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# Aerospace Medicine and Human Performance

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# Aerospace Medicine and Human Performance

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## Live from Paris: The 1<sup>st</sup> International Conference of Aerospace Medicine

Susan Northrup, M.D., M.P.H., FAsMA

The First International Conference of Aerospace Medicine 2022 (ICAM 2022) was a resounding success! While the planners hoped 400 people would attend, the final total was 848 from over 70 countries. The meeting was co-hosted by the AsMA, European Society of Aerospace Medicine, International Academy of Aviation and Space Medicine, and French Society for Aviation and Space Medicine. It was the first meeting in three years for all except AsMA. The organizations owe a huge thanks to Jeff and Deborah Sventek, as well as Giselle Vargus and Sheryl Kildall in the Home Office, who handled registrations in two currencies, overcoming digital and time zone challenges. Further, with the two delays for the Paris meeting, each task was performed several times over the years. The dedication of all the organizers and the French Society greatly contributed to the success of the meeting and they deserve our thanks!

The meeting itself, after the Allard Lecture and the JS Ernsting Panel, broke into three concurrent sessions covering everything from fatigue to diabetes to mental health to mishap investigation and space. The Ernsting Panel reviewed many of the initiatives the world and aviation medical community undertook in response to COVID-19. We hope to have the same group come to our May meeting and discuss ending a pandemic and returning to normal operations. The Scientific Program Committee did an outstanding job creating a robust program of papers.



One paper on fatigue was especially interesting. Three high school students from Indonesia presented research to determine level of fatigue based on voice. The ladies, working with a teacher, taught an app to indicate when an individual was fatigued

based on the pronunciation of vowels. Each subject had to record several statements with varying times since their last sleep event. In their limited population, the app was able to then determine time since last sleep when subjects were kept awake for periods of time. The concept that our phone can indicate fatigue based on our speech patterns is exciting—and from high school students! If we can find more young scientists like this, our society and profession will do well.

On a personal note, I thoroughly enjoyed the comradery and collaboration with the international community of aviation and space medicine experts. I met people whom I had been working with for years via Zoom. The ability to exchange ideas and discuss pathways forward for our professional challenges in person was sorely missed as we weathered the pandemic. Many of the attendees will be joining us in New Orleans. We are very lucky to have such a glorious organization.

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# Potential of Neuromuscular Electrical Stimulation as a Bone Loss Countermeasure in Microgravity

Thomas J. Abitante; Mary L. Boussein; Kevin R. Duda; Dava J. Newman

- INTRODUCTION:** For future long-duration spaceflight missions, additional methods of loading the skeleton may be required to supplement exercise to minimize bone loss. Neuromuscular electrical stimulation (NMES) can elicit muscular contractions that create strain on bone. However, the potential effectiveness of NMES on the proximal femur during disuse is not known.
- METHODS:** We measured the maximum isometric force of NMES-induced contractions of the rectus femoris and the hamstrings of 10 subjects (5 male, 5 female), sitting with the hips and knees at 90 degrees of flexion. We employed 2-D biomechanical models of the knee and hip to estimate the hip joint reaction forces, applied these forces to a generic femur finite element analysis model, and qualitatively compared the peak principal strains of the proximal femoral neck to the peak strains modeled in previous studies for other forms of exercise.
- RESULTS:** The average peak tensile/compressive strains were  $1380 \pm 719 \mu\epsilon$ / $-2179 \pm 1130 \mu\epsilon$  and  $573 \pm 345 \mu\epsilon$ / $-900 \pm 543 \mu\epsilon$  for the male and female subjects, respectively. While results varied between studies, the strains achieved during NMES generally were comparable to those achieved during walking or stairs, with some individuals matching higher intensity activities.
- DISCUSSION:** This study demonstrated that isometric NMES contractions of the thigh muscles can create strain in the proximal femoral neck similar to that achieved during low impact activities. While NMES alone will unlikely create a sufficient daily strain stimulus to prevent bone loss, it will likely improve the current spaceflight countermeasures by adding more frequent loading throughout the day.
- KEYWORDS:** strain model, exercise countermeasures, long duration spaceflight.

Abitante TJ, Boussein ML, Duda KR, Newman DJ. *Potential of neuromuscular electrical stimulation as a bone loss countermeasure in microgravity.* *Aerospace Med Hum Perform.* 2022; 93(11):774–782.

