Exercise Testing of Adolescents and Young Adults With Sickle Cell Disease: Perceptual Responses and the Gas Exchange Threshold

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Abstract

For individuals with sickle cell disease (SCD), mild to moderate exercise is advised, but self-regulation of these intensities is difficult. To regulate intensity, one SCD recommendation is to stop exercising at the first perception of fatigue. However, perceived effort and affect (how one feels) are perceptual cues that are commonly used to guide exercise intensity. This study (a) examined perceived effort, affect, and fatigue in relation to metabolic state (gas exchange) in adolescents and young adults (AYAs) with SCD, (b) explored guidelines AYAs use to self-regulate exercise, and (c) compared perceived effort and affect at gas exchange threshold (GET) with healthy counterparts. Twenty-two AYAs with SCD completed an incremental cycle test. Perceived effort, affect, and fatigue were assessed every 2 minutes. A mixed-effects linear model was conducted to model changes in effort, affect, and fatigue across time. Mean scores of effort and affect at GET were compared with published data of healthy counterparts. Participants were queried about self-regulation exercise strategies. Findings indicated that both perceived fatigue and effort at GET was lower than expected. Perceived effort was lower ($p < .0001$), and perceived affect was significantly higher ($p = .0009$) than healthy counterparts. Interviews revealed that most participants (95%) do not stop exercising until fatigue is moderate to severe, and many (73%) do not stop until symptoms are severe (chest tightness, blurry vision). Nurses should review guidelines for safe exercise with AYAs with SCD. Exercise training may be beneficial to AYAs with SCD for learning how to interpret bodily responses to exercise to improve self-regulation.

Keywords

Fatigue, adolescents and young adults (AYA), exercise, sickle cell disease

Sickle cell disease (SCD) is an inherited hemoglobinopathy that results in the hallmark sickling of red blood cells and lifelong painful vaso-occlusive crisis. Globally, SCD affects millions, and the number of infants born with SCD is expected to increase approximately 30% by 2050 (Piel, Hay, Gupta, Weatherall, & Williams, 2013). Research and treatment have focused on survival, with health promotion as secondary; thus, health promotion has been understudied. However, recent advances in treatment have significantly increased life expectancy (Quinn, Rogers, McCavit, & Buchanan, 2010), underscoring the need to focus on health promotion.

Exercise plays an important role in health promotion and is recommended for individuals with SCD to enhance physical and mental health (National Heart Lung and Blood Institute [NHLBI], 2002). Unfortunately, these individuals are less fit and engage in less physical activity

than healthy peers (Moheeb, Wali, & El-Sayed, 2007; Wali & Moheeb, 2011). Although inactivity is associated with poorer health outcomes (U.S. Department of Health and Human Services, 2008), exercise can be challenging because the disease reduces exercise capacity (Chaudry, Bush, Rosenthal, & Crowley, 2013; Liem, Nevin, Prestridge, Young, & Thompson, 2009). In addition, strenuous or vigorous-intensity exercise, defined as causing rapid breathing and a significant increase in heart rate (HR; Haskell et al., 2007), is contraindicated because of the potential to trigger a vaso-occlusive crisis. Examples

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of vigorous-intensity activities are jogging, tennis singles, and playing in a basketball or soccer game. Nonetheless, exercise has numerous benefits such as improving cardiovascular and musculoskeletal health and reducing obesity (U.S. Department of Health and Human Services, 2008). In SCD, exercise can lead to a reduction in the red blood cell disaggregation threshold, which may have a beneficial effect on blood flow (Waltz et al., 2012). Exercise can temporarily increase nitric oxide (Barbeau et al., 2001), which can cause vasodilation. Furthermore, exercise may decrease pain and improve respiratory muscle strength and quality of life (Tinti, Somera, Valente, & Domingos, 2010).

There are no formal evidence-based guidelines for exercising safely with SCD, but there are recommendations. Existing recommendations provide information on how to avoid complications but do not address how to improve exercise capacity or performance, thus making self-management (i.e., monitoring and self-regulation) of exercise intensity challenging. Examples of recommendations are “avoid vigorous exercise, and drink plenty of fluids” (Connes, Machado, Hue, & Reid, 2011; NHLBI, 2002). Another recommendation is “to stop exercising at the first sign of fatigue.” Perceived fatigue is used as a guide for exercise cessation because, in theory, it provides an indication of the transition in metabolic state from aerobic to anaerobic metabolism. However, this explanation of exercise fatigue that is limited to physiologic effects has been questioned.

