

# The Effects of Basal Insulin Suspension at the Start of Exercise on Blood Glucose Levels During Continuous Versus Circuit-Based Exercise in Individuals with Type 1 Diabetes on Continuous Subcutaneous Insulin Infusion

Dessi Zaharieva, MSc,<sup>1</sup> Loren Yavelberg, MSc,<sup>1</sup> Veronica Jamnik, PhD,<sup>1</sup> Ali Cinar, PhD,<sup>2,3</sup> Kamuran Turksoy, PhD,<sup>2</sup> and Michael C. Riddell, PhD<sup>1,4</sup>

## Abstract

**Background:** Exercise causes glycemic disturbances in individuals with type 1 diabetes (T1D). Continuous moderate-intensity aerobic exercise (CON) generally lowers blood glucose (BG) levels and often leads to hypoglycemia. In comparison, circuit-based exercise (CIRC) may attenuate the drop in BG. The goal of this study is to contrast the effects of basal insulin suspension at the onset of two different forms of exercise (CON vs. CIRC).

**Methods:** Twelve individuals (six men and six women) with T1D on insulin pump therapy were recruited for the study. All participants completed a maximal aerobic fitness test and two 40-min exercise sessions, consisting of either continuous treadmill walking or a circuit workout. Basal insulin infusion was stopped at the onset of exercise and resumed in recovery. After providing an initial reference value, volunteers were blinded to their [BG] and were asked to estimate their levels during exercise.

**Results:** Oxygen consumption ( $47.5 \pm 7.5$  vs.  $54.5 \pm 13.5$  mL·kg<sup>-1</sup>·min<sup>-1</sup>,  $P=0.03$ ) and heart rate ( $122 \pm 20$  vs.  $144 \pm 20$  bpm,  $P=0.003$ ) were lower in CON vs. CIRC. Despite the lower workload, BG levels dropped more with CON vs. CIRC ( $\Delta$  BG =  $-3.8 \pm 1.5$  vs.  $-0.5 \pm 3.0$  mmol/L for CON vs. CIRC, respectively,  $P=0.001$ ). Participants were able to estimate their BG more accurately during CON ( $r=0.83$ ) vs. CIRC ( $r=0.33$ ) based on a regression analysis.

**Conclusion:** Despite a lower intensity of exercise, with full basal insulin suspension at the start of exercise, CON results in a larger drop in BG vs. CIRC. These findings have implications for single hormone-based artificial pancreas development for exercise. While this study does not negate the importance of frequent capillary BG monitoring during exercise, it does suggest that if persons are knowledgeable about their pre-exercise BG levels, they can accurately perceive the changes in BG during CON, but not during CIRC.

**Keywords:** Hypoglycemia, Exercise, Insulin pump, Continuous glucose monitoring.

## Introduction

REGULAR PHYSICAL ACTIVITY (PA) is recommended for improving insulin sensitivity, blood lipid profiles and for reducing the risk of cardiovascular disease for individuals with type 1 diabetes (T1D).<sup>1</sup> Exercise can increase the like-

lihood of hypoglycemia and may also lead to challenges in maintaining blood glucose (BG) control overall.<sup>2</sup> Without insulin dose adjustments or carbohydrate intake, continuous moderate-intensity aerobic exercise (CON) typically leads to large reductions in [BG] concentrations,<sup>3</sup> whereas intermittent high intensity circuit-based exercise (CIRC) either

<sup>1</sup>School of Kinesiology and Health Science, Faculty of Health, Muscle Health Research Centre and Physical Activity and Chronic Disease Unit, York University, Toronto, Canada.

<sup>2</sup>Department of Biomedical Engineering and <sup>3</sup>Chemical and Biological Engineering, Illinois Institute of Technology, Chicago, Illinois.

<sup>4</sup>LMC Diabetes & Endocrinology, Toronto, Canada.

attenuates the decrease, or may even cause a small rise in [BG] levels.<sup>4,5</sup> While both CON and CIRC can lead to specific training adaptations, individuals with T1D now routinely perform CIRC for a variety of reasons, including enhanced fitness without promoting hypoglycemia.<sup>4,6</sup>

Tsalikian et al.<sup>7</sup> demonstrated that the risk of developing exercise-associated hypoglycemia could be effectively reduced with the suspension of insulin infusion (i.e., pump suspend) in children on continuous subcutaneous insulin infusion (CSII) therapy. In contrast, Admon et al.<sup>8</sup> found that pump suspension did not attenuate the drop in glycemia compared to leaving the pump on with a reduced basal rate (i.e., 50%). In a more recent study, McAuley et al.<sup>9</sup> reported that a basal rate reduction of 50% performed 60-min before the start of exercise failed to cause a significant reduction in circulating insulin levels during exercise compared to baseline. In all of these studies, only one type of exercise was performed (i.e., CON).

The primary purpose of this study was to examine the effects of basal insulin suspension at the onset of two different forms of prolonged exercise (i.e., CON vs. CIRC). The secondary purpose was to assess the accuracy of [BG] estimations when participants were provided with their measured [BG] value 10-min before the onset of exercise. Our hypothesis was that suspending basal insulin at the onset of CON would lead to a greater drop in glycemia compared to CIRC because of the higher reliance on anaerobic metabolism in the latter activity. We also hypothesized that participants could accurately estimate their BG concentrations during both forms of exercise.

## Methods

### Study participants

The experimental protocol conformed to the standards set by the Declaration of Helsinki and was approved by the Research Ethics Board at York University. The study was registered at clinicaltrials.gov in 2017 (identifier: NCT03034798). Twelve participants with T1D were recruited for the study. All of the participants engaged in regular PA, including structured exercise and reported monitoring BG levels regularly with capillary testing and a handheld glucose meter (4+ times per day). The inclusion criteria included the following: T1D for >1 year; on CSII for at least 3 months; at least in fair glycemic control (last HbA<sub>1c</sub> ≤9.0% or 75 mmol/mol). Exclusion criteria included the following: frequent and unpredictable hypoglycemia; unable to exercise on a regular basis due to an injury; having conditions that may make exercise unsafe (i.e., high blood pressure, late pregnancy, etc.).