Astronauts aboard long duration spaceflight missions are at risk of detrimental effects associated with micro-gravity, including a substantial loss of bone mineral density (BMD), as high as 1–2% per month, in the lower body.<sup>21</sup> Currently, exercise is prescribed as the primary countermeasure to reduce the rate of bone loss,<sup>22</sup> with heavy resistance training and proper nutrition increasing the efficacy.<sup>37,39</sup> Nevertheless, the rate of bone loss varies greatly among astronauts, with many at an increased risk of fracture<sup>41</sup> on a future mission beyond Low Earth Orbit (LEO) to the Moon or Mars.<sup>31</sup> The difficulty in maintaining BMD can be attributed to the fact that astronauts experience negligible skeletal loading outside of the exercise block, whereas the mechanisms that trigger bone maintenance are more responsive to more frequent skeletal loading spread throughout a given day.<sup>35</sup> Unfortunately, the

solution cannot be simply adding more exercise. The current exercise regimen (2 h per day) results in an increased need for water, food, and carbon dioxide removal, which may not be as logistically feasible beyond LEO.<sup>36</sup> Furthermore, an additional increased energy expenditure may be difficult to compensate for, creating a negative caloric balance which can hinder the benefits of the exercise.<sup>19</sup> Additionally, future long duration

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spacecraft will be significantly smaller and will not be able to accommodate the mass and power of the three exercise machines currently in use, potentially reducing the variability and intensity of exercises one can perform. While pharmacological countermeasures have been recently explored<sup>20,37</sup> and smaller integrated exercise devices<sup>44</sup> and new exercise regimens are in development,<sup>13</sup> investigations into nonexercise based methods to maximize the daily loads on the skeletal system are warranted.

Neuromuscular Electrical Stimulation (NMES) is a technique that uses electrical pulses to cause involuntary muscular contractions.<sup>6</sup> Repetitive daily muscular contractions with NMES can attenuate the bone loss in the tibia and the femur associated with disuse from spinal cord injury,<sup>11</sup> as well as increase bone parameters in rodent hind limbs.<sup>16</sup> NMES can also potentially address some of the shortcomings of the current spaceflight exercise countermeasure regimen. The energy expenditure during isometric NMES contractions of the lower limbs is less than that seen with the ISS cycle ergometer,<sup>15,42</sup> and it can be used in microgravity with minimal discomfort and equipment such that other work can be performed simultaneously, allowing NMES to be administered throughout the day outside of the exercise block. Additionally, simultaneous co-contractions of agonist-antagonist muscles such as the quadriceps and hamstrings muscles can reduce the net joint movement, which would be crucial for safe application in microgravity.<sup>26</sup>

The potential effectiveness of NMES as a bone loss countermeasure in healthy individuals is unknown. The currently accepted theory concerning bone health is that mechanosensors at the cellular level detect mechanical loading in the form of strain.<sup>14</sup> The total amount of loading that is required to maintain bone mass and structure is often referred to as the daily strain stimulus, which is determined by the magnitude of the strain, and the number of loading cycles or repetitions.<sup>33</sup> To better understand how to reduce BMD loss in the proximal femur in postmenopausal women, the bone strain associated with low impact activities like walking<sup>4,12,17</sup> and high intensity resistance training have been modeled using finite element analysis.<sup>24,32</sup> Presently, no finite element analysis model has been created to estimate the strain on the proximal femur from the internal forces produced by isometric NMES contractions in humans. Like the models used for exercise in postmenopausal women, the peak strains from the NMES contractions could indicate NMESs potential to reduce bone loss on long duration spaceflight.

Exercise interventions to prevent bone loss report varying results, but generally high impact activities like running or jumping and high intensity resistance training can inhibit bone loss.<sup>5</sup> If NMES can create sufficiently high strains comparable to that of high impact or resistive exercise, it could replace some components of the current exercise regimen or allow for a greater frequency of exercise-like forces throughout a given day. Low impact activities such as walking alone are not sufficient to inhibit bone loss unless at very high repetitions,<sup>7</sup> but walking in combination with other activities such as high impact or resistance training can potentially reduce bone loss.<sup>25</sup> If NMES can

only replicate low impact activities such as walking, it could be used to supplement exercise by adding additional loading throughout the day, without compounding the negative side effects of excessive exercise. In short, is it possible to add “walking” throughout the astronauts’ day?

The purpose of the current study was to model the internal forces produced by isometric NMES contractions of the rectus femoris and hamstring complex on the bone and estimate the strain induced on the proximal femur using finite element analysis to allow a qualitative comparison of the peak strains to that of other exercises modeled in previous studies in order to access the potential of NMES as a spaceflight countermeasure, and whether it could supplement, or even replace some of the current spaceflight exercise regimen.

