Blood Glucose Alterations and Continuous Glucose Monitoring in Centrifuge-Simulated Spaceflight

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INTRODUCTION: Sympathetic stimulation is known to be associated with transient alterations of blood glucose (BG) concentration; spaceflight acceleration may be similarly associated with alterations of BG, potentially posing a risk to diabetic individuals engaging in future spaceflight activities. Despite prior studies demonstrating diabetic subjects' tolerance to centrifuge-simulated spaceflight, data are lacking regarding blood glucose response to hypergravity. It remains unclear whether hypergravity or associated physiological response may pose a risk to diabetics. Continuous glucose monitors (CGM) offer a means of noninvasive glucose monitoring and may be useful in spaceflight and analog environments. Here, we describe the results of continuous glucose monitoring during centrifuge-simulated spaceflight.

METHODS: Subjects participated in 1–5 centrifuge-simulated spaceflight profiles (maximum +4.0 G_z, +6.0 G_x, 6.1 G resultant). Data collection included heart rate, blood pressure, electrocardiogram, continuous glucose via CGM, intermittent fingerstick BG, and postrun questionnaires regarding symptoms related to hypergravity exposure.

RESULTS: CGM data were collected from 26 subjects, including 4 diabetics. While diabetic subjects had significantly higher BG compared to nondiabetics, this was not associated with any difference in symptoms or tolerance. Transient hypergravity-associated CGM glucose alterations did not affect tolerance of the centrifuge experience. CGM data were found to be reliable with occasional exceptions, including four instances of false critical low glucose alarms.

DISCUSSION: While further study is necessary to better characterize CGM fidelity during hypergravity and other spaceflight-related stressors, CGM may be a feasible option for spaceflight and analog settings. As in prior studies, individuals with well-controlled diabetes appear able to tolerate the accelerations anticipated for commercial spaceflight.

KEYWORDS: acceleration, G exposure, spaceflight participant, commercial spaceflight, diabetes mellitus, blood glucose, continuous glucose monitor, blood sugar.

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As the commercial spaceflight industry expands, broader and commercialized access to space will increasingly allow those with financial means to participate in sub-orbital and orbital flight, including those with medical conditions traditionally seen as contraindications to such activities. Understanding of the physiological response and tolerance to hypergravity in individuals with traditionally disqualifying conditions has been the subject of substantial interest and recent study, with previous investigation demonstrating that individuals with even extensive medical history are likely capable of tolerating the physiological stressors of spaceflight.[2–4] One medical condition of interest, traditionally disqualifying for spaceflight, is diabetes mellitus (DM).

While historically considered a contraindication to spaceflight, individuals with DM have successfully managed their medical condition in other austere environments or during extreme activities, including high-altitude trekking,[7] diving,[5,24] motorsports,[10] and commercial aviation piloting activities.[13,28] However, changes in diabetes management may be necessary during such experiences. For example, at high altitudes, blood glucose (BG) may vary compared to baseline at sea level and

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insulin dosage may require adjustment.[7] Simultaneously, insulin delivery systems may deliver larger doses due to altered calibration from ambient pressure changes.[17] Changes in the timing of diabetic medication administration may be necessary when traveling across time zones or similarly shifting waking hours or circadian rhythm.[22] Previous spaceflight analog studies have shown that individuals of a wide range of ages and health conditions, including type 1 and type 2 DM,[3,4,18] can safely tolerate centrifuge-simulated spaceflight. Subjects in these studies were able to maintain safe BG levels throughout hypergravity exposures, including simulated spaceflight launch and landing profiles. Further, subjects using exogenous insulin experienced no reported adverse effects, including no significant malfunctions in automated insulin delivery systems exposed to hypergravity.[18] Given the small sample size in these studies, more investigation is warranted regarding the monitoring and management of diabetes during simulated launch and landing. Prior studies lacked controlled monitoring of BG in diabetic or control subjects.

Traditionally, BG is monitored via glucometer, a small handheld device which uses fingerstick capillary blood sampling to determine glucose concentration.[20] While reliable and quick for routine DM management, glucometers are not ideal for extreme environments, including spaceflight, due to the need for patient action (fingerstick, glucometer deployment and use) and the availability of resources (lancets, testing strips, glucometers, biohazardous disposal). Further, glucometers provide BG only at a single time and, without significant time commitment and repeated measurements, glucometers do not provide easy monitoring of glucose concentration changes or trends related to activity, stressors, or medication use.