### Experimental design

Participants completed a total of three exercise visits at the Human Performance Laboratory at York University. The first visit was for the determination of maximal aerobic capacity (VO<sub>2</sub>max) followed by two prolonged exercise visits consisting of either CON or CIRC, performed in random order. Participants were asked to avoid alcohol and caffeine consumption and refrain from all forms of exercise >3 metabolic equivalents for 24 h before each visit. To accommodate participant scheduling, the experimental visits (CON and CIRC) were conducted either in the late morning (~1100 h,

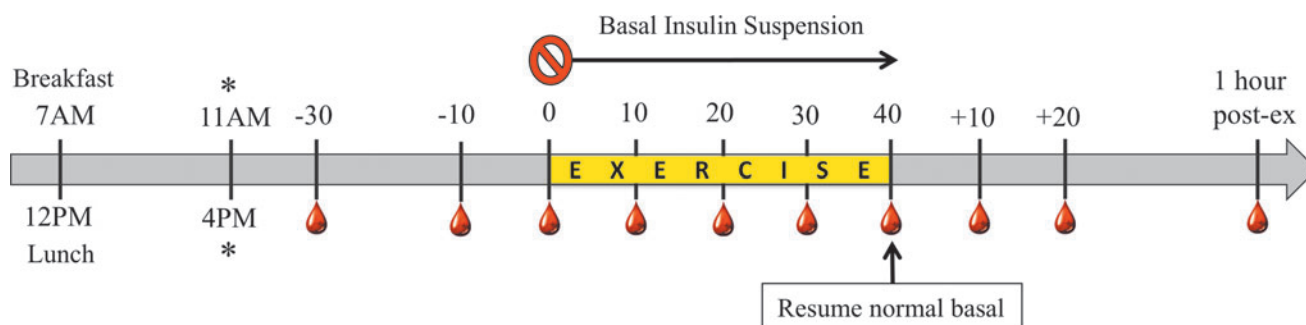
*n*=6) or in the late afternoon (~1600 h, *n*=6). For each participant, the timing of both CON and CIRC visits were standardized to try and control for as many variables as possible (pre-exercise meal, time of day, and circulating insulin levels). Participants were asked to consume the same meal of their choice, at least 4 h before coming to the laboratory, and take their regular insulin bolus for the meal before the exercise start time. Participants were asked to refrain from food or drink following their last meal before the exercise session, unless hypoglycemia developed ([BG] <3.9 mmol/L). There were no reported incidents of hypoglycemia pre-exercise for CON and CIRC conditions and it was confirmed by examining the participants pump history that no additional insulin bolus was given after the last meal. This protocol ensured that participants arrived at the laboratory with little or no “on-board” or active bolus insulin based on the pharmacokinetics of their rapid acting insulin analog.<sup>10</sup> Basal insulin was kept to the usual rate until the exercise start time.

### Fitness assessment (visit 1)

During the initial visit, anthropometric measurements (height, body mass, and body fat percentage) were completed. Participants were screened for any cardiovascular complications using the Physical Activity Readiness Questionnaire for Everyone (PAR-Q+).<sup>11</sup> VO<sub>2</sub>max and peak heart rate (HR) were measured using an incremental-to-maximum effort treadmill protocol. Participants also completed a supramaximal workload with increasing incline to confirm the attainment of VO<sub>2</sub>max following a 2-min break.<sup>12</sup> After the exercise, an enhanced Enlite™ sensor with iPro2 continuous glucose monitor (CGM) (retrospective, non real-time analysis) was placed on the abdomen using an Enlite Serter according to the manufacturer's instructions (Medtronic MiniMed®, Northridge, CA). Participants wore the CGM for one week and were instructed to use the glucose meter provided (Contour® Next Link, Ascensia Diabetes Care, ON, Canada) for self-monitoring of [BG] (SMBG) throughout the study. Following an initial calibration 1-h after sensor insertion, participants were advised to calibrate four times daily with no more than 12-h in between each calibration. The timing of the CGM placement was at least 24 h before exercise visits 2 and 3. If visit 3 was scheduled more than one week after the VO<sub>2</sub>max test, a new CGM was inserted at least 24 h before the exercise visit.

### Exercise sessions (visits 2 and 3)

Participants completed either 40-min of CON or CIRC in a randomized and counterbalanced design, with each visit separated by at least two days. Figure 1 represents a timeline and study design for both CON and CIRC visits. The CON visit consisted of treadmill walking/light jogging at 40%–50% of the participant's predetermined VO<sub>2</sub>max, while the CIRC visit included treadmill walking (4 min); marching on the spot with dumbbells (45 s); squats with front sweep (60 s); four jumping jacks; quadruped (30 s); two jumping jacks; four push-ups; prone forearm planks (20 s); marching on the spot with dumbbells (30 s); weighted ball lifts (60 s); four push-ups; prone forearm plank (20 s), and cycling at a moderate workload (4 min). This CIRC was performed three times (~13 min each time), lasting a total of 40 min (any time lost or gained by



**FIG. 1.** Timeline for CON and CIRC exercise sessions. Both of the exercise sessions were conducted at either 1100 or 1600 h depending on participant availability (this was consistent for each individual). Basal insulin was suspended at the onset of both CON and CIRC exercise conditions and resumed to the normal rate immediately postexercise ( $n=12$ ). \*Arrival to laboratory.

the participant doing the CIRC was made up for by varying the duration of cycling at the end of each CIRC.

For both CON and CIRC, basal insulin delivery was stopped at the onset of both exercise modalities (using the “suspend insulin” feature) and resumed to the usual rate immediately postexercise, as is the customary approach by many patients who exercise regularly. Capillary [BG] and lactate measurements were determined approximately every 10-min throughout exercise using a handheld glucose meter (Contour<sup>®</sup> Next Link; Ascensia Diabetes Care) and lactate analyzer (Scout+; EKF Diagnostics, Cardiff, UK), respectively. Participants were told their measured [BG] value 10-min before the onset of exercise in both CON and CIRC visits and then they were blinded to their measured glucose meter values until 20 min into recovery. Participants were asked to estimate their [BG] concentration at each measured glucose time point (i.e., every 10-min). The discrepancy between estimated and measured [BG] concentrations was assessed according to Clarke Error Grid analyses<sup>13</sup> (using measured and perceived BG levels) and a modified Bland Altman plot<sup>14</sup> ( $[\text{measured BG} - \text{estimated BG}]/\text{measured BG}$ ). If a participant developed hypoglycemia (whole BG of  $<3.9$  mmol/L), they were instructed to stop exercising (if it was during exercise) and 16 g of oral dextrose (Dex4<sup>®</sup>; AMG, QC, Canada) was provided.