## METHODS

### Subjects

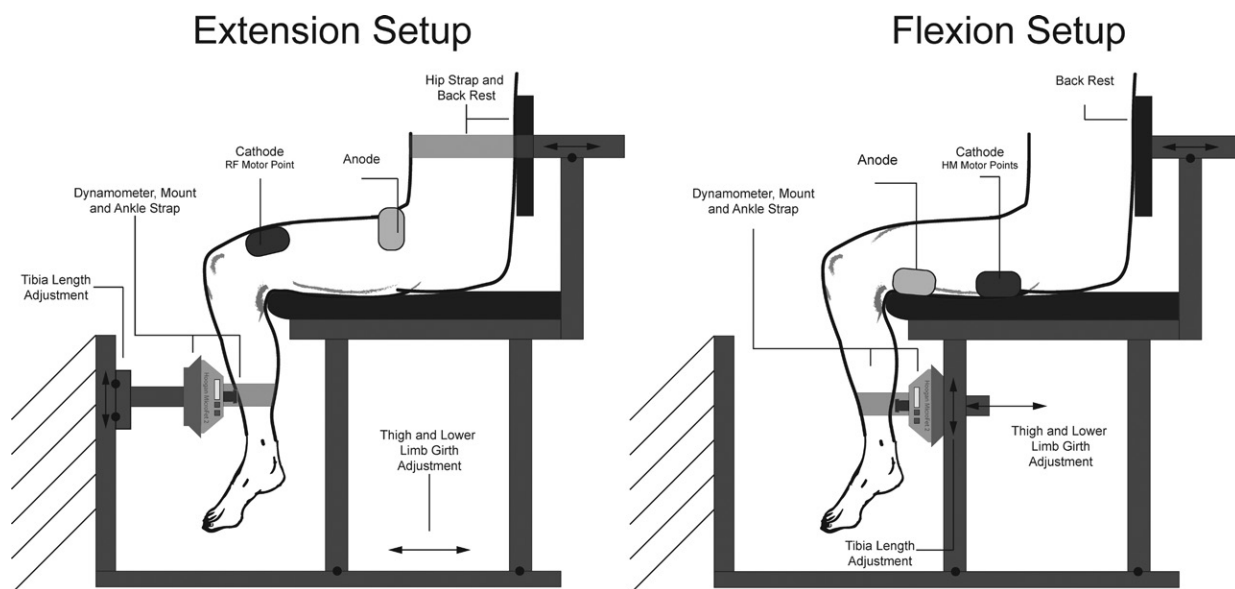
There were 10 subjects who volunteered to participate in this study (5 male,  $27 \pm 2.7$  yr old, and 5 female,  $28.5 \pm 4$  yr old). The experimental procedures were approved by the Institutional Review Board at the Massachusetts Institute of Technology, protocol number 1810570889. All subjects were recruited from the Massachusetts Institute of Technology student population. All subjects were required to be free of any ongoing knee injury and provided written informed consent prior to participating in the study. Subjects were instructed to avoid strenuous lower body exercise for at least 24 h prior.

Upon arrival, we recorded anthropometric measurements, including weight, femur length, medial distal femoral condyle radius (measured from the center of knee rotation to the lower edge of the condyle while the knee is at 90°), and pelvic height (measured as the distance from the greater trochanter of the femur to the superior edge of the lateral iliac crest while seated with the hip at 90°).

### Equipment

The NMES device we used in this study was a custom built, single channel, voltage-controlled device developed at the Massachusetts Institute of Technology (MIT) Human Systems Lab (HSL) in collaboration with MIT Portugal. The device is comprised of an Arduino microcontroller, controlled via the Arduino software,<sup>27</sup> and a muscle stimulation unit (MSU), which has two connections for cutaneous electrode attachment. The electrodes used were 4” x 2” rectangular electrodes (Ultrastim X, Axelgaard Manufacturing Co., Fallbrook, CA). The MSU delivers a biphasic pulse with four individually customizable parameters: pulse amplitude (V), pulse frequency (Hz), and positive and negative pulse widths ( $\mu$ s), which when combined are referred to jointly as the pulse width or pulse duration. Additionally, the duty cycle can be customized through the Arduino software.

We built a custom knee dynamometer rig in the MIT HSL for use in this study (**Fig. 1**). The rig was designed to prevent movement, resulting in isometric, thigh muscle contractions.



**Fig. 1.** NMES dynamometer rig built in the Massachusetts Institute of Technology Human Systems Lab for this study. The Hoggan MF2 dynamometer could be adjusted vertically to account for different lower limb lengths, the seat could be adjusted horizontally to account for different lower limb girths, and the backrest could be adjusted horizontally to account for different thigh lengths.

Therefore, the NMES administered in this fashion can be considered NMES against a fixed resistance (NMES-FR). The rig utilizes a Hoggan MicroFET 2 (MF2) handheld dynamometer for force measurement, which was secured with a 3D printed mount. The rig could be set up in either knee extension, or knee flexion configuration. The seat of the rig could be slid forward or backward to ensure that firm, constant contact between the lower leg and MF2 was achieved. A backrest was utilized to prevent hip extension during hamstring contractions, and a seatbelt was utilized to prevent hip flexion during rectus femoris contractions.