As an alternative to fingerstick BG, continuous glucose monitors (CGMs) were approved by the U.S. Food and Drug Administration in 1999 and were marketed for public use shortly thereafter, with the number of available devices and reliability increasing with time.[1,8,23] CGMs are adhered to the skin, with the deployment of a thin catheter into the subcutaneous tissue that allows for continuous sampling of interstitial fluid for glucose concentration. The CGM then transmits information to a separate receiver (typically smartphone or dedicated monitoring device) that collects and stores data. Once functional, some CGMs do not require calibration at all; others use fingerstick BG sampling at variable intervals.[1] Continuous glucose monitoring has been used to facilitate DM management, including during motorsports[10] and commercial aviation;[13,28] further, under recent Federal Aviation Administration guidance for Special Issuance of Medical Certification, diabetic pilots who can demonstrate disease stability and control for at least 6 mo, verified by CGM, can be approved for first-class medical certification.[9] A search of prior literature did not reveal any previous studies regarding the validity or utility of CGMs in the spaceflight environment or high-fidelity analogs, although glucose monitoring was reported to have occurred on a commercial spaceflight.[30] In a case report regarding use of CGM in motorsports, the subject notably endured transient hypergravity exposures of +2.5–4.5 G_z during banking turns;[10] however, literature documenting use of such devices under sustained acceleration exposures is lacking.

A variety of stressors can provoke alterations in BG, including physical activity and sympathetic stimulation.[12,16,27] Prior study has demonstrated significant elevation of heart rate (HR) and blood pressure during centrifuge-simulated spaceflight, indicative of sympathetic stimulation during such experiences.[2–4] Further, $+G_z$ exposure is often accompanied by the use of an anti-G straining maneuver (AGSM), with sustained isokinetic and anaerobic muscular activity that may further drive transient alterations to BG.[19,25] Existing literature has reported alterations of BG associated with motorsport racing and concurrent sympathetic stimulation as evidenced by increased urine catecholamines.[10,27] While motorsports are an imperfect analog to spaceflight or centrifuge, there are similarities, including excitement and adrenaline response, high acceleration, isokinetic muscular activity, and mental and physical stress. It is reasonable to suspect that layperson experience of centrifuge acceleration could similarly be associated with alterations of BG.

During a larger study that sought to characterize layperson responses to hypergravity exposure in centrifuge-simulated spaceflight, we sought to evaluate BG trends and the use of CGM for continuous glucose monitoring in sustained hypergravity environments. We monitored subjects using a U.S. Food and Drug Administration-approved CGM to evaluate CGM utility in glucose surveillance in subjects with and without diabetes during human centrifugation as an analog to spaceflight.

METHODS

Subjects

Subjects were a subset of individuals previously screened into a larger prospective study approved by the University of Texas Medical Branch Institutional Review Board. In the larger trial, adult subjects (age ≥ 18 yr) were identified for participation for a prospective study in physiological training at the National Aerospace Training and Research Center centrifuge (Southampton, PA). The general screening process was similar to that described in prior publications[18,21,29] and required a self-reported medical history questionnaire, a physical exam by a personal physician, a resting electrocardiogram, and documentation of effective control of pre-existing medical conditions, including diabetes. All medical documentation was reviewed and approved by an aerospace medicine specialist, with study volunteers either approved directly, excluded, or asked to provide additional documentation, including blood work, chest radiography, cardiac screening documentation, and other medical records or operative reports. Subjects were advised to take all home medications per their usual schedule throughout their participation in the study.

Subjects with a history of DM were included in a diabetic cohort based on a preexisting diagnosis of type 1 or type 2 diabetes controlled with diet, oral agents, insulin injections, or by

insulin pump. For study inclusion, diabetic volunteers were required to provide home preprandial fingerstick BG or CGM logs demonstrating current glucose trends, recent (≤ 6 mo) blood chemistry and metabolic panels, and a recent (≤ 6 mo) glycosylated hemoglobin (HbA1c) demonstrating reasonable control defined as HbA1c ≤ 8.0%. Volunteers diagnosed as "pre-diabetic," with HbA1c < 6.5% and no diet alterations or pharmaceutical control of BG were not considered diabetic for the purposes of this study.