### Statistics

The [BG] measurements between CON and CIRC, as measured by the handheld glucose meter, were compared using two-way (time by trial) repeated measures analysis of variance. Bonferroni post hoc tests were used if significant interactions were found and statistical significance was set at  $P < 0.05$ , unless otherwise indicated. Participant anthropometric and descriptive characteristics were reported using mean and standard deviation. Two-way paired  $t$ -tests were used to compare energy expenditure (in kilocalories or kcal) and percent of  $\text{VO}_2\text{max}$  during CON and CIRC. A linear regression was used to compare the measured BG concentrations with perceived [BG] concentrations during CON and CIRC. The percent of time spent in different BG ranges (i.e., hypoglycemia, euglycemia, and hyperglycemia) 12-h after CON and CIRC, as measured by CGM, were compared using the Mann–Whitney test for nonparametric statistics. For this analysis, euglycemia was defined by the iPro2 CGM as

a BG concentration of 3.9–10.0 mmol/L, hypoglycemia as  $<3.9$  mmol/L, and hyperglycemia as  $>10.0$  mmol/L. All statistical analyses were conducted using STATISTICA 7.0 (StatSoft) and GraphPad Prism software (Version 7.0). Fingertstick capillary BG was measured with the glucose meter and used as a reference to evaluate the accuracy of the Enlite/iPro2 CGM. The mean absolute relative difference (MARD) was calculated as the absolute relative difference between the glucose meter value and sensor value over the glucose meter value multiplied by 100. Two-way paired  $t$ -tests were used to compare the absolute relative difference between CON and CIRC conditions pre-, during, and postexercise.

### Results

Anthropometric measurements of all participants (six men and six women) are shown in Table 1. Most participants were young adults (mean age  $32 \pm 11$  years [mean  $\pm$  SD]), lean (body fat  $21.8\% \pm 9.4\%$ ), and in excellent metabolic control ( $\text{HbA}_{1c}$   $7.0\% \pm 0.9\%$ ). Disease duration ranged from 2 to 43 years and total daily insulin dose averaged  $39 \pm 14$  U in the group. Participants were using Medtronic<sup>®</sup> ( $n=6$ ), Animas<sup>®</sup> ( $n=4$ ), or OmniPod<sup>®</sup> ( $n=2$ ) insulin pumps.

Both BG ( $7.5 \pm 2.6$  to  $9.9 \pm 4.4$  mmol/L) and lactate levels ( $1.0 \pm 0.3$  to  $13.2 \pm 4.2$  mmol/L) increased from pre to post  $\text{VO}_2\text{max}$  ( $P < 0.05$  for both). Figure 2 shows the change in BG from pre-exercise ( $-10$  min) to recovery ( $+30$  min) during both CON and CIRC visits. During the CIRC visit, pre-exercise BG was  $8.2 \pm 0.4$  mmol/L (mean  $\pm$  SD), dropping to  $6.8 \pm 0.6$  mmol/L by the end of the activity. During CON, the pre-exercise BG was  $9.5 \pm 0.7$  mmol/L, dropping to  $5.7 \pm 0.4$  mmol/L by the end of exercise. The drop during CON was greater than the drop during CIRC in 10 of the 12 participants (83%) and for the group as a whole ( $P < 0.05$ ). Figure 3 represents the mean energy expenditure (in kcal) during CON and CIRC visits (panel a) and the percent of  $\text{VO}_2\text{max}$  during CON and CIRC (panel b). On average, participants worked at a higher percent of their  $\text{VO}_2\text{max}$  during CIRC compared to CON ( $P=0.03$ ) and tended to expend greater energy during CIRC than in CON ( $P=0.07$ ). Figure 4 shows the lactate concentrations before, during, and immediately after exercise in both visits. Lactate concentrations were significantly higher during CIRC compared to CON ( $P=0.001$  at  $t=20$  and  $t=40$ , respectively).

TABLE 1. INDIVIDUAL ANTHROPOMETRIC AND CLINICAL CHARACTERISTICS

Subject ID	Age (years)	Gender (M/F)	Height (cm)	Body mass (kg)	Diabetes duration (years)	TDD (units)	Basal insulin (%)	Body fat (%)	VO <sub>2</sub> max (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )	HR peak (bpm)	HbA <sub>1c</sub> (%)
1	35	M	174	80.5	12	50	37	22.0	49.9	203	7.9
2	34	F	182	78.0	31	46	57	27.9	37.9	195	7.7
3	27	F	167	70.0	19	35	49	29.4	41.6	199	7.1
4	49	M	184	75.1	35	24	71	16.6	47.7	188	7.4
5	19	M	177	72.7	5	50	35	11.3	65.0	201	6.8
6	44	M	173	72.8	41	23	38	8.3	59.8	175	5.5
7	26	F	170	75.6	9	47	49	34.6	35.6	189	8.0
8	19	M	187	74.6	7	48	42	9.8	74.5	200	6.9
9	24	M	183	78.0	14	65	55	14.5	56.7	208	8.2
10	53	F	156	56.6	3	23	42	30.8	42.7	160	5.9
11	24	F	170	75.1	2	29	37	31.3	40.5	184	6.2
12	31	F	165	65.3	3	25	46	25.6	39.7	174	6.1
Mean ± SD	32 ± 11	M=6 F=6	174.9 ± 9.1	72.9 ± 6.5	16 ± 13	39 ± 14	47 ± 11	21.8 ± 9.4	50.1 ± 13.7	191 ± 14	7.0 ± 0.9

HR, heart rate; TDD, total daily insulin dose; VO<sub>2</sub>max, maximal aerobic capacity.

Figure 5 demonstrates the accuracy of perceived to measured BG concentrations via Clarke Error Grids (a) and Bland–Altman plots (b) for the two exercise sessions. Table 2 represents BG estimations separated by zones A–E of the Clarke Error Grids during CON and CIRC. These zones depict the likelihood of inappropriate treatment based on the perceived versus measured BG values.<sup>13</sup> Based on regression analyses and our assessment using Clarke Error Grid analyses, participants were able to more accurately estimate their BG throughout CON ( $r=0.83$ ) compared to CIRC ( $r=0.33$ ),

although both conditions showed reasonably “safe” BG estimations overall, with 97% of the values within zones A and B of the Clarke Error Grid (Figure 5). Figure 6 (panel a) represents the 12-h recovery CGM data following the CON and CIRC sessions ( $n=8$  only because of technical limitations in data capture from CGM) and (panel b) the percentage of time spent in each of the following zones: euglycemia (3.9–10.0 mmol/L); hypoglycemia (<3.9 mmol/L); and hyperglycemia (>10.0 mmol/L). Compared to CIRC, CON elicited greater BG variability and led to a higher percentage of