### Procedures

We recorded the isometric muscle contraction force of two different muscles: the rectus femoris (RF), and the hamstring complex (HM). We placed the distal RF electrode longitudinally on the muscle belly, as identified with the leg at full extension, and the proximal electrode transversely across the proximal thigh, below the hip crease and in line with the distal electrode. We placed the distal HM electrode laterally above the knee crease, just medial to the bicep femoris tendon, and the proximal electrode over the muscle bellies of the HM muscles, as found when the subject was flexing the HM while standing. Both electrodes were placed longitudinally. The HM muscles were treated as a singular unit based on the inability to place the electrode in a way that would reliably delineate between the bicep femoris long head, semitendinosus, and the semimembranosus. Each muscle was activated individually with the rig either in the extension or flexion configuration for the RF or HM respectively. We followed an identical calibration and testing protocol for the RF and the HM.

First, with the subject not sitting within the knee dynamometer rig, three NMES-FR contractions were delivered at a

cadence of 1 s on, 3 s off at a low power. The power level of the pulse was determined by changing the pulse width of the electrical signal with the amplitude held constant. The pulse width was then slightly increased, and the three NMES-FR contractions were delivered again. We repeated this process until the subject stated that the intensity of the three contractions was at a maximum tolerable level. The maximum tolerable level was a subjective metric, defined as the point at which the subject felt they would be able to talk or read without distraction from the contractions. This metric was used as the goal would be that astronauts could perform other tasks during the administration of a NMES treatment. During this process, we instructed the subjects to either read or talk during the contractions to aid in this determination.

Following the determination of the peak power for a particular muscle, we slightly reduced the intensity of the NMES-FR, and the subject was positioned within the dynamometer rig. The intensity was reduced to ensure that any discomfort from the contractions was at a tolerable level. For both muscles, we measured the knee angle and the distance from the knee center of rotation to the MF2. Additionally, when in the extension configuration, we measured the vertical distance from the hip joint (measured as the greater trochanter of the femur) to the center of the seatbelt, and when in the flexion configuration, we measured the vertical distance from the hip joint to the top of the posterior edge of the iliac crest (assumed to be the center of pressure on the back rest). The subject then received two bouts of four contractions at a cadence of 1 s on, 3 s off, with the isometric force being recorded by the MF2.

To estimate the internal forces from the measured external muscle forces, we constructed simple biomechanical models of the knee and hip. The knee model was used to take the external measured force and determine the internal muscle forces for

the RF and the HM. The hip model was used to take the internal muscle forces as determined by the knee model and estimate the hip joint reaction forces (HRF) from the RF and HM. Additionally, we used these models to estimate the net joint torques at the knee and hip, which could result in unwanted movement while in microgravity.

The knee was treated as a 2-D joint, with no forces acting in the transverse plane. The hip model was also treated as 2-D, with only the sagittal moments arms of the muscle being included, as the muscles overwhelmingly acted in the direction of the femur. This allowed the seatbelt and back rest reaction forces to be calculated. However, the joint reaction forces in the hip model were treated as 3-D, with the transverse joint reaction forces being equal to the transverse components of each of the HM and RF muscle forces. Additionally, in both the knee and hip, we assumed the joint reactions were placed at the center of the joint to greatly simplify the calculations. This was deemed acceptable as the differences in the estimated muscle forces were minute. OpenSim static optimization was also used to determine the muscle activation of the individual muscles in the HM contractions.<sup>8</sup>

Due to the nature and capabilities of this study, we were unable to obtain accurate anthropometric data of the internal structures of the knee and hip for each subject. Therefore, we used literature derived moment arms of the muscles and joints in question: male knee extension,<sup>38</sup> female knee extension,<sup>30</sup> knee flexion,<sup>38</sup> hip rectus femoris,<sup>10</sup> male and female hip hamstrings.<sup>10,29</sup> When female data were not available, we extrapolated it based on the numerical differences between male and female moment arms found in other muscles.

To account for the different anthropometric characteristics across individuals, we then scaled the literature-derived moment arms based upon the anthropometric measurements taken: knee moment arms based upon the medial distal femoral condyle radius and hip moment arms based on pelvic height. The moment arm was scaled an equal number of standard deviations of the literature derived moment arm to the number of standard deviations of the individual's anthropometric measurement from the average of the group.<sup>28</sup>

With the Abaqus CAE software (Dassault Systems), we created a finite element model of the femur to model the

effects of the muscle contractions. A 4<sup>th</sup> generation standard model femur geometry was obtained with literature derived and validated material properties applied.<sup>23</sup> The hip reaction force from the RF and HM were applied to 20 nodes on the superior surface of the femoral head in the direction of the knee. We applied physiologically realistic boundary conditions in accordance with Speirs *et al.*<sup>40</sup> to minimize femoral head deflection. The model was then meshed with tetrahedral elements, sized in accordance with a performed convergence test (1.2 mm for the femoral head, neck and trochanter, and 3 mm elsewhere).

