SHORT COMMUNICATION

Preflight Screening Techniques for Centrifuge-Simulated Suborbital Spaceflight

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Introduction: Historically, space has been the venue of the healthy individual. With the advent of commercial spaceflight, we face the novel prospect of routinely exposing spaceflight participants (SPFs) with multiple comorbidities to the space environment. Preflight screening procedures must be developed to identify those individuals at increased risk during flight. We examined the responses of volunteers to centrifuge accelerations mimicking commercial suborbital spaceflight profiles to evaluate how potential SFPs might tolerate such forces. We evaluated our screening process for medical approval of subjects for centrifuge participation for applicability to commercial spaceflight operations. ***Methods:*** All registered subjects completed a medical questionnaire, physical examination, and electrocardiogram. Subjects with identified concerns including cardiopulmonary disease, hypertension, and diabetes were required to provide documentation of their conditions. ***Results:*** There were 335 subjects who registered for the study, 124 who completed all prescreening, and 86 subjects who participated in centrifuge trials. Due to prior medical history, five subjects were disqualified, most commonly for psychiatric reasons or uncontrolled medical conditions. Of the subjects approved, four individuals experienced abnormal physiological responses to centrifuge profiles, including one back strain and three with anxiety reactions. ***Discussion:*** The screening methods used were judged to be sufficient to identify individuals physically capable of tolerating simulated suborbital flight. Improved methods will be needed to identify susceptibility to anxiety reactions. While severe or uncontrolled disease was excluded, many subjects successfully participated in centrifuge trials despite medical histories of disease that are disqualifying under historical spaceflight screening regimes. Such screening techniques are applicable for use in future commercial spaceflight operations.

Keywords: medical screening, medical risk, hypergravity, commercial spaceflight participant, hypertension, cardiovascular disease, pulmonary disease, diabetes.

THROUGHOUT THE history of manned spaceflight, astronauts and cosmonauts have been selected based upon their ability to pass rigorous screening that identified only those that met the highest physical and psychological standards. During the early space program, the first astronauts were selected from military service backgrounds that ensured not only the physical endurance to withstand the G forces of launch and reentry, but also the mental fortitude to withstand any psychological challenges. While early biomedical concerns focused on crew survival during short-duration missions lasting hours or days, longer-duration missions raised additional questions regarding long-term effects of microgravity, radiation, and human factors on crew performance (7). Preflight screening for career astronauts has evolved over this time period, with a focus on identifying potentially incapacitating conditions such as nephrolithiasis or dysrhythmia, as well as conditions that may limit the operational lifetime of an astronaut candidate, including malignancy, cardiovascular disease, or similar progressive disorders. However, these established screening regimes may not be applicable to commercial spaceflight.

The mission profile for commercial spaceflight more closely mirrors the early, suborbital, and short-duration missions from the pre-Apollo era, as currently proposed commercial suborbital profiles will be measured in minutes instead of days. Unlike the NASA astronauts who first embarked on those missions, it is anticipated that commercial spaceflight participants (SFPs) will be of a wider age range, with potential physical limitations and a full spectrum of medical comorbidities (4). Though the commercial space industry will soon offer regular spaceflights to the population at large, medical practitioners currently have little information regarding effective prescreening methods for commercial SFPs. Thus, the development of preflight screening criteria with a focus on identifying the potential for incapacitating events during a short-duration flight is appropriate. In particular, concern has been raised regarding physical tolerance of the launch and re-entry phases of flight, where acceleration forces are greatest. Given these factors, screening techniques were derived from standards designed by NASA as well as recommendations that have been offered by aerospace medical experts from the Federal Aviation Administration, Aerospace Medical Association, and Space Medicine Association to identify potentially incapacitating conditions within high-risk populations expected to be routinely encountered within the SFP population (1,2,5). Screening criteria were developed for conditions believed to have the greatest capacity for adverse events during short-duration exposure to hypergravity, including hypertension, cardiovascular

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disease, diabetes, pulmonary disease, and back and neck conditions. These screening criteria were employed as a part of a larger study examining the physiological effects of centrifuge-induced simulated launch and reentry forces on subjects with a variety of medical backgrounds (3).