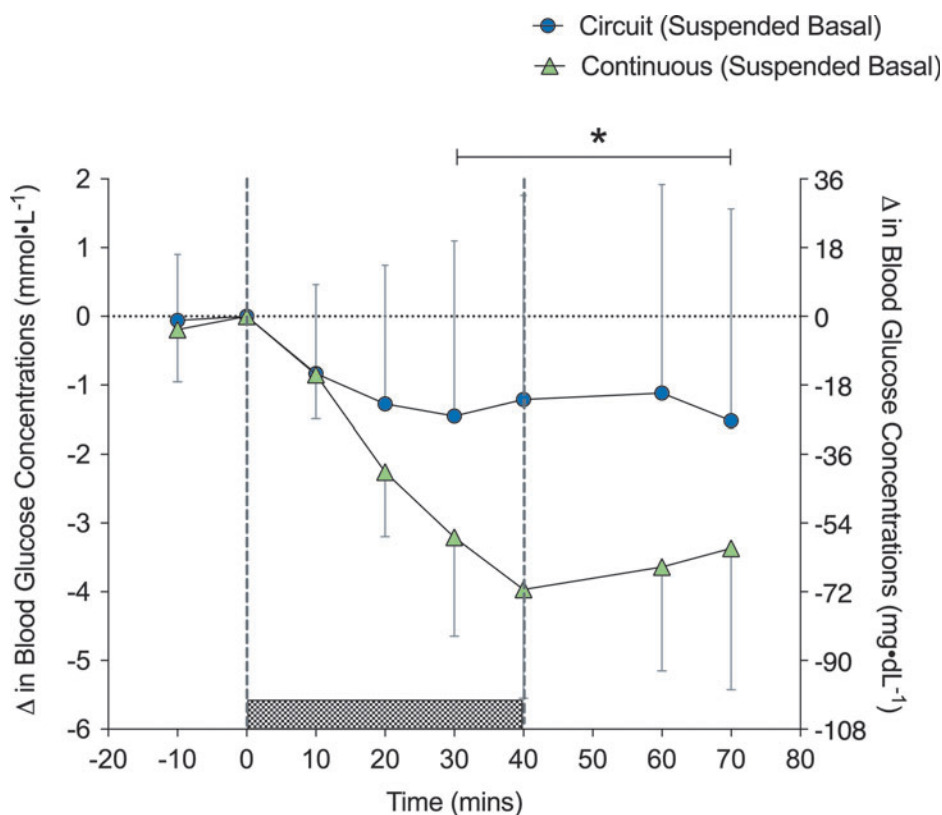
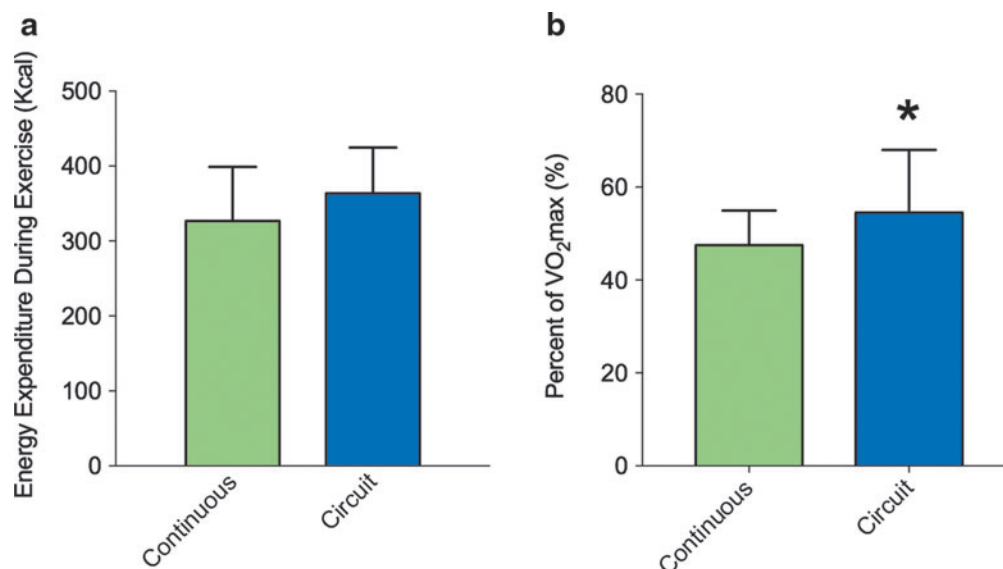


FIG. 2. Relative (delta) change in BG with CIRC exercise (circle) and CON exercise (triangle) pre-, during, and postexercise ( $n=12$ ). Hashed box represents the exercise session (40-min). Data are expressed relative to the BG levels at the onset of exercise (time=0). Data are expressed as mean ± SD; \*  $P < 0.05$ .



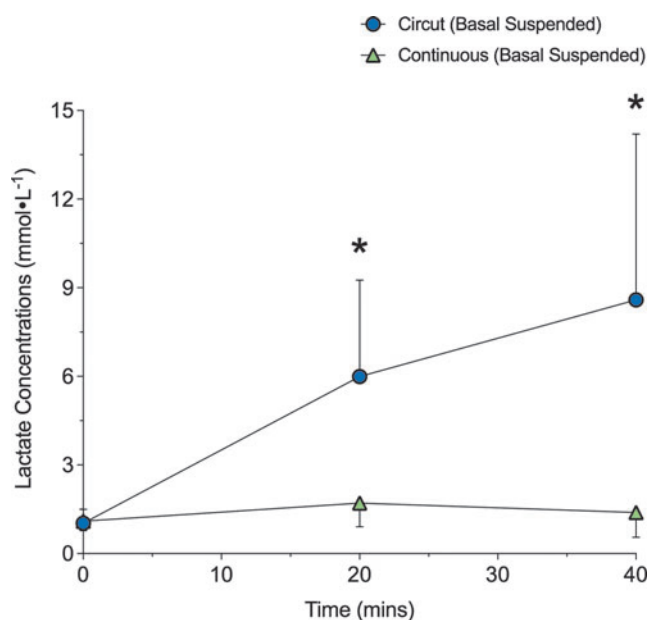
**FIG. 3.** (a) Energy expenditure in kilocalories (kcal) during CIRC and CON exercise sessions and (b) the percent of VO<sub>2</sub>max during CON and CIRC exercise ( $n=12$ ). Data represent mean  $\pm$  SD; \* $P<0.05$ .

time spent in hypoglycemia postexercise (3% vs. 10% of the time in hypoglycemia, respectively).