A convenience sample of subjects who were included in the larger trial were further selected for CGM monitoring. All subjects provided informed consent before participating in the larger trial; additional informed consent was obtained before inclusion in the CGM cohort.

Equipment

A long-arm (7.6 m arm length) high-performance human centrifuge (National Aerospace Training and Research Center AFTS-400) was used for simulation of hypergravity. Commercial glucometers (Accu-chek®, Roche Diabetes Care Inc., Indianapolis, IN, USA; and Freestyle Lite®, Abbott Diabetes Care Inc., Alameda, CA, USA) were used to measure fingerstick BG. Continuous glucose monitoring was performed using the Dexcom G6© (Dexcom Inc, San Diego, CA, USA), with data synchronized to a corresponding application on subjects' personal smartphones and shared directly with study investigators. Smartphones were not carried into the centrifuge gondola; instead, devices were left in an observation area in direct line-of-site to the centrifuge to allow continuous wireless connection during spins. Diabetic subjects used their own medication and supplies for their normal management, which was not supervised by medical monitors, and later shared CGM, BG trends, and insulin dosing with study investigators. Apart from designated calibration times, CGM was not monitored in real time except in cases of critical low-glucose alarm events. Subjects were informed that data would not be used for medical advice or treatment guidance and diabetic subjects were instructed to manage their DM as they normally would for light-to-moderate exercise activities as recommended by their personal physician. In addition to planned glucometer testing times, a glucometer was made available to diabetic subjects for use if desired throughout the day.

Procedures

Resting HR, blood pressure, pulse oximetry, and fingerstick BG were measured upon arrival at the training facility. Prior to centrifuge runs, participants were taught AGSM, including sustained contraction of lower extremity skeletal muscles and the "hook" (L-1 closed glottis variant) respiratory maneuver. They were advised to strain only during $+G_z$ exposures in Runs 1 and 4; all participants were advised to use both the extremity muscular strain and the hook maneuver during their first $+G_z$ exposure (maximum +3.8 G_z), but were given the option to decrease their AGSM effort (for example, use of only muscle strain without hook) or eliminate AGSM altogether on subsequent $+G_z$ exposures based on whether they experienced $+G_z$-related symptoms (light-headedness, tunnel vision, greyout, etc.). Subjects were monitored at all times by a study medical monitor via continuous video and two-way voice communication as well as continuous 3-lead electrocardiogram, beat-to-beat HR, and respiratory rate telemetry.

Application of CGMs occurred either the night before participation or the morning of the centrifuge runs. CGMs were worn by subjects during the full study day as well as a minimum of one 24-h period after completion of their centrifuge runs. CGMs were placed on the abdomen lateral to the umbilicus at a site between the lateral border of the rectus abdominis and the midaxillary line. Care was taken when possible to minimize interaction between the CGM, clothing waistbands, and gondola harness positioning.

Subjects participated in up to five centrifuge profiles (referred to as Runs 1–5; **Table I**) in a single day. Profiles were designed to simulate suborbital spaceflight or orbital launch and landing sequences with corresponding hypergravity exposures similar to those that would be experienced in winged or capsule spacecraft. Acceleration onset rates for all profiles were ≤0.5 G/s in the $+G_z$ direction and ≤1.5 G/s in the $+G_x$ direction. Runs 1 and 4 simulate suborbital spaceflight in a winged vehicle and are identical to profiles previously described in prior studies.[2–4] These profiles were 5–7 min in duration, with peak G of +3.8 G_z and +6.0 G_x during Run 1 and a simultaneous exposure of +4.0 G_z and +4.5 G_x (resultant vector 6.1 G) during Run 4. Individuals identified during screening as higher risk due to pre-existing medical conditions could be spun at 50% intensity during Run 1 (peak +2.2 G_z and +3.0 G_x) based on medical monitor discretion.

Table I. Centrifuge Profile Overview.