Exercise fatigue has been explained by peripheral fatigue—that is, fatigue in skeletal muscle due to buildup of lactic acid. This explanation would lead one to believe that the sense of fatigue during exercise is based solely on physiologic changes in skeletal muscle. Noakes (2012) refers to this as the “brainless” model, meaning that the brain is not involved in sensing exercise fatigue. A review by Gandevia (2001) suggests that skeletal muscle fatigue is not explained by changes in the muscle alone but that there are changes in the central nervous system as well. Noakes (2012) expands the concept of exercise fatigue and suggests that there is an emotional (sensation) as well as a physiological component. He puts forth a model to explain exercise regulation, the central Governor Model of Exercise Regulation, which proposes that “the brain regulates exercise performance” based on numerous conscious and unconscious factors such as to warn the body when to cease exercising in order to avoid “a catastrophic failure of homeostasis” (Noakes, 2012p. 5). As part of the model, exercise fatigue is conceptualized as an unpleasant sensation to warn the individual of their physiologic capacity. But, most important, this sensation of fatigue can be controlled by individuals so that they can achieve maximum performance if they so desire. In other words, they can push through this sensation of fatigue such as in

competition where they have a “burst” of energy at the end. Whether the perception of fatigue during exercise for AYAs with SCD indicates a transition to anaerobic metabolism (i.e., peripheral fatigue), as the exercise recommendation assumes, or something else is unknown.

Metabolic state during exercise encompasses three phases: aerobic metabolism, anaerobic threshold (gas exchange threshold [GET]), and anaerobic metabolism. Exercising at an intensity above GET can be unsafe in SCD because it can lead to sickling, a vaso-occlusive crisis, metabolic acidosis, and hyperventilation (Moheeb et al., 2007; Myers & Ashley, 1997). Thus, exercising at or below GET (mild to moderate intensity) comprises the guide for safe exercising. It is not only a parameter of safety but also may be an effective approach for improving exercise capacity (Lear et al., 2017; Wen et al., 2011). However, several studies indicate that individuals with SCD may be in an anaerobic state before they sense fatigue and cease exercising (Balayssac-Siransy et al., 2011; Callahan et al., 2002; Moheeb et al., 2007), suggesting that the perception of fatigue may consist of multiple factors and may not be the most sensitive or reliable perceptual cue of GET.

In healthy individuals and other clinical populations, perceptual cues to exercise such as perceived effort (i.e., what one feels) and affect (i.e., how one feels) are used to gauge exercise intensity and guide exercise prescription (American College of Sports Medicine, 2014). Effort is defined as the amount of exertion one perceives one is experiencing with exercise. Affect refers to one’s mood during exercise, or how good or bad one feels. Perceptual cues of effort and affect have exhibited consistent patterns or trends across metabolic states, which is why they are useful for guiding exercise intensity. These trends have been empirically derived (Acevedo, Kraemer, Haltom, & Tryniecki, 2003; Ekkekakis, Hall, & Petruzzello, 2004; Hall, Ekkekakis, & Petruzzello, 2002). In healthy individuals, there has been extensive research on trends of perceived effort and affect in relation to biomarkers of metabolic state (e.g., gas exchange, blood lactate) and to other physiologic markers of exercise intensity (e.g., maximal HR, oxygen uptake reserve) (Ekkekakis & Acevedo, 2006; Ekkekakis et al., 2004; Ekkekakis, Lind, & Vazou, 2010). In general, HR and perceived effort respond to increasing exercise intensities (with changes in metabolic state) in a linear fashion, whereas affect responds to increasing exercise intensities in a curvilinear fashion. Affect—how good or bad one feels during exercise—is positive (feeling good) and generally shows no significant change during aerobic metabolism, but it demonstrates a quadratic decline when exercise intensities surpass the GET. However, a few studies suggest that affect may begin to decline soon after the start of exercise in deconditioned individuals (Ekkekakis et al., 2010; Sheppard & Parfitt, 2008b).