The FE model was solved for each subject. The model assumed the knee and hip extensors and flexors would be contracted simultaneously in an agonist-antagonist co-contraction, and that the forces produced during the co-contraction would equal the forces produced when contracted individually. For each subject, we extracted the peak maximum (tensile) and peak minimum (compressive) principal strains on the cortical femoral neck. As each subject model utilized the same femur geometry as well as the same HRF input vector, differences in strain will be attributed solely due to differences in muscle force production during the NMES-FR.

**Table I** lists the six studies that measured or modeled the strain in the proximal femur during various exercises that we used as comparison to the results of the NMES-FR. Low Impact includes walking and stair climbing and descending. Resistance Exercise includes exercises such as squats with or without added weight. Where possible, resistance exercises that exceed 70–80% of maximum effort were used, due to the increased likelihood of positive results for bone maintenance.<sup>5</sup>

Due to the variability in study methods and materials, as well as the unavailability of individual data points from the associated studies, we could only perform a qualitative comparison. Additionally, the qualitative comparison was performed due to an inability to concretely compare the osteogenic potential of any individual activity modeled in one study to another, as there remains many unknowns concerning the interactions of peak strain, loading cycle count, and loading cycle distribution on a total daily strain stimulus and the subsequent osteogenic effect, especially when one activity is used in combination with another.

**Table I.** List of the Six Studies Obtained for the Qualitative Comparison.

STUDY	MUSCLE DATA SOURCE	FEMUR MODEL SOURCE	SUBJECT POPULATION	LOW IMPACT	VERTICAL JUMP	RESISTANCE EXERCISE
Aamodt 1997 <sup>1</sup>	In-Vivo	N/A	Women (N = 2)	X		
Martelli 2014 <sup>24</sup>	Obtained Model Simulation*	Obtained Model†	N/A	X	X	X
Edwards 2016 <sup>12</sup>	Obtained Model Simulation	Obtained Model	N/A	X		
Kersh 2018 <sup>17</sup>	Subject Inverse Kinematics/ Dynamics	Individual Subject CT	Post-Menopausal Women (N = 20)	X	X	
Pellikaan 2018 <sup>32</sup>	Subject Inverse Kinematics/ Dynamics	Obtained Model	Post-Menopausal Women (N = 14)	X	X	X
Altai 2021 <sup>4</sup>	Subject Inverse Kinematics/ Dynamics	Individual Subject CT	Post-Menopausal Women (N = 5)	X		

\*Obtained Model Simulation states that muscle forces were obtained computationally using subject kinematics or dynamics inputs from a previous study.

†Obtained Model states that a previously constructed femur geometry was obtained.



## RESULTS

### Knee and Hip Torques

For each subject, we assumed that the thigh muscles would be simultaneously contracted, resulting in both knee and hip extension and flexion. To aid in predicating the feasibility of using NMES in microgravity, we calculated the net knee torques and hip torques using the estimated internal muscle forces and moment arms. Positive torque denotes extension and negative torque denotes flexion. In 9 of 10 subjects, the rectus femoris produced a greater force than the hamstrings, resulting in net knee extension and hip flexion. **Table II** displays the net joint torques for each subject.

### Peak Strains

The peak maximum (tensile) strains occurred on the distal portion of the superior femoral neck, and the peak minimum (compressive) strains occurred on the proximal portion of the inferior femoral neck (**Fig. 2**). The peak strain locations were at identical nodes for all subjects as we had a single femur FEA model and used identical HRF vector across each subject.

This also resulted in a direct correlation between the sum of the modeled HRFs and the peak strains. The average peak tensile strains were  $1380 \pm 719 \mu\epsilon$  and  $573 \pm 345 \mu\epsilon$  for the male and female subjects, respectively. The average peak compressive strains were  $-2179 \pm 1130 \mu\epsilon$  and  $-900 \pm 543 \mu\epsilon$  for the male and female subjects, respectively. All of the peak strains by subject are listed in **Table III**.