	VEHICLE / PROFILE SIMULATED	AGSM	MAXIMUM ACCELERATION	TOTAL PROFILE TIME
Run 1	Winged, suborbital launch and landing	AGSM required for $+G_z$, including Hook	+3.8 G_z +6.0 G_x	7 min
Run 2	Capsule, launch	None	+3.2 G_x	3.5 min
Run 3	Capsule, reentry	None	+4.2 G_x	11 min
Run 4	Winged, suborbital launch and landing	AGSM as needed for $+G_z$, including Hook	+4.0 G_z +4.5 G_x (6.1 G resultant)	5 min
Run 5	Capsule, launch abort	None	+3.3 G_x	8 min

Subjects experienced up to five centrifuge profiles simulating winged and capsule vehicles, with variable $+G_z$ and $+G_x$ exposures. Total profile time and use of AGSM is provided; subjects were required to use AGSM during Run 1 but used their own discretion to determine whether it was necessary during the two $+G_z$ exposures of Run 4. AGSM: anti-G straining maneuver.

The remaining profiles were designed to simulate hypergravity exposures in a capsule-type spacecraft during launch, reentry, or launch abort events. Capsule profiles included only $+G_x$ exposure. Run 2 (3.5 min) simulated a capsule single-stage launch sequence with a slow build of hypergravity to a maximum of +3.2 G_x. Run 3 (11 min) simulated a capsule reentry, with a slow $+G_x$ acceleration/deceleration with sustained hypergravity duration of 4 min, 45 s and a maximum of +4.2 G_x. This period of sustained $+G_x$ was followed by intermittent transient $+G_x$ exposures simulating drogue parachute and main parachute deployments, and, finally, a transient $+G_x$ exposure followed by a sinusoidal $+G_x$ waveform simulating a landing impact on water and subsequent capsule water motion. Peak transient $+G_x$ exposure was +2.2 G_x. Run 5 (8 min) simulated a launch abort sequence that was initially identical to Run 2, but during the launch acceleration the subject experienced a transient acceleration peak of +3.3 G_x, simulating the initiation of a launch escape system. Following this acceleration peak, the subject experienced a prolonged idle period (1 min, 40 s) simulating capsule loft, followed by a brief sustained acceleration/deceleration (duration 50 s, maximum +1.9 G_x), simulating reentry. The sustained reentry acceleration was followed by transient $+G_x$ exposures simulating parachute deployment and water impact, then a sinusoidal $+G_x$ waveform simulating capsule water motion, similar to those experienced in Run 3.

Fingerstick BG was obtained before and after Run 2 and Run 4 for device calibration and validation of CGM data. The CGM device requires a 2-h acclimation period after insertion for resolution of insertion trauma prior to reliable readings. While the CGM does not require calibration to fingerstick BG for use, for the purposes of the study CGM was calibrated to fingerstick BG after the initial acclimation period and prior to Run 2. Additional fingerstick BG measurements were obtained in the case of a critically low (<55 mg · dL^{-1}) CGM glucose alarm and at the discretion of medical monitors, including in circumstances where medical monitors suspected inaccurate readings from the CGM. CGMs were occasionally recalibrated in circumstances including a low glucose alarm and observation that CGM differed ≥10 mg · dL^{-1} from fingerstick BG.

Data Processing and Statistical Analysis

Data processing and analysis followed collection, using descriptive statistics, logistic regression, Student *t*-tests, Fisher's exact test, and nonparametric Mann-Whitney U. CGM raw data for all subjects (including glucose measurements, date and timestamp, calibration events, alarm thresholds, and alarms) were retrieved from corresponding applications and preprocessed in GNU Octave© (www.gnu.org) code. Run times were aligned for all subjects based on the time of spin start. Baseline glucose was defined as the CGM glucose value at or immediately before the time of spin start. CGMs typically report delayed interstitial glucose concentration compared to real-time serum glucose due to delay in diffusion of serum glucose into the interstitial space, delay in diffusion of glucose onto the sensor itself, and processing lag, culminating in a maximum lag time of 10–15 min.[11,26] The brand of CGM used in this study has a range of reported lag times from 3.7–13min[6,14,31] and reports concentrations at 5-min intervals. Thus, CGM glucose concentrations considered reflective of interstitial glucose concentration changes from hypergravity experiences included the time period from 5 min after profile start to 15 min after profile end. Maximum and minimum CGM values within that window were used to calculate delta glucose (largest absolute change from baseline to maximum or minimum) and interval to maximum absolute change. CGM mean absolute relative difference (MARD)[15] was calculated from all fingerstick BG and corresponding CGM glucose values recorded immediately prior to fingerstick. All plots were generated by GNU Octave©.