The utility of these perceptual cues has not been examined in individuals with SCD. In addition, although one of the recommended guidelines for exercise cessation for individuals with SCD is when they first sense fatigue, the perception of fatigue in relation to metabolic state during exercise has not been explored. The dearth of research raises the question as to the extent to which individuals with SCD are aware of perceptual cues of GET, particularly given the potential multifactorial dimensions of exercise fatigue.

The primary objective of this pilot study was to examine perceived effort, affect, and fatigue in relation to metabolic state during an incremental exercise protocol in adolescents and young adults (AYAs) with SCD. The focus is on AYAs because they have reported seeking more explicit guidelines to self-manage exercise to improve fitness (Ameringer & Austin, 2014). We hypothesized that perceived effort and fatigue will increase significantly linearly across time (exercise intensity), and perceived affect will decrease significantly nonlinearly across time (exercise intensity). Secondary objectives were to (a) explore the guidelines that AYAs are currently using to self-manage their exercise and (b) to compare perceived effort and affect at anaerobic threshold of AYAs with SCD to perceived effort and affect reported in published reports on healthy counterparts.

Method

The study was approved by the Institutional Review Board of Virginia Commonwealth University. Minor assent and written permission were obtained from participants who were younger than 18 years and parents, respectively, and written informed consent was obtained from adult participants.

Design, Setting, and Participants

This cross-sectional observational pilot study was conducted at an academic medical center in the Mid-Atlantic. Participants were recruited from pediatric and adult SCD clinics. Inclusion criteria were AYAs who were aged 15 to 39 years, who had hemoglobin SS or HbS β 0 thalassemia disease. Exclusion criteria were participant's or minor's parent's inability to read and write in English; pregnancy; hemoglobin ≤ 6.0 and/or no more than 1 g/dL change from baseline in the past 6 months; illness or sickle cell crisis in the past 2 weeks; acute chest syndrome in the past 2 months and chronic blood transfusions; history of bone marrow transplant, asthma, other pulmonary or cardiac conditions; and/or use of stimulants. The participant's provider conducted a physical exam to confirm eligibility and approve participation. Participants completed a health history form to identify any additional

exclusion criteria (e.g., use of stimulants). Participants were instructed to abstain from vigorous physical activity and to maintain regular eating and hydration habits for 24 hours prior to the study visit.

A mixed-effects linear model was conducted to model changes in perceived effort, affect, and fatigue across time. Using the longitudinal data from our initial feasibility study that included three male AYAs with SCD aged 19 to 23 years, the standard deviations and correlations for perceived effort, affect, and fatigue were (3.29, 0.62), (3.50, 0.52), and (2.73, 0.53), respectively. Using nQuery Advisor (Elashoff, 2007) with the type I error set at 0.05, a proposed sample size of 30 was estimated to have a greater than 95% power to detect a difference in effort, affect, and fatigue means across time using a single-group repeated-measures analysis of variance.

Measures

Demographic, disease, and physical characteristics were obtained from either medical records or self-report. Height, weight, blood pressure, HR, and oxygen saturation using pulse oximeter readings were obtained. Participants completed the International Physical Activity Questionnaire (n.d.), a 21-item self-report measure used to categorize physical activity level as high, moderate, or low. After completing the exercise protocol, participants were asked three questions about self-regulation strategies they use when exercising: (a) "When you exercise, what guidelines do you use to take a break or stop exercising?" (b) "Are there any other guidelines that your provider suggested you use?" and (c) "On a scale of 0 to 10, what level of fatigue do you use to decide when to stop exercising?" Participants were asked these questions after completing the exercise protocol as opposed to beforehand so that their answers would not influence their ratings of their perceptions during the exercise testing, which was the primary focus.

Perceptions of effort, affect, and fatigue as well as HR were assessed during the exercise testing protocol. Perceived effort was assessed with the Rating of Perceived Exertion scale (RPE) (Borg, 1974; Borg, Hassmen, & Lagerstrom, 1987; Borg, Ljunggren, & Ceci, 1985). Scores range from 6 (*very, very light*) to 20 (*very, very hard*). Perceived affect, how good or bad one feels, was assessed with the Feeling Scale (FS), (Hardy & Rejeski, 1989). Scores range from -5 (*very bad*) to +5 (*very good*). Perceived fatigue was assessed with an 11-point numeric rating scale ranging from 0 (*not tired at all*) to 10 (*as tired as can be*) from the Brief Fatigue Inventory (BFI; Mendoza et al., 1999). The measures were displayed on a board held in front of the participant so that the participant could point to the response while exercising. Participants were assessed for potential adverse