### Comparative Metrics

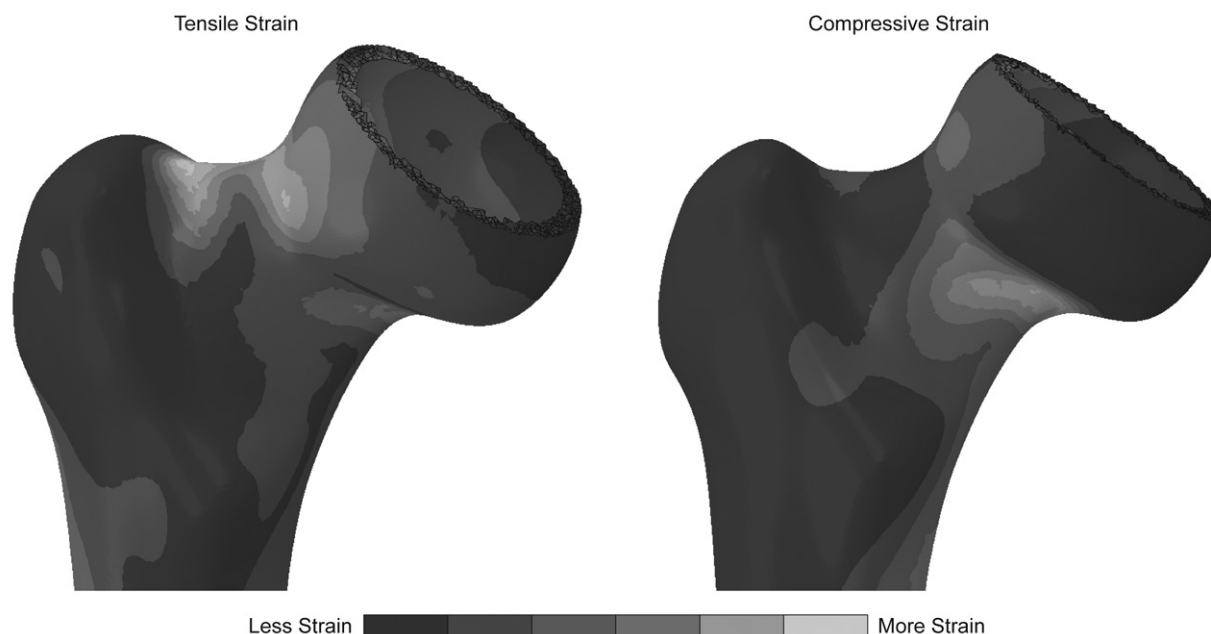
We obtained the peak strains on the cortical proximal femur from six prior studies. When not published, the exact quantitative data was obtained from the authors, with the

**Table II.** The Net Torques of the Knee and Hip for Each Subject, as Calculated from the Estimated Internal Rectus Femoris and Hamstring Complex Muscle Forces and Measured Anthropometric and Experimental Data.\*

	NET TORQUE (N-cm)	
	KNEE	HIP
Male		
1	918.176	-1246.5
2	156.670	-132.45
3	1543.408	-1854.13
4	168.270	-79.5462
5	-486.223	2306.756
Female		
1	891.434	-936.135
2	772.864	-1155.67
3	860.066	-1049.37
4	258.150	-335.458
5	647.700	-1011.44

\*Positive net torque denotes extension, and negative net torque denotes flexion.

exception of the Pellikaan 2018 study,<sup>32</sup> where we visually estimated the average peak strains from the published figures. We created four different categories for the qualitative comparison: Walking, Stairs, Vertical Jump, and Resistive Exercise. The following resistive exercises were used: Weighted Squat (Sq), Hip Extension (HE), Hip Flexion (HF), Knee Extension (KE), and Knee Flexion (KF). The only exercises with a listed percentage of maximum effort were HE and HF in Pellikaan 2018.<sup>32</sup> All studies, with the exception of Martelli 2014,<sup>24</sup> published both superior proximal (tensile) and inferior proximal (compressive) peak strains. If a study further divided the superior and inferior peak strains of the proximal femur by sub region, those most closely matching this study's FEA results were used (superior-distal, inferior proximal). **Fig. 3** displays the peak strains of the various activities to the peak strains achieved by the male and female subject groups.



**Fig. 2.** Strain on the proximal cortical femoral neck as calculated by the Abaqus finite element analysis model. The strain profile was equal across all 10 subjects. A section of the femoral head was removed to eliminate nodes with erroneous peak strains resultant from the loading boundary condition.

**Table III.** Peak Strains for Each Individual Subject.\*

SUBJECT	PEAK STRAINS ( $\mu\epsilon$ )			
	MALE		FEMALE	
	MAXIMUM	MINIMUM	MAXIMUM	MINIMUM
1	965	-1520	1110	-1750
2	786	-1240	505	-794
3	2290	-3600	589	-925
4	844	-1330	152	-238
5	2040	-3200	508	-797
Average	1380	-2170	573	-900
SD	719	1130	345	543

\*Maximum peak strains refer to the peak tensile strain on the superior cortical femoral neck, and minimum peak strains refer to the peak compressive strain on the inferior cortical femoral neck.