Table 3 shows the CGM sensor performance data during the CON and CIRC trials. Sensor performance was good overall, with MARD values all below 15% pre-, during, and postexercise in both trials. However, during the exercise period itself, the MARD was significantly lower during CIRC versus CON ( $P=0.03$ ).

## Discussion

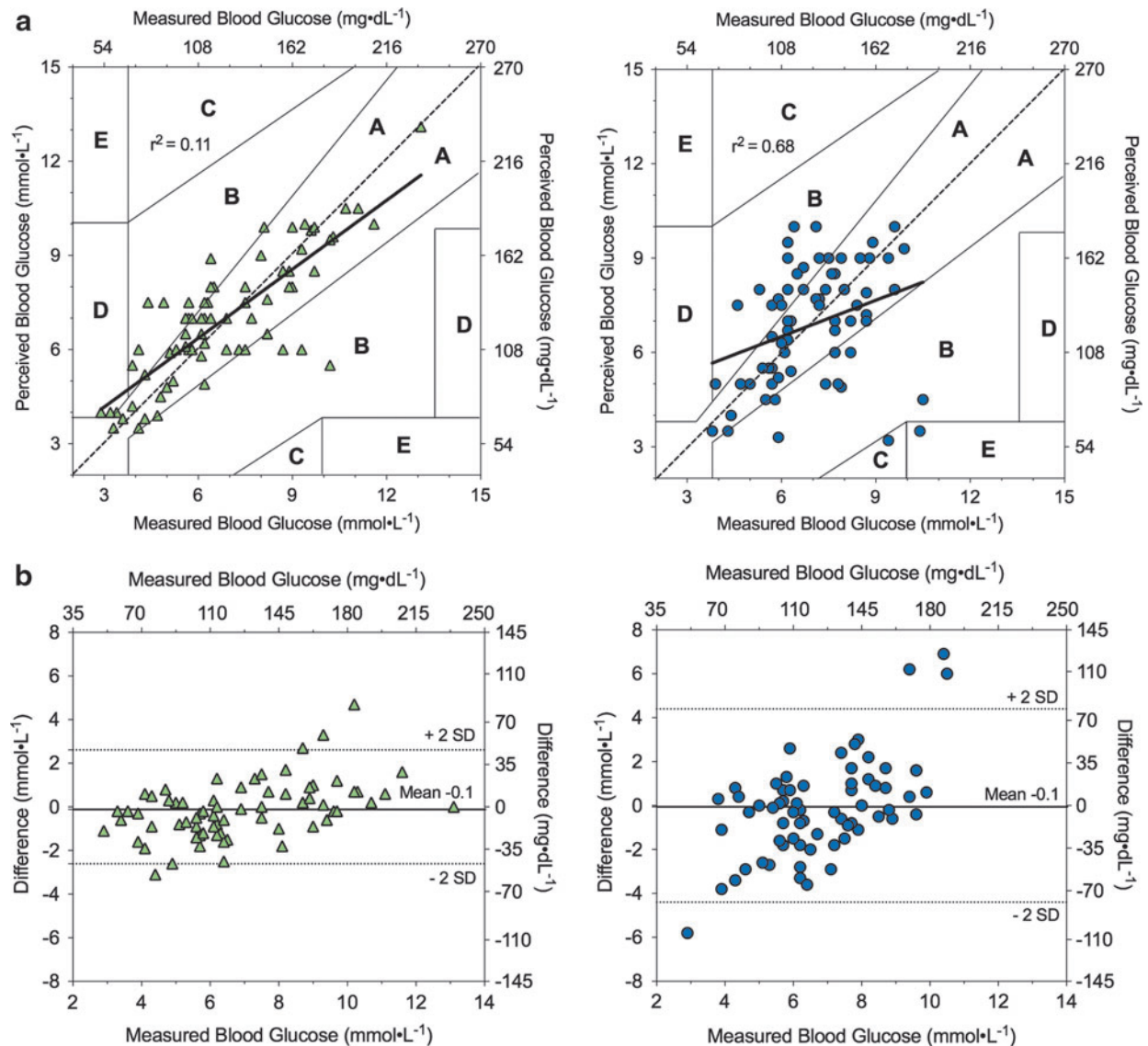
It is recommended that basal insulin reductions be performed 30–90 min before exercise to allow for circulating



**FIG. 4.** Lactate concentrations (mmol/L) at the start ( $t=0$ ), middle ( $t=20$  min), and end ( $t=40$  min) of exercise during both CIRC and CON conditions ( $n=11$ ). Data represent mean  $\pm$  SD; \* $P<0.05$ .

insulin levels to drop by the onset of exercise.<sup>1,15,16</sup> However, in reality, many individuals with T1D suspend basal insulin at the start of exercise with varying degrees of success for hypoglycemia prevention.<sup>17</sup> This study demonstrates that with basal insulin suspension at the onset of exercise, the mean drop in BG is greater during CON versus CIRC ( $P=0.001$ ), as seen in Figure 2. Similarly, Moser et al.<sup>18</sup> found that the drop in BG levels with intermittent high-intensity exercise (IHE) was less than with CON in MDI patients. Interestingly in our study, the energy expenditure (measured in kcal) during exercise was similar between conditions ( $P=0.09$ ); however, the intensity of exercise, as measured by the percent of VO<sub>2</sub>max was slightly, but significantly greater in CIRC versus CON ( $P=0.03$ , Figure 3). These findings suggest that basal insulin suspension at the onset of exercise is more protective against the drop in glycemia for mixed activities when compared to activities that are primarily aerobic in nature. These findings also reveal that CON is likely a more challenging form of exercise for the development of automated insulin delivery system that rely on single hormone therapy and technologies that trigger changes in an algorithm at the time of exercise start (like HR or accelerometry).<sup>19</sup>

We first performed a pilot study, in a subset of participants ( $n=3$ ), to determine whether CON could be performed safely without any changes to the usual basal rate. All participants developed moderate hypoglycemia within 30 min of starting CON. Thus, for safety and ethical reasons, this arm of the intervention was eliminated. The failure to have data collected with pump on for both CON and CIRC conditions limits our capacity to clearly demonstrate that pump off reduces the risk of hypoglycemia compared to pump on. However, with this study design, it was still possible for us to determine whether participants respond differently to CON versus CIRC with basal insulin suspension. Another limitation in our study is that we did not include plasma free insulin measurements and this information would have provided insight regarding the impact of basal insulin suspension at the start of two different forms of exercise. A number of groups have recently demonstrated that exercise increases circulating free insulin



