $\geq +5$ or -5 the 80% CIPCS. A designation of 'not improved' was given to those persons whose change scores did not exceed the 80% CIPCS in either direction.

Initially, a univariate linear regression analysis was performed with the criterion set at $p \leq 0.20$ to include the predictors in the subsequent multivariate analysis. Following this, multiple linear regression analyses (stepwise-backward elimination method) were conducted separately for the TSS and SSS respectively. All possible 2-way interactions between the predictor variables were also included in both models. The selection of the overall model fit was based on the Bayesian information criterion (BIC) which penalises models for the number of parameters estimated. A level of significance was set at $p < 0.05$ to identify the individual predictor contribution in the models for the TSS and SSS.

Results

A total of 260 participants (males=146, females=114) completed this study. The average age of the participants was 20.33 years ($SD=1.71$, range=18 to 28). The pre-exercise and post-exercise scores for TSS and SSS for all participants were 4.2 ($SD=4.1$) and 5.0 ($SD=4.1$), and 7.3 ($SD=8.9$) and 8.7 ($SD=8.3$) respectively. The descriptive statistics for the exercise parameters are presented in Table 1. The change in the post concussion-like symptoms (TSS & SSS) from pre-to post-exercise is presented separately for males and females in Table 2. The results revealed that nearly two-thirds of all participants did not have a change (increase or decrease) in TSS (77.9%) and/or SSS (81.9%) from pre to post-exercise/training. In general, males had an apparent increase in symptoms following exercise/training compared to females.

In the univariate analysis, the following predictor variables were found to be significant in both the TSS and SSS models: gender, intensity of exercise (RPE), duration of exercise, type of

exercise and volume of exercise (training load). However, when these were included in the multivariate models, only gender and volume of exercise were found to be significant. On average, females endorsed 4.03 units' fewer symptoms (TSS) compared to males (Table 3). The volume of exercise (training load) was moderated by gender to explain a small proportion of variance in the model. Specifically, volume of exercise did not have any impact on the TSS in males, but did have an effect in the females.

Discussion

This study investigated the symptom response following participation in exercise or rugby training in non-concussed individuals. The results differed from previous studies (Alla et al., 2010; Covassin et al., 2007) that documented an increased symptom response following exercise under laboratory conditions. Alla and colleagues (2010) reported that SSS increased following moderate intensity exercise and the symptoms further increased following high intensity exercise. Meanwhile, Covassin et al (2007) also selectively reported on a single symptom (fatigue), which was found to have increased following exercise. Contrarily, most of the participants in this study did not demonstrate any change (increased or decreased) in the symptom response (TSS & SSS). These findings could have resulted because participants chose either a single exercise activity or a combination of activities (e.g. aerobics and/or weights), that would have resulted in different intensities of exercise being performed. It is likely that the participants may not have exercised at an intensity high enough to result in symptoms and its provocation.

There was a 'cool down' or recovery period towards the end of, or immediately following the exercise/training session for most individuals. Hence, the time of reporting of symptoms took place at different times post-exercise, and there is a possibility that the data collection may have varied between participants. Moreover, the majority of the participants reported that they exercised 2-3 times a week; thus, they were probably familiar with the exercise activities they chose to perform, and likely would have had decreased physical and psychological stressors. This is in contrast to previous studies where the participants were asked to perform an exercise program under controlled conditions, with a possibility of exercise activities designed to provide a physiological stress leading to increased symptom production. The perceived benefits of exercise on the psychological wellbeing have been demonstrated elsewhere (Fox, 1999; Penedo & Dahn, 2005). Similarly, de-stressing effects associated with regular participation in exercise

has been reported in school students, particularly in females (Currie, 2010). These potential factors could have possibly played a significant role in our findings with a majority of participants not having a change in the symptom response.

These results show that no change in the symptom response occurred despite that all participants engaged in at least a minimum duration of 15 minutes. The findings of this study is partially supported by the authors elsewhere (Leclerc et al., 2002), who showed that varsity athletes who performed exercise at 84% maximum heart rate did not have a change in symptoms from baseline to post-exercise. However, direct comparisons cannot be made, considering that the athletes in their study (Leclerc et al., 2002) exercised under controlled conditions for a period of 5 minutes. Furthermore, the results have been reported for the entire McGill Abbreviated Concussion Evaluation (ACE) scale and not for the symptom subscale (Leclerc et al., 2002). Although, a majority of participants did not have a change in symptoms following exercise/training, it must be noted that one-third of participants did have a change, which is a significant proportion.