Of the four studies with walking (Fig. 3A), the male subject's peak maximum and minimum strains were similar to three studies<sup>1,4,17</sup> and less than one,<sup>32</sup> and the female peak strains were less than all but one.<sup>1</sup> Of the three studies with stairs (Fig. 3B), the men again had peak strains similar to if not greater than all three, whereas the female peak strains were less than all but one.<sup>1</sup> For the three studies with vertical jumping (Fig. 3C), both the male and female's peak strains were similar to one study,<sup>17</sup> and less than the other two.<sup>24,32</sup> Lastly, for resistive exercises (Fig. 3D), the male peak strains were similar to Weighted Squats and Knee extension per Martelli 2014,<sup>24</sup> and less than all others. The female peak strains were less than all recorded exercises.<sup>24,32</sup>

## DISCUSSION

The aim of this study was to estimate the feasibility of using Neuromuscular Electrical Stimulation (NMES) as a bone loss countermeasure in space. This feasibility was determined by qualitatively comparing the strain induced on the femur by NMES of the rectus femoris and hamstring muscles to that of other exercises.

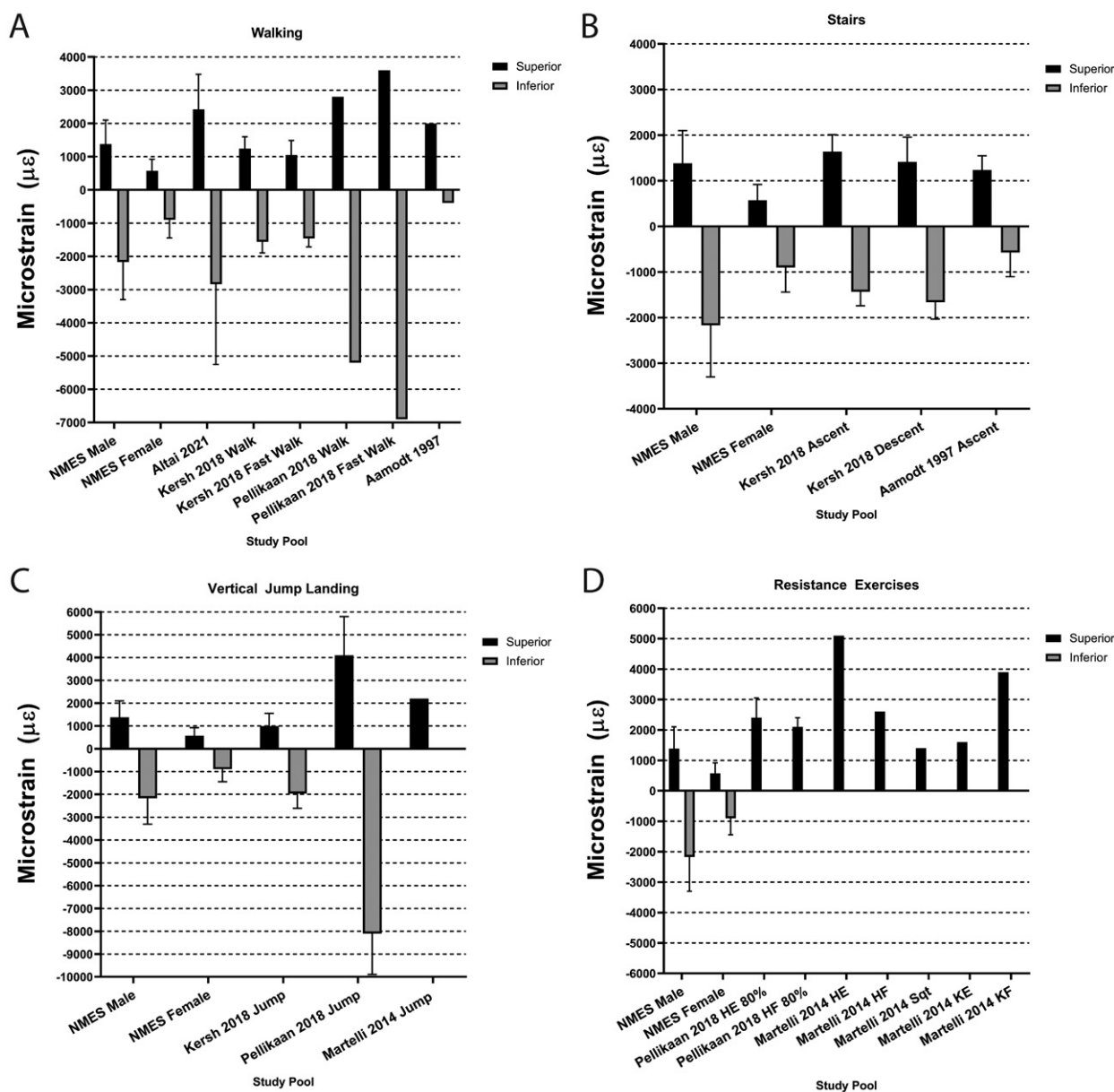
Our results show that NMES, or in this case NMES-FR, could produce peak strains on the femur similar to those of low impact activities, including walking and stair ascending/descending, potentially replicate the strain from higher impact activities like jumping, but could not replicate the strains from most resistive exercises. The ability of these NMES-FR contractions, or an equivalent co-contraction in microgravity without a fixed resistance, to prevent bone loss, however, is still unknown. The current theory of the bone mechanostat states that the total daily strain stimulus, which is determined by the peak strain of a loading cycle and the total number of loading cycles, drives the osteogenic response in bone tissue.<sup>33</sup> However, it is still not known if there is an exact threshold that must be reached, or how such a threshold can vary between individuals, as noted by the wide range of BMD changes following resistive exercise regimens targeting bone loss in older individuals.<sup>5</sup> Also less understood is the influence of lower strain, but higher frequency loading. For example, studies of vibration therapies, where low magnitude, high frequency loading is applied have had mixed