Figure 1. Exemplar of Ratings of Perceived Exertion (RPE), Feeling State (FS), and Brief Fatigue Inventory (BFI) and responses of heart rate (HR) across exercise intensity for a single participant. From the exemplar, one can see that the gas exchange threshold (GET) is estimated at 55.7. This exemplar has three observations before GET and five observations after GET. Because participants' number of observations before and after GET differ, the standardized number of observations chosen was based on the frequency of responses across participants; thus, the two points prior to GET, observation at GET, and three points post GET were chosen.

events immediately, at 24 hours, and 1 week after completing the protocol.

Metabolic state was determined by measuring gas exchange from expired oxygen during a progressive incremental exercise protocol on a stationary bike. A Parvo Medics TrueOne metabolic measurement system was utilized to quantify pulmonary ventilation (VE), oxygen consumption (VO₂), and carbon dioxide produced (VCO₂). Aerobic fitness was defined as the peak oxygen uptake (VO₂ peak) during the graded exercise protocol. Anaerobic threshold was operationalized as the GET. The GET was determined with a computerized version (Winbreak 3.7, Ames, IA) of the procedure described by Gaskill et al. (2001).

Exercise Protocol

After a 2-minute warm-up (no resistance) on a stationary bike, the workload was increased in 2-minute stages, using an incremental ramp protocol (7, 10, or 15 watts). The increases in workload continued until the participant reached volitional exhaustion—that is, until the individual felt that she or he could not continue. HR, blood pressure, and perceived effort, affect, and fatigue were obtained from the participant at baseline, just prior to each 2-minute increase in workload during the exercise protocol and immediately after completing the exercise protocol. Heart rate and rhythm were continuously monitored. After completing the exercise protocol, participants rested for approximately 15 minutes and completed the postprotocol measures.

Statistical Analyses

Descriptive statistics were used to characterize the sample. Because duration of exercise protocol varied across participants, standardized time points were used in the analysis.

The primary objective was to examine perceived effort, affect, fatigue, and HR in relation to metabolic state (GET) across exercise intensity. To address this objective, each participant was asked to exercise to volitional exhaustion. Using the resulting physiologic data, the individual GETs were calculated, and graphs of perceptual cues and physiologic responses (RPE, FS, BFI, and HR) across exercise intensity were created for each participant. Using the GET as anchor point, data across subjects were aligned, and the following standardized time points were retained: 4 minutes before GET (GET -2), 2 minutes before GET (GET -1), minute of GET (GET), 2 minutes after GET (GET +1), 4 minutes after GET (GET +2), and 6 minutes after GET (GET +3). The time to volitional exhaustion differs for each individual; therefore, these standardized time points were retained because they captured the majority of observations before and after GET for all participants. The plot in Figure 1 exemplifies the profile of a single participant, showing the perceptual cues and physiologic responses (RPE, FS, BFI, and HR) across exercise intensity. Note that in this exemplar, this participant has three observations prior to their GET of 55.7 (GET -3, GET -2, and GET -1) and five observations after GET (GET +1, GET +2, and GET +3, GET +4, and GET +5). In this example,

observations that were retained for the analyses were GET -2, GET -1, GET, GET +1, GET +2, and GET +3. Using these standardized time points, a graph depicting group means and standard error bars of perceptual cues (RPE, FS, BFI) and physiologic response (HR) were examined. Next, to examine the trends, a mixed-effects linear model was used to model changes across time for RPE, FS, BFI, and HR. Time, modeled as a polynomial (linear and quadratic effects), constituted fixed effects, and the participant was modeled as a random effect. All analyses were performed using SAS and JMP software (SAS Institute, n.d.-a, n.d.-b).