RESULTS

A total of 50 volunteer subjects met criteria for inclusion in the larger centrifuge study. Of these, a convenience sample of 26 individuals were selected for continuous glucose monitoring during hypergravity exposure. Subjects monitored by CGM included 14 men, 11 women; average age 40.2 ± 11.6 yr (men: 41.9 ± 16.4 yr; women: 39.5 ± 12.3 yr), average body mass index (BMI) of 24.6 ± 3.9 kg · m^{-2} (men: 25.1 ± 3.5 kg · m^{-2}; women: 24.4 ± 4.2 kg · m^{-2}). Of these subjects, four (three men, one woman) had a preexisting diagnosis of Type 1 DM and were on insulin therapy at the time of the study; average age of diabetic subjects was 32.8 ± 8.9 yr, and average BMI 25.1 ± 1.8 kg · m^{-2}. Diabetic subjects had an average HbA1c of 6.45 ± 0.73% and average preprandial BG of 127.1 ± 17.2 mg · dL^{-1}. Diabetic subjects reported no recent hospitalizations (past 5 yr) for diabetes or related conditions.

Subjects were observed during their participation in up to five centrifuge runs in a single day, as described above. Data collection quality was considered adequate; instrument malfunction, motion artifact, or minor technical constraints caused rare omissions that were not considered sufficient to compromise result integrity. CGMs were applied as described either the night prior to centrifuge trials or the morning of participation. As a result, some CGMs (those applied in the morning of testing) were not fully acclimated after insertion trauma and, as a result, some Run 1 CGM data were unavailable for inclusion. One nondiabetic CGM subject participated only in Run 1 at 50% intensity before withdrawing from the study; this subject applied the CGM the night before participation and thus was included only in Run 1 CGM data analysis.

The remaining 25 subjects participated in two or more centrifuge runs. There were 3 additional subjects (including 1 diabetic subject) who opted out of 1 or more centrifuge runs; the remaining 22 subjects completed all 5 centrifuge runs. There was no significant difference between subject CGM glucose before or after any spin in those that opted out of runs vs. those who completed all centrifuge runs. There were no episodes of clinically significant hypoglycemia in any subject during any phase of the study. CGM data was calibrated against fingerstick BG at 1–5 time points during the trial day for each subject; there was no significant difference between fingerstick BG and CGM readings during

the study day for the cohort as a whole. However, in three nondiabetic subjects (11.5% of CGM cohort), critical low CGM alarms prompted fingerstick BG; comparison of CGM to BG demonstrated substantial difference for each alarm (Alarm 1: CGM = 55 mg · dL^{-1}, fingerstick = 113 mg · dL^{-1}, Alarm 2: CGM = 52 mg · dL^{-1}, fingerstick 106 mg · dL^{-1}, Alarm 3: CGM = 41 mg · dL^{-1}, fingerstick = 90 mg · dL^{-1}). All subjects were asymptomatic at the time of alarm. These deviating CGMs were recalibrated at the time of the fingerstick comparison and had no other alarms or notable deviations after recalibration. At study completion, validation of CGM readings was performed by obtaining MARD.[15] The CGM readings determined to be false alarms caused by sensor disturbance (for example, impact trauma) rather than true hypoglycemia were omitted. Adjusted MARD for our cohort of CGM-wearing subjects resulted as 10.84%; if no omission of known false alarms, MARD was 12.05%.

Average prespin CGM glucose was significantly higher for diabetic subjects compared to nondiabetic subjects (diabetics: 179.9 ± 52.3 mg · dL^{-1}, nondiabetics 109.7 ± 15.6 mg · dL^{-1}, U = 28, $P < 0.001$). Average postspin CGM glucose was significantly higher for diabetic subjects compared to nondiabetic subjects (diabetics: 173.0 ± 51.9 mg · dL^{-1}, nondiabetics 104.7 ± 11.4 mg · dL^{-1}, U = 7, $P < 0.001$).