**FIG. 5.** (a) Clarke Error Grids comparing measured BG concentrations with perceived [BG] concentrations during CIRC exercise (circles) and CON exercise (triangles). The BG values are separated into zones A–E that represent the clinical implications of estimation errors. (b) Bland–Altman plots comparing the difference between measured and perceived BG values within two standard deviations. A BG measurement was taken 10-min before the onset of exercise and participants used this value as a reference during exercise. In general, participants could accurately estimate their BG levels during exercise, particularly during CON exercise. During CON exercise, the best-fit y-intercept was  $1.97 \pm 0.44$  mmol/L and CIRC exercise y-intercept was  $4.20 \pm 0.95$  mmol/L ( $P < 0.05$ ).

concentrations in patients on CSII when basal insulin rates are kept constant,<sup>20</sup> lowered,<sup>9</sup> or suspended altogether<sup>21</sup> before exercise start. It is likely that increases in adipose tissue blood flow with exercise<sup>22</sup> may be facilitating tissue depot uptake of insulin, which may contribute to an increased risk for exercise-associated hypoglycemia. The greater drop in glycemia during CON versus CIRC is likely related to higher levels of counterregulatory hormones released and/or greater lactate production during CIRC.<sup>23</sup>

Al Khalifah et al.<sup>24</sup> showed that individuals with a good level of aerobic fitness (based on the norms for age and sex) are more susceptible to hypoglycemia during exercise, possibly due to their better insulin sensitivity and their higher work capacity. In our study, we terminated exercise

on three occasions because of documented hypoglycemia (twice during CON; once during CIRC). However, one participant had a  $\text{VO}_2\text{max}$  of  $59.8 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$  and the other  $39.7 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ , so fitness level likely did not explain the incidence of hypoglycemia in our study.

Due to the increased risk for exercise-associated dysglycemia, the usual clinical recommendation is to increase the frequency of BG monitoring before, during, and following PA participation.<sup>25,26</sup> However, it can be difficult, or undesirable at times, to perform SMBG during exercise, especially in competition where the activity must be stopped to “test.” In fact, in activities such as swimming, cycling, and skydiving, it becomes incredibly challenging, and in some cases impossible, to test BG levels frequently while exercising.

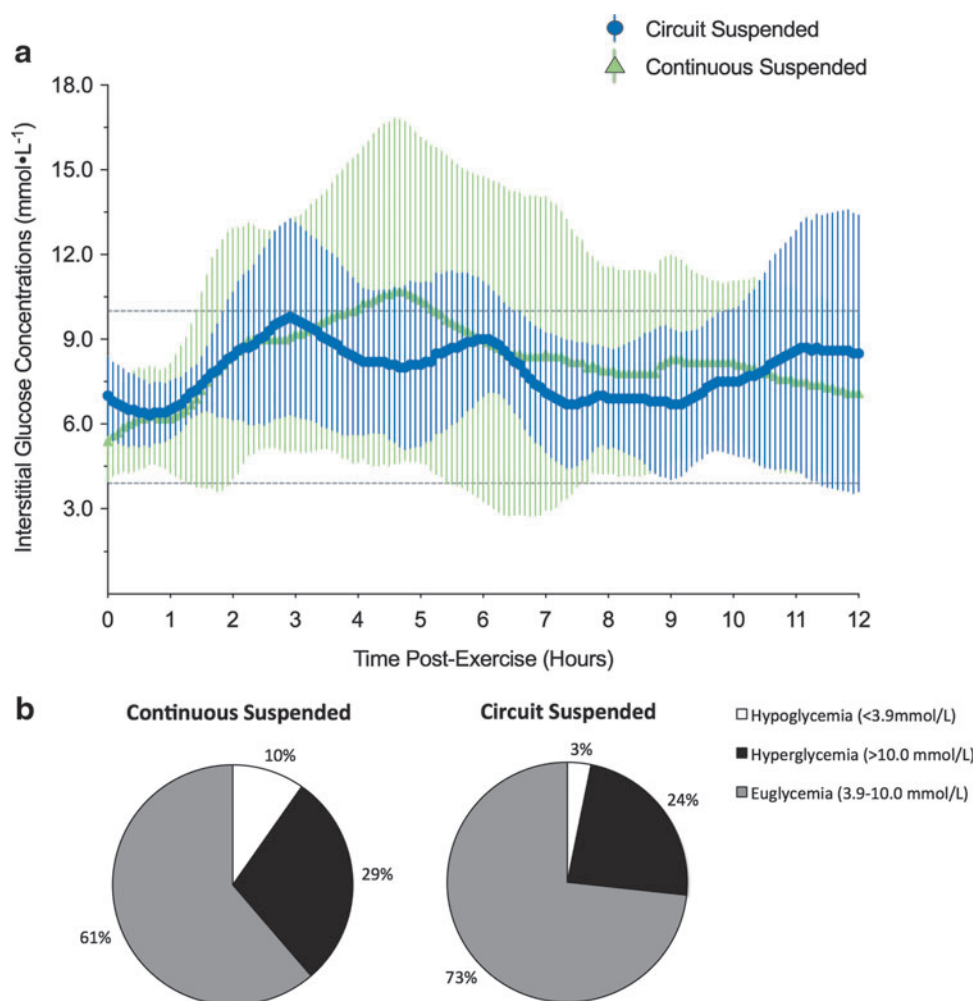
TABLE 2. CLARKE ERROR GRID ANALYSES

Zones	Continuous (CON) exercise	Circuit-based (CIRC) exercise
A	50/70 (71%)	44/70 (63%)
B	18/70 (26%)	24/70 (34%)
C	0/70 (0%)	1/70 (1%)
D	2/70 (3%)	0/70 (0%)
E	0/70 (0%)	1/70 (1%)

Clarke Error Grid zones A–E during CON versus CIRC exercise. Zone A, values within 20% of the measured BG (CON 71%, CIRC 63%); Zone B, points are outside of 20%, but would not lead to inappropriate treatment (CON 26%, CIRC 34%); Zone C, points leading to unnecessary treatment (CON 0%, CIRC 1%); Zone D, points indicate potentially dangerous failure to detect hypo- or hyperglycemia (CON 3%, CIRC 0%); Zone E, points that would confuse treatment of hypo- for hyperglycemia and vice versa (CON 0%, CIRC 1%).