METHODS

A prospective cohort study, approved by the University of Texas Medical Branch Institutional Review Board, was designed to recruit volunteers for physiological training at the National AeroSpace Training and Research (NASTAR) Center centrifuge (Southampton, PA). Prescreening techniques reported here were performed as a part of this larger study (3). Potential subjects were recruited through a media outreach campaign involving webpage advertisement, email list distribution, and television news cast. Disease cohorts were comprised of only well-controlled conditions as classified by study criteria and an exam by their own physician. Cohort groups included hypertension (HTN), cardiovascular disease (CV), diabetes (DM), pulmonary disease, and chronic back or neck injury or compromise (BN) (3). Volunteers were subjected to 2 d of centrifuge trials, with maximum acceleration exposures of +6 G_x (chest-to-back) and +4.0 G_z (head-to-toe), mimicking a suborbital spaceflight profile, from January through November of 2013 (3).

All respondents were asked to complete a medical history questionnaire detailing personal medical history, family history, exercise tolerance (none, minimal, moderate, high), physical limitations, allergy profile, tobacco use, surgical history, and psychiatric history. Volunteers were provided a physical exam form and instructed to have the form completed by a physician of their choosing. All applicants received a generalized physical exam, with disease-specific criteria detailed as follows.

HTN group applicants were required to provide documentation of resting blood pressure (BP), a list of currently administered medications, and time on therapy for each. HTN exclusion criteria included baseline systolic pressures $>$ 180 mmHg, diastolic $>$ 105 mmHg, and preflight systolic values $>$ 190 mmHg. Participants were instructed to hold all alpha-blockade and peripheral vasodilator agents for a minimum of 24 h prior to centrifuge runs.

Subjects with any history of CV disease were required to provide reports from any stress testing, echocardiography, or percutaneous cardiovascular intervention(s). Surgical reports relating to CV history, including coronary artery bypass grafting or congenital malformation repair, were required. BP trends were required of all CV applicants even in the absence of a diagnosis of HTN. Inclusion criteria established a minimum left ventricular ejection fraction (LVEF) $\geq$ 50% and accepted a history of dysrhythmia, valvular heart disease, past myocardial infarction, and implanted continuous pacemakers. Exclusion criteria included patients with history of cardiac transplant, automated implantable cardioverter-defibrillator placement, and LVEF $<$ 50%. No exclusion threshold was established for right ventricular systolic pressure, relying instead on functional status as described by the examining physician. Patients with a known history of ischemic heart disease with intervention (percutaneous or coronary artery bypass grafting) were additionally required to provide exercise stress test results performed post-intervention. Lipid profiles were requested, but not exclusionary.

DM volunteers were accepted with either insulin dependent or noninsulin dependent diabetes. Applicants controlled with diet, oral agents, insulin injections, or by insulin pump were included in the cohort. For study inclusion, subjects were required to provide home fingerstick blood glucose (BG) logs showing current BG trends, as well as a recent ($\leq$ 6 mo) glycosylated hemoglobin (HbA1c) showing reasonable control, defined as HbA1c $\leq$ 8.0%. Applicants diagnosed as "pre-diabetic," without medical intervention (diet alterations or medication) and with recent HbA1c $<$ 6.5%, were excluded from the DM group for the purposes of this study.

Applicants with a history of pulmonary disease were accepted with a wide variety of underlying lung pathology, including asthma, chronic obstructive pulmonary disease, chronic restrictive lung disease, and any history of lung surgery for any reason. Asthmatic subjects were required to keep a short-acting beta-agonist rescue inhaler easily accessible on their person during centrifuge profile runs. Chest radiography and current pulmonary function test (PFT) results were requested, though abnormal PFT findings alone were not exclusionary as long as reasonable control and oxygenation could be demonstrated. Exclusion criteria consisted of a history of a single episode of spontaneous or traumatic pneumothorax, remote and without evidence of bullae or sequelae, as well as any dependence on continuous supplemental oxygen therapy. Active tobacco use was not exclusionary, but was recorded for analysis purposes.

BN applicants were considered from a range of possible disease profiles as well, including chronic back/neck muscle strain, degenerative disk disease or disk herniation (current or recurrent/past), nerve root impingement, a history of trauma with or without surgical intervention, scoliosis, or sciatica. Surgical spinal fixation or other hardware implantation was not exclusionary as long as subjects were outside of the postoperative period, defined for the purposes of this study as 6 wk post-intervention. While additional imaging was not required, radiology reports of the most recent spinal imaging performed were requested to supplement the basic documentation outlined above. Acute spinal injuries and applicants $<$ 6 wk post-surgery were excluded.