There was no significant correlation between delta HR and delta CGM during any phase of any run, nor was there any significant association between age and delta CGM during or after any run. Further, there was no significant difference between delta CGM during or after any run for diabetic vs. nondiabetic subjects. However, CGM glucose was noted to change immediately following centrifuge runs, in both positive and negative directions (see **Fig. 1** and **Fig. 2**). Delta CGM, number of subjects with glucose rise vs. fall, and time to maximum CGM delta are presented in **Table II**. There was no significant difference in delta CGM response to spins or time to maximum delta CGM in diabetics vs. nondiabetics. There was no association between symptoms and delta CGM, time to delta CGM, or rise vs. fall of CGM, nor was CGM change or time to delta predictive of subjects opting out of any runs. On two occasions, two different nondiabetic subjects registered a prespin CGM of >200 mg · dL^{-1} followed by a steady decline of CGM readings to >50 mg · dL^{-1} during and after profiles. Given the high initial CGM, this decline returned subjects to normal ranges and no hypoglycemic event occurred. There were no symptoms associated with either event. Other abrupt vertical drops in CGM values corresponded to known calibration events; more gradual and sustained CGM decline frequently was associated with longer downward trends after meals.

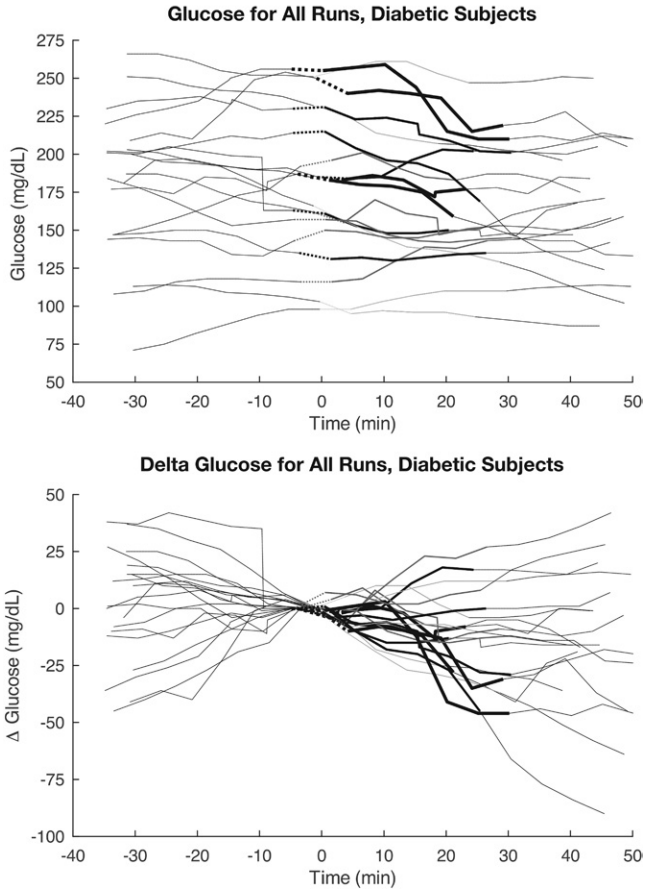

Fig. 1. Top: glucose for all runs, diabetic subjects; bottom: delta glucose for all runs, diabetic subjects. Continuous glucose monitor (CGM) data are presented for diabetic subjects across all runs, normalized to profile start time. Absolute CGM glucose is normalized by the CGM glucose reading at or immediately prior to the start of the profile. Thick dashed lines designate profile start. Thick solid lines represent the time period from 5 min after profile start to 15 min after profile end in which the CGM glucose reflects the blood glucose during the profile. Thin gray lines show CGM glucose from 30 min before and after the centrifuge run.

DISCUSSION

Overall, subjects tolerated simulated spaceflight profiles well and CGM monitoring did not seem to adversely impact subject tolerance of the centrifuge experience. CGM devices successfully transmitted continuous glucose data throughout the study data collection period despite hypergravity exposures and distance between the CGM and receivers. An adjusted MARD of 10.84% is higher than the ideal range preferred for insulin dosing adjustment, which is generally considered adequate at <10% MARD.[11] Notably, prior literature has indicated that MARD can increase to an average of 13% with aerobic exercise;[14,31] MARD observed in this study may indicate inaccuracy from sympathetic stimulation and/or aerobic activity, or may be indicative of poor device function related to the hypergravity environment. Further study is warranted to determine whether CGM accuracy is consistently affected by the hypergravity environment or another confounding factor.