Previous studies have assessed the accuracy of perceiving BG levels in individuals with T1D<sup>27,28</sup> but few have focused on exercise per se. Cox et al.<sup>27</sup> found that although BG estimations were highly variable across participants, very few dangerous errors were made in estimating BG levels. In

another study that assessed the BG estimation accuracy in adolescents, a poor correlation ( $r=0.35$ ) was found between measured and perceived BG during 60-min of CON steady-state cycling exercise.<sup>29</sup> In general, adolescents tended to underestimate their own BG when they were hyperglycemic and overestimate their own BG when they were hypoglycemic during exercise. This phenomenon was also more apparent with CIRC in this study (Figure 5). In the conditions of which our study was designed, the majority of participants were found to accurately estimate their own BG during both forms of exercise when they were provided with a reference BG value 10-min before exercise. We also found that the accuracy of the BG estimations was better during CON ( $r=0.83$ ) compared to CIRC ( $r=0.33$ ) (Figure 5). The reason for this difference is unclear, but may be attributed to the frequent variation in exercise intensities throughout the 40-min CIRC session, which may mask the capacity to estimate BG. Another limitation is that it is unclear how critical a reference value is for improving an individual's estimations of BG concentrations during exercise. Future studies should include a subset of participants that are not provided with a reference BG value before exercise as a comparison, or perhaps a visit in which participants are blinded to their own pre-exercise BG.



**FIG. 6.** (a) Twelve-hour recovery CGM glycemia following CON (light shade) and CIRC exercise (dark shade). Data represent mean  $\pm$  SD of 12-h postexercise from 1200–0000 or 1800–0600 h. (b) Time spent (%) in hypoglycemia, euglycemia, and hyperglycemia following CON versus CIRC exercise sessions ( $n=8$ ). CGM, continuous glucose monitor.

TABLE 3. SENSOR PERFORMANCE DATA PRE-, DURING, AND POSTEXERCISE

	<i>Continuous (CON) exercise</i>	<i>Circuit-based (CIRC) exercise</i>	P
Pre-exercise MARD (%)	9.86 ± 0.08	8.15 ± 0.07	0.37
During exercise MARD (%)	12.00 ± 0.12	6.96 ± 0.06	0.03
Postexercise MARD (%)	10.44 ± 0.10	10.02 ± 0.14	0.89

MARD, mean absolute relative difference expressed as a percentage (%) ± SD.

Previous studies have investigated the accuracy of various CGM systems during IHE versus CON, although findings remain inconclusive.<sup>30–32</sup> Bally et al.<sup>31</sup> found comparable CGM accuracy during IHE and CON whereas Moser et al.<sup>30</sup> revealed CGM overestimation during IHE. More recently, Taleb et al.<sup>32</sup> compared the performance of two current and widely used CGM systems (Dexcom G4<sup>®</sup> Platinum, Medtronic Enlite with MiniLink<sup>®</sup> transmitter) at rest and during exercise; finding that both products had lower performance during exercise compared to rest. Similarly in this study, CON revealed lower performance in comparison to rest and recovery periods. The higher MARD during CON may be attributed to the more rapid drop in glycemia compared to CIRC (Table 3). However, based on the overall MARD values in our study, the enhanced Enlite/iPro2 CGM performance appears more accurate than the real-time CGM systems used in the previous study.<sup>32</sup> The limitation with iPro2 CGM, however, is that glucose values are not reported in real-time and as such can only be used for retrospective analysis.

Numerous studies have demonstrated delayed hypoglycemia postexercise, typically occurring from 8 to 12 h in recovery from prolonged activity.<sup>33–36</sup> Similarly in our study, 12-h postexercise, the percent of time spent hypoglycemic (defined as a sensor glucose <3.9 mmol/L) tended to be higher following CON (10%) versus CIRC (3%) (Figure 6b). Some common suggestions to help reduce nocturnal hypoglycemia include reducing basal insulin rates overnight, reducing fast-acting insulin with the evening meal, and/or consuming low glycemic index food at bedtime, although further research in this area is required.<sup>33</sup>

In conclusion, basal insulin suspension at the onset of exercise leads to a greater drop in glycemia during CON versus CIRC. CON also tends to increase the percent of time spent in hypoglycemia 12-h following exercise. More effective strategies are needed to reduce the barriers associated with exercise such as the fear of hypoglycemia.<sup>37</sup> In addition, the type of exercise performed may also impact an individual's estimations of their BG levels. Following a baseline glucose meter reading, estimating BG levels during exercise should be done with caution, particularly in those individuals with hypoglycemia unawareness. Both frequent SMBG and CGM use for exercise are highly recommended for active individuals with T1D to increase safety and to help with decision support from healthcare providers.<sup>1</sup> Based on our findings that circuit-based exercise deteriorates BG estimations com-

pared to continuous moderate-intensity aerobic exercise, this study supports the need for increased vigilance around monitoring BG levels during activities that are interspersed with frequent variation in exercise intensities.

### Acknowledgments

This work was supported by the National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Grant No.: 1DP3 DK101075.

### Author Disclosure Statement

M.C.R. has received speaker's fees/honoraria from Medtronic Diabetes, Lilly, Ascensia Diabetes Care, and Insulet Corporation. D.Z. has received speaker's fees/honoraria from Medtronic Diabetes and Ascensia Diabetes Care.

### References

- Riddell MC, Gallen IW, Smart CE, et al.: Exercise management in type 1 diabetes: a consensus statement. *Lancet Diabetes Endocrinol* 2017. Jan 24. pii: S2213-8587(17)30014-1. doi: 10.1016/S2213-8587(17)30014-1.
- Guelfi KJ, Ratnam N, Smythe GA, et al.: Effect of intermittent high-intensity compared with continuous moderate exercise on glucose production and utilization in individuals with type 1 diabetes. *Am J Physiol Endocrinol Metab* 2007;292:E865–E870.
- Tansey MJ, Tsalikian E, Beck RW, et al.: The effects of aerobic exercise on glucose and counterregulatory hormone concentrations in children with type 1 diabetes. *Diabetes Care* 2006;29:20–25.
- Guelfi KJ, Jones TW, Fournier PA: The decline in blood glucose levels is less with intermittent high-intensity compared with moderate exercise in individuals with type 1 diabetes. *Diabetes Care* 2005;28:1289–1294.
- Harmer AR, Chisholm DJ, McKenna MJ, et al.: Sprint training increases muscle oxidative metabolism during high-intensity exercise in patients with type 1 diabetes. *Diabetes Care* 2008;31:2097–2102.
- Cassidy S, Thoma C, Houghton D, et al.: High-intensity interval training: a review of its impact on glucose control and cardiometabolic health. *Diabetologia* 2016;60:7–23.
- Tsalikian E, Kollman C, Tamborlane WB, et al.: Prevention of hypoglycemia during exercise in children with type 1 diabetes by suspending basal insulin. *Diabetes Care* 2006; 29:2200–2204.
- Admon G, Weinstein Y, Falk B, et al.: Exercise with and without an insulin pump among children and adolescents with type 1 diabetes mellitus. *Pediatrics* 2005;116:E348–E355.
- McAuley SA, Horsburgh JC, Ward GM, et al.: Insulin pump basal adjustment for exercise in type 1 diabetes: a randomised crossover study. *Diabetologia* 2016;59:1636–1644.
- Heinemann L, Nosek L, Kapitza C, et al.: Changes in basal insulin infusion rates with subcutaneous insulin infusion: time until a change in metabolic effect is induced in patients with type 1 diabetes. *Diabetes Care* 2009;32:1437–1439.
- Jamnik VK, Warburton DE, Makarski J, et al.: Enhancing the effectiveness of clearance for physical activity participation: background and overall process. *Appl Physiol Nutr Metab* 2011;36:S3–S13.