Screening Process

In addition to the above criteria, a baseline electrocardiogram (EKG) was required for all subjects, including controls. Examining physicians were provided with an outline of simulated flight profiles and the associated physiological stressors their patient would encounter, including anticipated acceleration timing and magnitude. Psychiatric history was required by screening

questionnaire; in addition, an attempt was made to identify subjects without a confirmed psychiatric diagnosis who expressed possibly debilitating psychological instabilities with regards to their tolerance of study activities, such as severe anxiety or claustrophobia. While such histories were not necessarily exclusionary, they did prompt a more thorough review of medical and psychological documentation to ensure stability on current medication regimens.

All medical documentation was reviewed by a study investigator and medical monitor, with study participants either being approved directly, excluded, or requested to undergo further testing or provide additional data (3). Baseline hemodynamic values were taken upon arrival at the testing facility. Study medical monitors ultimately had final decision-making ability for subject inclusion. During centrifuge trials, study monitors observed subjects via real-time audiovisual display as well as 3-lead EKG (3). Termination criteria included evidence of clinically significant dysrhythmia or appearance of extreme distress by video monitoring (3).

RESULTS

Of 355 registered volunteers, 176 were excluded for failure to complete the preliminary medical questionnaire by the study deadline. An additional 55 were excluded for incomplete medical documentation, resulting in 124 eligible study applicants. Of these, 15 were excluded for exceeding study weight maximum, set at 250 lb due to limitations of centrifuge-compatible medical monitoring equipment. Five applicants were ultimately excluded for medical conditions. Of the remainder, 7 were excluded due to scheduling conflicts precluding travel to the centrifuge facility and 11 for lack of response to scheduling attempts. The remaining 86 subjects participated in centrifuge trials (**Fig. 1**).

Of the five subjects screened out for medical conditions, one was excluded from the BN group due to proximity to surgery (< 3 wk since intervention). Another was screened out from the CV cohort due to recurrent atrial fibrillation with rapid ventricular rate requiring cardioversion. The subject had a history of paroxysmal atrial fibrillation in the past and arrhythmia was triggered during prior cardiac stress testing. A third subject was excluded from the DM group due to uncontrolled type II diabetes, with a current HbA1c $> 10\%$ and BG trends ranging from 250-300 mg $\cdot$ dl^{-1}.

Two subjects were excluded due to psychiatric concerns. The first was screened out by interview and documentation of explosive personality disorder, with recommendations from the volunteer's psychiatrist that the individual not participate in the study. The physiological stress and confined environment of the centrifuge combined with the unpredictable nature of the subject's behavior was deemed high risk for both the subject and investigators, precluding participation. The second applicant carried a diagnosis of bipolar disorder, which by itself was not exclusionary, but the subject was ultimately excluded based upon recommendations from the personal physician and a documented history of inconsistency on medication and instability when off medication.

Of the 86 subjects screened in for study inclusion, 26 individuals were required to provide additional medical documentation beyond the medical questionnaire, physical exam, and resting EKG. For inclusion in the CV cohort, 10 applicants were required to provide records of cardiac stress testing and recent echocardiography or