As in prior studies,[2–4] diabetic subjects successfully self-managed their condition with no hypoglycemic episodes or other adverse medical events. In both diabetic and nondiabetic subjects, CGM glucose values were altered following centrifuge runs; however, such alterations were highly variable with no significant overall trends and variable rise or fall of glucose observed among subjects and even within a single subject from one profile to the next. Additionally, there was no correlation between

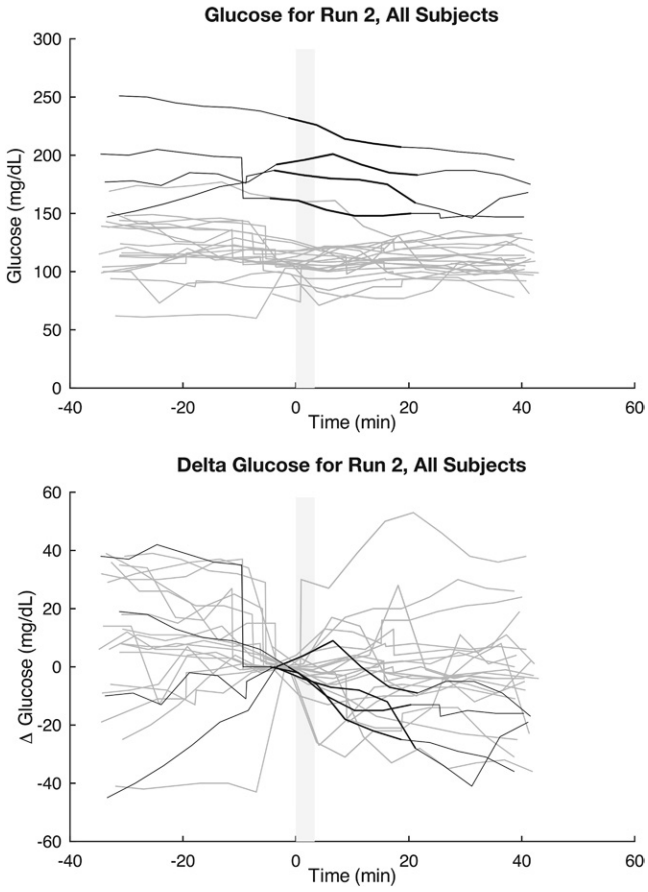

Fig. 2. Top: run 2 continuous glucose monitoring (CGM); bottom: run 2 delta CGM glucose. CGM data are presented for diabetic (gray lines) and nondiabetic (black lines) subjects. Profile duration is indicated by the shaded bar; thick dashed lines indicate CGM value at or immediately before run start, solid thick lines indicate the period from 5–15 min after spin completion in which lagging CGM data reflects hypergravity glucose effect.

glucose alterations and any change in subject tolerance, symptoms, or any clinical sequelae in either diabetic or nondiabetic subjects. This suggests that transient alterations of glucose related to hypergravity exposure do not promote clinically relevant alterations of BG or associated symptoms.

This study was undertaken to provide some understanding of BG alterations resulting from hypergravity exposure and to demonstrate the utility of CGM in monitoring glucose levels in a spaceflight analog. As discussed above, subjects experienced no adverse events or clinically significant alterations of BG despite minor alterations in CGM glucose readings throughout a day of intermittent acceleration exposure, suggesting that any BG alterations induced by spaceflight accelerations are likely tolerable for most individuals. CGM was demonstrated to be potentially useful, with glucose values generally valid and data collection to be, in most cases, unaffected by the centrifuge environment. However, the occasional incidence of error in critically low glucose readings noted in three subjects does indicate the potential for inaccuracy; in a clinical setting, such events could drive inappropriate treatment adjustments if fingerstick BG is not available as a confirmatory test. Similarly, elevated MARD in our study may indicate inaccuracy such that CGM may not be reliable for adjustment of insulin dosage or other treatment considerations during or after hypergravity exposures. Potential contributors to deviant CGM readings include hydration status, localized monitor or underlying tissue trauma from impact or restraint interference, need for calibration despite device approval for noncalibrated use, inaccuracy induced by repetitive hypergravity exposure, or other device malfunction. Further study is necessary to determine expected frequency of such deviation events and whether any factor in the centrifuge or spaceflight environment increases the potential for inaccuracy.