12. Howley ET, Bassett DR, Welch HG: Criteria for maximal oxygen uptake: review and commentary. *Med Sci Sports Exerc* 1995;27:1292–1292.
13. Clarke WL, Cox D, Gonder-Frederick LA, et al.: Evaluating clinical accuracy of systems for self-monitoring of blood glucose. *Diabetes Care* 1987;10:622–628.
14. Bland JM, Altman DG: Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–310.
15. Colberg SR, Sigal RJ, Yardley JE, et al.: Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. *Diabetes Care* 2016;39:2065–2079.
16. Robertson K, Riddell MC, Guinhouya BC, et al.: ISPAD Clinical Practice Consensus Guidelines 2014. Exercise in children and adolescents with diabetes. *Pediatr Diabetes* 2014;15 Suppl 20:203–223.
17. Pinsker JE, Kraus A, Gianferante D, et al.: Techniques for exercise preparation and management in adults with type 1 diabetes. *Can J Diabetes* 2016;40:503–508.
18. Moser O, Tschakert G, Mueller A, et al.: Effects of high-intensity interval exercise versus moderate continuous exercise on glucose homeostasis and hormone response in patients with type 1 diabetes mellitus using novel ultra-long-acting insulin. *PLoS One* 2015;10:E0136489.
19. Turksoy K, Paulino TML, Zaharieva DP, et al.: Classification of physical activity: information to artificial pancreas control systems in real time. *J Diabetes Sci Technol* 2015;9:1200–1207.
20. Mallad A, Hinshaw L, Schiavon M, et al.: Exercise effects on postprandial glucose metabolism in type 1 diabetes: a triple-tracer approach. *Am J Physiol Endocrinol Metab* 2015;308:E1106–E1115.
21. Franc S, Daoudi A, Pochat A, et al.: Insulin-based strategies to prevent hypoglycaemia during and after exercise in adult patients with type 1 diabetes on pump therapy: The DIA-BRASPORT randomized study. *Diabetes Obes Metab* 2015;17:1150–1157.
22. Frayn KN, Karpe F: Regulation of human subcutaneous adipose tissue blood flow. *Int J Obes (Lond)* 2014;38:1019–1026.
23. Harmer AR, Chisholm DJ, McKenna MJ, et al.: High-intensity training improves plasma glucose and acid-base regulation during intermittent maximal exercise in type 1 diabetes. *Diabetes Care* 2007;30:1269–1271.
24. Al Khalifah RA, Suppère C, Haidar A, et al.: Association of aerobic fitness level with exercise-induced hypoglycaemia in type 1 diabetes. *Diabet Med* 2016;33:1686–1690.
25. American Diabetes Association: Physical activity/exercise and diabetes. *Diabetes Care* 2004;27 Suppl 1:S58–S62.
26. Goldstein DE, Little RR, Lorenz RA, et al.: Tests of glycemia in diabetes. *Diabetes Care* 2004;27:1761–1773.
27. Cox DJ, Clarke WL, Gonder-Frederick L, et al.: Accuracy of perceiving blood glucose in IDDM. *Diabetes Care* 1985;8:529–536.
28. Freund A, Johnson SB, Rosenbloom A, et al.: Subjective symptoms, blood glucose estimation, and blood glucose concentrations in adolescents with diabetes. *Diabetes Care* 1986;9:236–243.
29. Riddell MC, Bar-Or O: Children and adolescents. In: Ruderaman N, Devlin JT, Schneider SH, eds. *Handbook of Exercise and Diabetes*. Alexandria, VA: American Diabetes Association, 2002, pp. 547–566.
30. Moser O, Mader JK, Tschakert G, et al.: Accuracy of continuous glucose monitoring (CGM) during continuous and high-intensity interval exercise in patients with type 1 diabetes mellitus. *Nutrients* 2016;8:E489.
31. Bally L, Zueger T, Pasi N, et al.: Accuracy of continuous glucose monitoring during differing exercise conditions. *Diabetes Res Clin Pract* 2016;112:1–5.
32. Taleb N, Emami A, Suppère C, et al.: Comparison of two continuous glucose monitoring systems, Dexcom G4 Platinum and Medtronic Paradigm Veo Enlite system, at rest and during exercise. *Diabetes Technol Ther* 2016;18:561–567.
33. Charlton J, Kilbride L, MacLean R, et al.: Delayed hypoglycaemia in people with type 1 diabetes after performing moderate intensity exercise before the evening meal. *Pract Diab* 2015;32:99–102.
34. Taplin CE, Cobry E, Messer L, et al.: Preventing post-exercise nocturnal hypoglycemia in children with type 1 diabetes. *J Pediatr* 2010;157:784–788.
35. Yardley JE, Kenny GP, Perkins BA, et al.: Resistance versus aerobic exercise: acute effects on glycemia in type 1 diabetes. *Diabetes Care* 2013;36:537–542.
36. Campbell MD, Walker M, Trenell MI, et al.: Large pre- and postexercise rapid-acting insulin reductions preserve glycemia and prevent early- but not late-onset hypoglycemia in patients with type 1 diabetes. *Diabetes Care* 2013;36:2217–2224.
37. Brazeau AS, Mircescu H, Desjardins K, et al.: The Barriers to Physical Activity in Type 1 Diabetes (BAPAD-1) scale: predictive validity and reliability. *Diabetes Metab* 2012;38:164–170.

Address correspondence to:

Michael C. Riddell, PhD  
School of Kinesiology and Health Science  
Faculty of Health  
Muscle Health Research Centre  
Physical Activity and Chronic Disease Unit  
York University  
4700 Keele Street  
Toronto, ON M3J 1P3

E-mail: [mriddell@yorku.ca](mailto:mriddell@yorku.ca)