The secondary objectives were to (a) compare RPE and FS scores at GET of AYAs with SCD to healthy AYAs and (b) describe guidelines AYAs report using to self-manage their exercise. To compare perceived effort and affect at GET of these AYAs with healthy AYAs, we identified published studies that used RPE (Acevedo et al., 2003; Demello, Cureton, Boineau, & Singh, 1987; Ekkekakis et al., 2004; Hetzler et al., 1991; Mahon, Duncan, Howe, & Del Corral, 1997; Purvis & Cukiton, 1981; Stoudemire et al., 1996; Welch, Hulley, Ferguson, & Beauchamp, 2007) and FS (Acevedo et al., 2003; Ekkekakis et al., 2004; Hall et al., 2002; Sheppard & Parfitt, 2008b; Welch et al., 2007), which were methodologically similar. The means from these studies were harvested and a pooled mean, weighted by sample size, was calculated for both RPE and FS. A single-group *t* test was used to compare the mean RPE and FS from study data with the published means. The use of data from published reports provided a historical control to allow comparison between AYAs with SCD and their healthy counterparts on RPE and FS at GET. Fatigue was not compared due to lack of published data. Content analysis and descriptive statistics were used to summarize the responses to the interview questions.

Results

Participant Characteristics

Of 57 AYAs with SCD who were eligible, a total of 33 enrolled and 24 completed the exercise protocol to volitional exhaustion. The 9 that did not complete the protocol were either ineligible following the physical exam or did not show for testing. Of the 24, two were excluded from the analysis due to equipment failure, experimenter error, or subject adherence to the protocol. Data from 22 participants (73% of the recruitment goal) were analyzed. The majority were males (64%), and the mean age was 23.7 years. See Table 1 for participant characteristics. Oxygen saturation demonstrated a statistically but not clinically significant drop (mean drop = 1.1, standard deviation [*SD*] 2.3, *p* = .038). Aerobic capacity was low as indicated by the mean (*SD*) VO_2 peak of 19.2 (5.43). Only 1 of the 22

Table 1. Sample Characteristics (*N* = 22).

Variable	<i>M</i> (<i>SD</i>)	Range
Age (years)	23.7 (6.70)	15-39
Height (cm)	169.6 (7.94)	146-183
Weight (kg)	65.4 (14.1)	45.9-91.2
BMI	22.7 (4.41)	16.4-33.1
Hgb (g/dL)	8.9 (1.43)	7.1-11.6
Duration of exercise (minutes)	13.7 (3.33)	7-21
Pulse oximetry		
Pre	96.5 (2.60)	89-99
Post	95.4 (2.97)	89-99
VO_2 peak (mL/kg/min)	19.2 (5.43)	12.0-34.8
Percent peak VO_2 at GET	59.0 (12.95)	35.5-85.8
Percent of expected max HR at GET	61.0 (9.92)	46.5-77.9
Variable	<i>n</i> (%)	
Hydroxyurea use		
Yes	15 (68)	
No	7 (32)	
Gender		
Male	14 (64)	
Female	8 (36)	
Genotype		
SS	19 (86)	
S β 0 Thalassemia	3 (14)	
IPAQ physical activity level		
High	13 (59)	
Moderate	6 (27)	
Low	3 (14)	

Note. BMI = body mass index; hgb = hemoglobin; IPAQ = International Physical Activity Questionnaire; GET = gas exchange threshold; HR = heart rate.

participants reported pain within 24 hours of testing. The participant went to the emergency department but did not require hospitalization. This episode could not be directly linked to the exercise testing. No serious adverse events were reported during or up to 1 week following the exercise testing by any other participant.

Perceptual Responses and Metabolic State

Figure 1 displays a graph showing the perceptual cues and physiologic responses (RPE, FS, BFI, and HR) across exercise intensity for an exemplar participant. The mean ratings for the perceptual cues and HR at GET are in Table 2. The mean RPE at GET was 9.4, and the mean BFI was 0.9. More than half (55%) rated their fatigue at 0 at GET. The mean FS at GET was 3.1. The mean terminal rating on the RPE was 16.6 (*SD* = 2.42), and on the FS it was -0.8 (*SD* = 2.63). The mean terminal rating on the BFI was 6.9 (*SD* = 2.33), and the range was 0 to 10.

Table 2. Means and Standard Errors of Perceptual Responses and Heart Rate.