Another important reason for these contrasting results could be explained due to the differences in the statistical methods adopted between this study and previous studies. The previous studies (Alla et al., 2010; Covassin et al., 2007) have conducted the analyses at a group level and have extended the generalizations to an individual level. Assessment and interpretation of changes are affected by factors such as practice effects associated with repeated measurements, test-retest reliability and regression to the mean (Collie et al., 2003). Therefore, this study estimated the reliable change score for each participant, thus accounting for both measurement error and practice effects, often problems associated with test-retest measurements (Iverson et al., 2003). The estimation of the reliable change score is an analysis conducted at an individual level, and as such is of strong clinical relevance as opposed to being statistically meaningful (Iverson et al., 2006).

From the results of the regression models, it was found that the predictor variable of 'gender' contributed to both the TSS and SSS. In general, males had a decline (increase) in symptom response (TSS & SSS) compared to females following exercise/rugby training. These gender specific findings are different to previous studies (Gaetz & Iverson, 2009; Mrazik et al., 2013) that found no differences in symptom reporting between genders following exercise participation.

However, direct comparisons cannot be made because both these studies (Gaetz & Iverson, 2009; Mrazik et al., 2013) were conducted under controlled laboratory conditions, whereas this study was conducted in typical real-world conditions. It has been postulated that based on the ‘competition of cues’ theory, females more often tend to focus on external cues (e.g. talking to friends while exercising) and are likely to get distracted, whereas males are known to concentrate more on their internal bodily sensations (Pennebaker, 2000). Given that this study was conducted in a real-world context, there are more possible distractions that may have allowed a majority of the females to divert their attention more towards the external environment. Additionally, the symptom perception model clearly described the different processes involved in the perception of symptom reporting and how they differ between the genders (van Wijk et al., 1997).

In the past, it has been well documented that exercise causes the release of endogenous opiate substances known as endorphins from the higher centres of the brain (Harber & Sutton, 1984), which are known to cause a euphoric effect in an individual. However, the endorphin hypothesis has been mainly supported only in participants who engage in cardiovascular exercise (Goldfarb et al., 1998; Kraemer et al., 1989) compared to resistance training (Pierce et al., 1994). In this present study, a greater number of females ($n=37$) participated in cardiovascular only exercise compared to males ($n=6$). Meanwhile, more males ($n=60$) participated in resistance (weight training) only exercise compared to women ($n=7$). The endorphin hypothesis (Goldfarb et al., 1998; Kraemer et al., 1989) may potentially explain why a greater number of females had an improved (reduced) response in symptoms compared to males. In addition, studies have reported that females tend to have higher levels of depression and anxiety prior to participating in exercise (Rocheleau et al., 2004) hence, subsequent mood enhancement occurs more in women (Yeung, 1996). This improved state of well-being (Thoren et al., 1990) following exercise could have led the females in this study to report an improved (decrease) symptom response.

It was anticipated that participants would report increased SSS due to the challenge induced by the volume of exercise (training load). However, the contribution of the volume of exercise to the reported SSS was very marginal (negligible). The exact reasons for only a marginal increase in SSS could not be ascertained, considering that participants engaged in different types of exercise at different intensities and also the time of reporting varied.

In spite of this being the first prospective study to document symptom response following exercise or sports participation in a real-world context, this study is not without its limitations. Potential extraneous factors such as prior physical fitness level and the level of participation of exercise (e.g. amateur and recreation) that could influence the symptom reporting were not screened for and controlled. Considering that the main focus was to conduct this study in a real-world framework, it was not reasonable and viable to control these factors. Although conducting a study in a real-world context has the general advantage of extrapolating results due to high external validity, the internal validity is however compromised. Thus, studies need to be conducted in both controlled conditions and a real-world environment with the same participants in order to precisely determine the true change in symptom scores following exercise program or sports participation. The symptom response (TSS & SSS) following exercise or sports participation did not change in the majority of participants. Gender contributed to the reporting of both the TSS and SSS, whereas the volume of exercise (training load) contributed only to the SSS.

Perspective

Clinicians need to be aware of the effects of exercise when they interpret symptom reports post-exercise, as they are important components of a graduated RTP exercise protocol. The findings from this study need to be taken into account considering that exercise leads to symptom production and provocation even in non-concussed individuals. This is in accordance with the latest consensus statement (McCrory et al., 2013) which states that symptom testing should be carried out 15 minutes' post-exercise due to the effects of fatigue and/or exertion. In this light, Alla and colleagues (2010) have already demonstrated that symptom production and provocation occur following controlled exercise in non-concussed individuals. Therefore, it is most likely that the symptom provocation could occur in concussed individuals when they engage in an RTP exercise protocol.