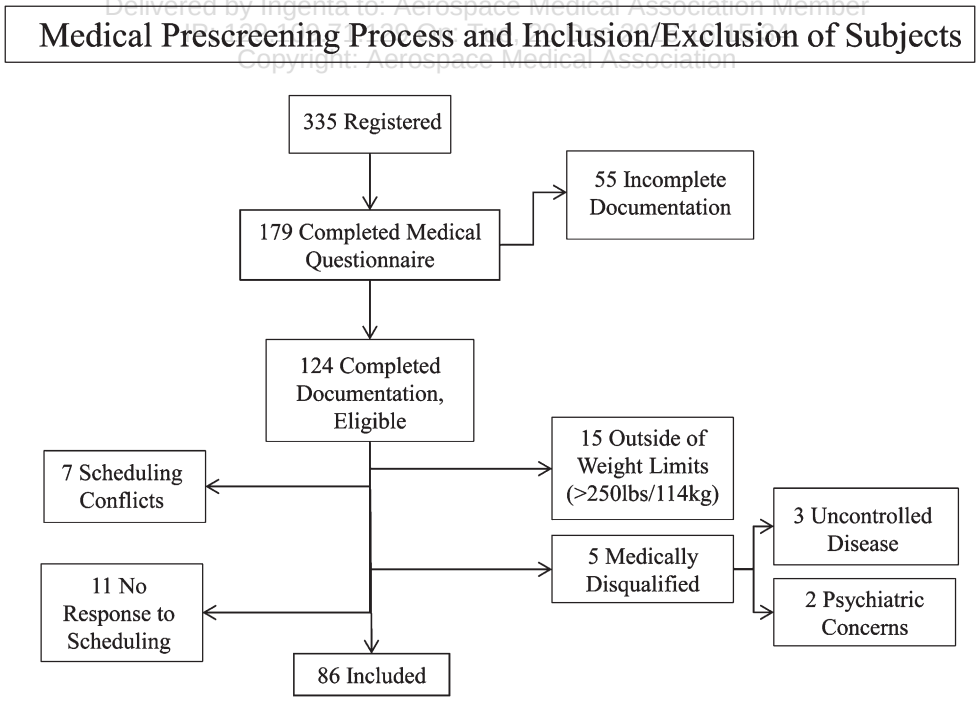

Fig. 1. Diagram of screening flow and inclusion/exclusion of subjects.

other cardiac function testing; an additional 10 subjects were required to provide documentation of recent fasting BG trends and HbA1c for inclusion in the DM cohort. DM subjects were told to maintain their normal medication, diet, and exercise regimens during the study period. During the trials, one brief episode of clinical hypoglycemia did occur shortly after an introductory $+G_z$ centrifuge run. Symptoms included dizziness, nausea, diaphoresis, and hypotension (nadir 80/53 mmHg) following the run, all of which were corrected with food intake. The subject had missed breakfast due to time constraints, but had taken his oral hypoglycemic agent (an oral sulfonurea) as per his normal schedule; the combination of these factors appeared to be causative (3). No subjects required to provide additional medical data or documentation were ultimately excluded from centrifuge trials. Furthermore, the 26 subjects required to undergo additional screening did not differ in their centrifuge tolerance compared to subjects who underwent only minimal screening.

Only 5 subjects (0.6%) failed to complete the study. Despite the inclusion of 20 subjects who subjectively reported an exercise tolerance of none (a score of 5) or minimal (a score of 15) on the medical questionnaire, there was no observed association between these scores and centrifuge tolerance. Three subjects withdrew due to anxiety, making anxiety the largest contributor to postscreening study dropout (6). One subject withdrew due to back strain suffered during Day 1 trials. The remaining subject was forced to withdraw due to scheduling constraints.

DISCUSSION

The screening methods used in this study were sufficient to identify individuals physically capable of tolerating simulated suborbital flight, but failed to identify individuals who aborted due to anxiety. The screening cutoff values employed for our study, especially with regard to the HTN group, effectively "screen in" a large segment of the general population as likely to tolerate a similar flight profile. With regard to BP, relatively high baseline values were accepted due to several factors, including $+G_z$ exposure during the profile, for which higher baseline BP appears mildly protective from greyout and G-induced loss of consciousness (G-LOC), as demonstrated in prior studies (3,4). As a correlate to the risk of hypoglycemia in the DM group, hypotension was deemed the greater risk to study participants. The decision to hold peripheral dilating and alpha-blocking agents was made with this in mind: the increased capacity with peripheral dilators for venous pooling and decreased afterload during $+G_z$ loading could place participants at increased risk for G-LOC and impaired anti-G straining maneuver (AGSM) effectiveness. Likewise, alpha-blockade of epinephrine and norepinephrine binding to peripheral receptors increases the risk of postural hypotension both by increasing peripheral dilation and blunting the compensatory response to catecholamine release. Additionally, the hypoglycemic episode in the DM group was illustrative of the risks associated with hypoglycemia in extreme environments. Tight glucose control is not an indicator of ability to tolerate such exposures and in future studies more liberal HbA1c values would not be expected to have worse flight profile tolerance.