Variable	GET stage											
	GET -2 (n = 18)		GET -1 (n = 22)		GET (n = 22)		GET +1 (n = 22)		GET +2 (n = 21)		GET +3 (n = 19)	
	M	±SE	M	±SE	M	±SE	M	±SE	M	±SE	M	±SE
BFI	0.22	±0.13	0.55	±0.19	0.86	±0.25	1.95	±0.37	3.24	±0.53	4.47	±0.50
RPE	7.00	±0.35	8.23	±0.46	9.41	±0.48	10.91	±0.49	12.48	±0.59	14.05	±0.62
FS	1.44	±0.47	2.09	±0.43	3.09	±0.35	2.45	±0.40	1.86	±0.48	1.00	±0.58
HR	94.4	±3.80	108.5	±6.20	120.0	±4.27	131.6	±4.56	144.3	±4.65	158.4	±4.60

Note. GET = gas exchange threshold, M = mean; SE = standard error, BFI = Brief Fatigue Inventory, RPE = Rating of Perceived Exertion, FS = Fatigue Scale, HR = heart rate.

Figure 2. Ratings of Perceived Exertion (RPE), Feeling State (FS), and Brief Fatigue Inventory (BFI) and responses of heart rate (HR) across gas exchange threshold (GET) stages. The figure shows the group means and standard errors at each stage for each variable.

Trend analysis showed that the linear trends were significant for RPE, $F(1, 101.7) = 334.9, p < .0001$; BFI, $F(1, 101) = 210.5, p < .0001$; and HR, $F(1, 101.4) = 325.3, p < .0001$, while quadratic trends were significant for FS, $F(1, 100.4) = 19.0, p < .0001$, and BFI, $F(1, 100.3) = 14.1, p < .0003$. See Figure 2.

For RPE, a trend analysis with a model that included a linear and quadratic effect showed that the quadratic effect was not significant, $F(1, 100.2) = 1.2, p < .2750$, whereas a trend analysis with the linear effect only showed that the linear trend was significant, $F(1, 101.7) = 334.9, p < .0001$. For FS, a trend analysis with a model that included a linear and quadratic effect showed that the linear effect was not significant, $F(1, 101.3) = 1.9, p < .1742$, but the quadratic effect was significant, $F(1, 100.4) = 19.0, p < .0001$. For BFI, a trend analysis with a model that included a linear and quadratic effect showed that both the linear BFI, $F(1, 101) = 210.5, p < .0001$, and the quadratic, $F(1, 100.3) = 14.1, p = .0003$, effects were significant.

Comparison of RPE and FS Scores

We compared the RPE and FS scores at GET of the 22 participants with healthy counterparts from published reports. The mean RPE at GET for the AYAs with SCD ($M = 9.4$, standard error [SE] = 0.48) was significantly lower than the pooled mean RPE at GET in healthy counterparts ($M = 12.73$) (CI [8.41, 10.41]; $p < .0001$). The mean FS at GET for the AYAs with SCD ($M = 3.09$, $SE = 0.35$) was significantly higher than the pooled mean FS at GET in healthy counterparts ($M = 1.73$) (CI [2.36, 3.83]; $p = .0009$).

Exercise Guidelines Used by AYAs

After completing the exercise session, we asked the participants what guidelines they use for guiding exercise cessation. Content analysis of the responses resulted in four categories: cardiorespiratory symptoms, fatigue symptoms, other symptoms, and do not use any. See Table 3 for examples of responses. When asked if there

Table 3. Categories of Guidelines Participants Report Using to Stop Exercising.

Category	<i>n</i>	Examples of responses
Cardiorespiratory symptoms	12	Chest gets tight and heavy Feels a burning in the chest Can't breathe Chest tightness Vision gets blurry Heart rate goes up Light headed, dizzy
Fatigue	4	Tired enough to throw up Gets too tired
Other	5	By the way my body feels When mouth gets dry Any pain
Nothing	4	No stopping Not really anything

were other guidelines that their providers recommend they use, most ($n = 13$) said that they received no other instructions. Nineteen participants responded to the question as to what level of fatigue from the BFI they usually use to decide when to stop exercising. Based on the categorization of fatigue as mild (1-3), moderate (4-6) and severe (7-10) (Mendoza et al., 1999), only 1 (5%) reported stopping at a mild level of fatigue, 9 (47.5%) at a moderate level, and another 9 (47.5 %) at a severe level.

Discussion

The primary objective was to examine how perceptions of effort, affect, and fatigue aligned with metabolic state during exercise in AYAs with SCD. We found that the patterns of RPE and FS across metabolic states were similar to healthy AYAs; however, the scores differed. Overall, RPE scores were lower, and FS scores were higher. The pattern of responses on the BFI indicated that fatigue was, on average, mild at GET and only mild to moderate at volitional exhaustion.