Incorporation of CGM into spaceflight activities would require additional considerations. For example, while we tried to place the CGM in a location that would minimize interactions between the device and subject restraints, restraint interaction could (and likely did) occur, and the device is large enough to potentially result in interference with a space suit. There is the possibility that the device could cause either localized crewmember injury during suit pressurization or even damage the device or the suit during suited and pressurized activities or don and doff procedures. Alternatively, if further study continues to confirm that glucose alterations induced by hypergravity exposures do not result in clinically significant sequelae, CGMs could instead be applied as needed during periods of spaceflight outside of suited activities, removing the risk of CGM interference or injury to subject or suit during suited periods. This would, of course, require removal of any CGM prior to suit donning activities; addition of such a step may pose a challenge in the case of emergency, with the potential for a crewmember to forget to remove a device during a

Table II. Blood Glucose Response to Centrifuge Profiles.

	ABSOLUTE CGM DELTA (MEAN ± SD; mg · dL^{-1})	NUMBER OF SUBJECTS WITH CGM RISE vs. FALL	RISE (NUMBER SUBJECTS, MEAN ± SD; mg · dL^{-1})	FALL (NUMBER SUBJECTS, MEAN ± SD; mg · dL^{-1})	TIME TO MAXIMUM DELTA (min)
Run 1	17.2 ± 12.8	18 | 5	12.9 ± 15.3	14.9 ± 10.0	15.5 ± 7.2
Run 2	17.4 ± 12.1	9 | 15	18.6 ± 14.8	16.7 ± 10.6	12.1 ± 5.9
Run 3	17.9 ± 10.9	7 | 17	15.7 ± 12.5	18.8 ± 10.5	21.2 ± 8.0
Run 4	16.0 ± 13.4	7 | 18	16.1 ± 14.9	16.0 ± 13.2	18.5 ± 7.9
Run 5	17.0 ± 10.9	10 | 12	16.9 ± 11.3	17.2 ± 11.1	17.1 ± 7.8

Comparative blood glucose responses to each of five runs, as measured by continuous glucose monitoring, is presented. Note that subjects experienced both rise and fall of glucose, variable by profile. Time to maximum delta blood glucose is additionally provided. Notably, there was no consistency in blood glucose alterations; subjects with a decline in blood glucose after one spin could experience a rise in the next, and vice versa. CGM: continuous glucose monitor; SD: standard deviation; mg: milligram; dL: deciliter; min: minutes.

rapid suit donning procedure and subsequent risk of injury or suit damage. The utility or desire for glucose monitoring during spaceflight must be weighed against such considerations.

There are many limitations to this study. First, while the use of centrifugation as an analog provides the opportunity to replicate acceleration forces similar to those experienced during spaceflight launch and landing, centrifugation can lead to artifacts, including Coriolis or other spatial disorientation, and replication of microgravity exposure is not possible in a terrestrial centrifuge setting. A convenience sample of subjects were selected for CGM monitoring; this sample cohort included all available diabetic subjects, but notably few diabetic subjects (a total of four) were included in the larger study. Nondiabetic subjects were selected primarily due to availability of CGM devices and the need to limit total number of monitored subjects in a single day and associated data collection burden. A larger sample size is necessary to provide increased power and analysis of CGM fidelity in spaceflight or analog environments for diabetic subjects. While care was taken to avoid interaction between the CGM and subject clothing and restraints, the devices were occasionally jostled or impacted, which may have altered the reliability of the CGM data. Application of the CGM in some subjects the morning of centrifugation resulted in some data points being unavailable due to the delay between CGM application and the acclimatization period of the device for accurate monitoring.

Despite these limitations, we feel the results of this study are an important step toward the evaluation and validation of glucose monitoring devices for use in the spaceflight environment and improving understanding of BG responses to hypergravity exposure, potentially enabling future access to spaceflight for diabetic individuals. Further, the data collected in this study seem to align with prior evidence[3,4,18] that the acceleration forces anticipated for commercial spaceflight are well-tolerated by individuals with well-controlled diabetes and that diabetics in otherwise good health are likely to be unencumbered by their medical condition should they choose to participate in future spaceflight activities.

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