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Conflicts of Interest

PM is a co-investigator, collaborator or consultant on grants relating to mild TBI funded by several governmental organisations. He is Co-Chair of the Australian Centre for Research into Sports Injury and its Prevention (ACRISP), which is one of the International Research Centres for Prevention of Injury and Protection of Athlete Health supported by the International Olympic Committee (IOC). He has a clinical and consulting practice in general and sports neurology. He receives book royalties from McGraw-Hill and was employed in an editorial capacity by the British Medical Journal Publishing Group from 2001 to 2008. He has been reimbursed by the government, professional scientific bodies and sporting bodies for presenting research relating to mild TBI and sports-related concussion at meetings, scientific conferences and symposiums. He received consultancy fees in 2010 from Axon Sports (USA) for the development of educational material (which was not renewed) and has received support since 2001 from CogState Inc for research costs and the development of educational material. He is a cofounder and shareholder in two biomedical companies (involved in eHealth and Compression garment technologies) but does not hold any individual shares in any company related to concussion or brain injury assessment or technology.

The other authors do not have any conflicts of interest to be declared

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Table 1

Descriptive Statistics for the Exercise Parameters

Variable	Participants					
	Males (n=146)			Females (n=114)		
	M (SD)	Min	Max	M (SD)	Min	Max
Duration of exercise (minutes)	68.3 (26.4)	15	150	61.6 (21.9)	25	120
Volume of exercise (training load) ^a	371.0 (248.8)	0	120	271.2 (162.9)	0	1200
Recovery period (minutes)	6.0 (6.0)	0	40	4.7 (5.1)	0	40
Intensity of exercise (pre-RPE)	3.0 (2.8)	0	10	2.5 (2.1)	0	10
Intensity of exercise (post-RPE)	5.2 (2.2)	0	10	4.4 (1.9)	0	10

Note. M=mean; Min=minimum; Max=maximum; SD=standard deviation

^aProduct of post-RPE (session RPE) and duration of exercise, hence has dimension less units

Table 2*Number and Percentage of Participants Who 'Changed' or 'Did not have a Change' in the Post-Activity Symptom Scores*

Participants	Mean (SD)		S _{diff}	80% CI ^a	% (n)	% (n)	% (n)
	Pre-exercise	Post-exercise			Improved	Declined	Not improved
Males ^b (n=146)							
TSS	3.60 (3.71)	5.40 (3.78)	3.88	4.97	6.8 (10)	19.9 (29)	73.3 (107)
SSS	5.82 (7.15)	9.36 (7.51)	7.88	10.10	6.2 (9)	15.1 (22)	78.8 (115)
Females ^b (n=114)							
TSS	5.04 (4.46)	4.62 (4.46)	4.79	6.14	9.6 (11)	7.9 (9)	82.5 (94)
SSS	9.28 (10.57)	7.87 (9.18)	12.19	15.62	8.8 (10)	6.1 (7)	85.1 (97)

Note. CI=confidence interval; TSS=total symptom score; SD=standard deviation; SSS=symptom severity score; S_{diff} =standard error of difference ^aValues obtained by multiplying the S_{diff} value with the Z-score value of 1.282 associated with 80% CI; ^bRounded to whole number to provide 80% confidence interval predictive cut-off value for males (TSS=5, SSS=10) and females (TSS=6, SSS=16) respectively.

Table 3

Multiple Linear Regression Analyses Predicting the Total Symptom Score and Symptom Severity Score

Predictor variable	Estimate	95% CI
TSS		
Intercept	1.285*	[0.050, 2.519]
Gender ^a	-4.033***	[-5.985, -2.081]
Volume of exercise (training load)	0.001	[-0.001, 0.004]
Gender x volume of exercise (training load)	0.007*	[0.001, 0.012]
SSS		
Intercept	0.028	[-2.582, 2.639]
Gender ^a	-4.003**	[-6.476, -1.530]
Volume of exercise (training load)	0.009***	[0.003, 0.015]

Note. CI = confidence interval.

^aMales (reference category).* $p < .05$, ** $p < .01$, *** $p < .001$.

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Author/s:

Balasundaram, AP;Athens, J;Schneiders, AG;McCrory, P;Sullivan, SJ

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