The physical fitness of these AYAs were fair to poor as indicated by the range of VO_2 peak values. The mean VO_2 peak of 19.2 mL/kg/min is similar to findings in other studies of AYAs with SCD, where mean VO_2 peaks have ranged from 23 to 28 (Liem et al., 2009; Liem et al., 2015; Watson et al., 2015), and notably lower than healthy AYAs, where VO_2 peaks have been ranged from 28 to 52 (Eisenmann, Laurson, & Welk, 2011; Liem et al., 2015; Robbins, Pender, Ronis, Kazanis, & Pis, 2004; Schneider, Dunn, & Cooper, 2009; Watson et al., 2015; Zamunér et al., 2011). Studies of sedentary individuals within this age category have reported VO_2 peaks ranging from 24 to 33 mL/kg/min (Welch et al., 2007; Zamunér et al., 2011).

However, VO_2 peaks in older overweight/obese women are more similar to the AYAs with SCD, with ranges from 16 to 23 (Ekkekakis et al., 2010; Hulens, Vansant, Lysens, Claessens, & Muls, 2001).

Perceived fatigue is one of the recommended cues for stopping exercise for individuals with SCD; thus, their perceptions of fatigue during exercise are important. During exercise, feeling fatigued is considered to be an indicator of lactic acid build up and the body's switch to anaerobic metabolism. While the SCD recommendations for exercising safely suggest resting at the first sign of fatigue (Connes et al., 2011; NHLBI, 2002), we found that the mean BFI score at GET was much lower than expected (0.9), and more than half did not report any fatigue until beyond GET. At stage GET +3, the mean BFI score was only in the moderate range (4.47).

Responses from the questions on self-regulation of exercise indicated that most of the participants did not even use fatigue as a guide for when to stop exercising but used other symptoms, such as cardiorespiratory symptoms, despite the fact that in the third interview question they provided a level of fatigue for when they stopped. Several of the symptoms they reported are worrisome as they may indicate that the individuals are exercising beyond a safe point, including that they do not stop until they experience difficulty breathing, chest tightness, or dizziness. Most (95%) of the participants also reported that their fatigue level was usually in the moderate to severe range when they stopped exercising, which based on the findings from this study would indicate that they would be in an anaerobic state for a time. However, the length of time that is dangerous for individuals with SCD to be in an anaerobic state is unclear.

If the intention of the recommendation to stop at the first sign of fatigue is to keep the individual from transitioning into an anaerobic state, then these findings suggest that this recommendation may be inadequate. There is no definition of fatigue that individuals with SCD can easily use to self-regulate exercise intensity. Furthermore, even the perception of muscle fatigue appears elusive. Other factors, such as emotions, may be contributing to their perception of exercise fatigue. Regardless, many reported that they do not use fatigue levels to guide exercise cessation. Fatigue may be useful in conjunction with other recommendations, but further clarification of this recommendation is needed to ensure that individuals with SCD exercise at an intensity below anaerobiosis. Evidence-based guidelines for safe exercise are greatly needed for individuals with SCD.

The results for the trend analysis of RPE indicated that RPE showed a similar linear trend to healthy AYAs and adults but the scores were lower overall. On the RPE scale, a score in the range of 12 to 14 indicates moderate exercise intensity, the individual senses they are working

“somewhat hard,” and these scores usually align with the GET (American College of Sports Medicine, 2014). A score of 9 or 10 would indicate that the person senses they are working “very lightly.” Our results revealed that most participants did not report an RPE of 12 to 14 until they were well beyond GET. The mean RPE at GET (9.4) of these AYAs was not only significantly lower than the pooled mean RPE at GET of healthy AYAs (12.7) but was also not in the expected range of 12 to 14. Mean RPE ratings at GET have been found to be similarly lower in younger children (Duncan, Mahon, Gay, & Sherwood, 1996). In essence, though the perceived effort increased linearly as expected, RPE did not correspond to GET as it has in other populations. However, HR also demonstrated a significant linear trend as expected, and rates were in the expected ranges across stages, supporting the validity of these GET values.