Within the CV cohort there were no exclusions due to supplemental documentation, testing, or medical history; even so, much of the required documentation was considered necessary for a thorough screening. Exercise stress testing and baseline/comparison EKGs were deemed critical for subject safety in those with ischemic heart disease. Echocardiography-confirmed LVEF $>$ 50% was chosen to ensure near-normal cardiac output, vital for maintaining cerebral perfusion during $+G_z$ exposure and AGSM. While subjects with LVEF $<$ 50% may potentially tolerate similar profiles without incident given the low maximum $+G_z$ exposure (+4.0 G_z) of the simulated suborbital profiles, we advise caution in any subject with impaired total cardiac output or outflow tract obstruction for any reason, including aortic stenosis, coarctation, or infiltrative or hypertrophic heart disease. Such subjects must be evaluated on a case-by-case basis.

In the pulmonary disease cohort, PFTs were not predictive of centrifuge run tolerance or in-flight Po_2 values. As the ability to perform normal physical activities off continuous oxygen therapy was a requisite for this study, our results suggest that, in the absence of oxygen therapy, PFTs may be of minimal use in medical screening for suborbital flight.

BN participants were screened nearly entirely on the basis of injury/disease history. Where imaging reports were requested, none resulted in study exclusion and no new imaging was requested for study participation. Proximity to surgical intervention or acute injury was considered reason for exclusion, as the acute postsurgical or injury period places the individual at the highest risk of re-injury. Even with relatively low peak Gs, the risk of re-injury was considered too great for inclusion of any subject within this period; similar recommendations would likely be appropriate for screening of suborbital passengers.

Within all groups, self-reported exercise tolerance did not appear to predict centrifuge profile tolerance. This may suggest that such subjective reports may be of limited use in similar applications; however, a larger sample size and a more thorough means of identifying exercise capacity is warranted before further conclusions can be drawn. Similarly, improved screening for psychological instability is recommended based on our findings, particularly as severe anxiousness or other psychological disturbances in flight can cause disruption of the flight experience for both fellow passengers and crewmembers (3,6). There was no correlation between history of psychiatric disease and psychological intolerance or anxiety within the centrifuge; therefore, it appears that simply identifying psychiatric diagnoses does not accurately identify those individuals at greatest risk for anxiety in the operational environment.

There are several limitations to this study. Our findings are limited to the five disease groups discussed, failing to represent a large segment of medical diagnoses. However, these disease groups were chosen to represent a large cross section of common chronic disease states in an aging population and to identify disease categories that are considered the highest risk based on prevalence and the potential for adverse events in the flight environment. Similar research in the future may address other concerning disease histories. Further, screening techniques were used to evaluate for subject tolerance to short-duration accelerations of relatively low magnitude; a more severe G profile may not be tolerated by subjects who experienced no difficulty with the profiles here. Though no incapacitation events were encountered during centrifuge trials, our screening criteria are not definitively validated. The limited number of test subjects per cohort limits the likelihood of observing a rare but medically significant event. In addition, this study examined only the effects of launch and reentry and did not address additional stressors of microgravity exposure or longer duration or orbital flight, each of which could affect tolerance. Finally, medical decision-making was performed by trained aerospace physicians. The ability of a general physician to make medical decisions regarding fitness-to-fly has not been evaluated here; however, we believe it appropriate that a certified aerospace physician be tasked with such decision-making in the commercial spaceflight industry.

As minimal medical histories and excellent physical conditioning have long been a prerequisite for astronaut candidates, the ability of those with chronic disease states to withstand the stress of spaceflight has been previously unaddressed. While screening criteria for this study were chosen primarily to screen out individuals at high risk for incapacitation or similarly severe adverse events during centrifuge operation, it is telling that, of all applicants who completed the required documentation, only 6% were rejected on the basis of medical concern, and only 5 of 86 total subjects failed to complete the demanding series of acceleration exposures. Additionally, though severe or uncontrolled disease was excluded, many subjects successfully participated in centrifuge trials despite medical histories of disease that were disqualifying under historical spaceflight screening regimes. These screening techniques are likely applicable for use in future commercial spaceflight operations and suggest that much of the general population may be capable of withstanding the physiological stresses of the launch and re-entry profiles of suborbital spaceflight.

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