An individual’s affective response to exercise—the pleasure or displeasure one experiences during exercise—may play an important role in both guiding exercise intensity and maintaining engagement with exercising. The research on the affective response to exercise suggests two important points. First, there is a negative relationship between exercise intensity and affective responses such that as exercise intensity increases, pleasure decreases, although not linearly but as a quadratic decline. Pleasure generally drops off soon after transitioning to anaerobiosis. Second, exercise usually remains pleasurable below the GET (Ekkekakis, Parfitt, & Petruzzello, 2011). While the quadratic trend for the FS was significant as it has been in other populations (Ekkekakis et al., 2004; Sheppard & Parfitt, 2008b), the mean rating on the FS at GET was significantly higher (3.1) compared with the pooled mean on healthy AYAs (1.7) and higher than healthy young adolescents (Sheppard & Parfitt, 2008a) and overweight/obese women (Ekkekakis et al., 2010). In both obese (Ekkekakis et al., 2010) and inactive young adult women (Welch et al., 2007), there was a decline in FS prior to GET, whereas with these AYAs with SCD, the decline occurred after GET. However, the mean VO_2 peak of the AYAs with SCD are somewhat similar to obese women (15.8-17.5) (Ekkekakis et al., 2010; Hulens et al., 2001).

There are general recommendations for exercising safely with SCD (Connes et al., 2011; NHLBI, 2002), but some are vague. Along with the guideline to stop exercising at the first sign of fatigue, other recommendations include gradually increase the frequency of exercise; engage in mild to moderate exercise but avoid intense exercise; rest at least every 20 minutes; hydrate prior to, during, and after exercise; avoid cold and heat stress; and avoid contact sports. The challenge with these guidelines, again, is that some of them are nebulous. What is intense exercise? What is moderate exercise? What do we mean by the first sign of fatigue? As findings from this study

indicate, whether and how perceived fatigue is used by AYAs to guide self-regulation of exercise is unclear. This highlights the need for initiating and having ongoing discussions with AYAs about not only the importance of exercising for health promotion but also exercising safely. The nurse should ask the AYA to describe what bodily cues they use to determine when they should rest. At the very least, determine whether the AYA understands the current general recommendations.

The interpretation of study findings is limited by the small sample size and use of a single institution. Using published reports to compare RPE and FS scores between AYAs with SCD and healthy counterparts has recognized weaknesses such as baseline differences, selection bias, methodological differences, and time differences. We acknowledge these weaknesses; however, the intention of the comparisons is to begin to gain a sense of whether these groups differ on their perceptions of effort and affect at GET. One limitation is that we were not able to compare fatigue scores at GET of AYAs with SCD to healthy AYAs, but that is because we could not identify any relevant literature. We were not able to achieve our recruitment goal of 30 within the time frame of the study but learned lessons that will inform recruitment approaches in future studies. For example, our eligibility criteria were relatively stringent, and these may be able to be relaxed in future studies. In addition, several who were enrolled did not show up for the exercise session despite multiple attempts to contact them, and the number of potential eligible AYAs was lower than expected. However, we were pleased that 42% of those eligible did participate.

In conclusion, it is difficult to interpret what the fatigue scores actually indicated, though muscle fatigue probably contributed to the scores. Fatigue is not commonly used to guide exercise prescription because it can be confused with numerous bodily responses. The patterns of responses for effort and affect during the incremental exercise protocol of these AYAs with SCD were similar to healthy individuals, but the RPE scores were generally lower, indicating less effort, and FS scores were generally higher, indicating greater pleasure. This could possibly be due to the lack of experience with reading their own bodily responses during exercise. It has been established that training may enhance these perceptions (Rose & Parfitt, 2008). Ekkekakis et al. (2011) has recommended a biopsychosocial approach grounded in biofeedback, using perceptual cues of effort and affect to improve self-monitoring and self-regulation of safe exercise. Across other conditions, such as heart disease, individuals have been trained successfully to discern their responses of effort and affect during exercise and use these perceptual cues as part of their regimen to self-regulate safe exercise. Future research should focus on determining whether AYAs with SCD can be trained to use perceptual

cues of effort and affect to guide safe exercise and examining the effects of mild to moderate exercise on improving fitness. Nurses who work in pediatric and adult hematology, primary care, and schools are in prime venues to provide guidance to AYAs with SCD on the importance of exercising and exercising safely.

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