results on preventing bone loss.<sup>18</sup> Therefore, while NMES can produce strains akin to walking, our data indicate that NMES alone would not reduce bone loss in microgravity, as walking alone generally does not produce sufficient daily stimulus to reduce bone loss unless at very high repetitions (10,000+).<sup>7</sup> Additionally, the fatigability associated with repetitive NMES contractions makes achieving a high enough number of productive repetitions difficult.<sup>2</sup>

However, it can be posited that adding a daily NMES regimen to the current or future exercise regimen could potentially improve the effects and further reduce bone loss in long duration spaceflight missions. The bone's mechanotransducers have a sensitivity that declines with repetitive loading cycles, and requires time to recovery this lost sensitivity.<sup>34</sup> Loading that is more distributed throughout a given day, therefore, has a significantly greater osteogenic response than the same volume of loading applied at a single time point.<sup>35</sup> While NMES alone may not generate strains that would fully replicate the loading one experiences on Earth, astronauts currently experience negligible forces on the lower body throughout the day outside of the prescribed exercise period.<sup>21</sup> A countermeasure that induced strains akin to walking periodically throughout the day could theoretically have significant benefits. It is recommended that a long term, head down bed rest study comparing the bone loss with an exercise block vs. an exercise block with distributed NMES be performed to investigate these possibilities. Additional metabolic analysis studies of multiple muscle repetitive NMES contractions should also be completed to further conclude that NMES will not exacerbate the negative energy balance seen with ISS astronauts.<sup>19</sup>

These potential benefits will vary significantly individual to individual, as observed by the variation in peak strains between subjects. The source of the individual variation can be attributed to an individual's potential force production, which is affected by the neuromuscular composition, muscle fiber type distribution and the muscle's maximum voluntary contractile force. Neuromuscular composition refers to the distribution of the motor endplates, where a particular motor neuron branches out to innervate its respective muscle fibers. Those who have more clustered motor endplates can have more under a given electrode size and therefore have more muscle fiber innervated by a given strength NMES electric field.<sup>3,6</sup> The muscle fiber type distribution refers to the spatial distribution of the high twitch, high force producing muscle fibers. As all muscle fiber within reach of the NMES electric field will contract, individuals with more of the high force producing fast twitch muscle, normally recruited during strenuous activity, near the electrodes could generate higher forces.<sup>6</sup> Last, the inherent strength of a muscle will determine the potential strength of a NMES contraction. A greater percentage of muscle fibers innervated, with a greater percentage of those fibers being fast twitch, will generate a greater percentage of the total maximum force capability. The individual variation in results can also be attributed to an individual's tolerance to NMES. The pain of NMES can be attributed to purely subjective measures as well as physical characteristics, such as body fat and hair. Thicker subcutaneous fat requires a

## Peak Principal Strains on the Superior and Inferior Cortical Femoral Neck During Activity



**Fig. 3.** Peak strains on the superior and inferior cortical femoral neck from NMES compared to A) walking, B) stairs, C) vertical jump landing, and D) various resistive exercises. Height of each bar represents the mean and the whisker represents 1 SD. If no whiskers are present, the data were not available or the study utilized a model rather than subjects. Data for the Pellikaan 2018<sup>37</sup> exercises were obtained visually from figures.

stronger electric field to innervate the motor endplates and results in more residual current entering tissue, resulting in pain.<sup>9</sup>

There were no strength, athletic, or body composition requirements for the subjects of this study, nor was any information recorded. Therefore, it is difficult to ascertain why certain subjects were more responsive and subsequently produced higher forces. However, factors like maximum voluntary contractile strength and body fat thickness likely played a role in the trend of the female peak strains being less those that of the men. Additionally, the limitations with using a single FEA

model for all subjects regardless of anthropometric measures was a likely contributor to the overall differences in modeled strain between the two groups.

This study also calculated the net knee and hip torques produced from the proposed co-contraction of the rectus femoris and hamstring muscles. In microgravity, these net joint torques could result in unwanted movement that could be hazardous to the spacecraft or self. Co-contractions of the quadriceps and hamstrings have previously been performed in microgravity aboard Mir and found that at lower NMES intensity levels the resultant movement was negligible.<sup>26</sup> However, this may not be



the case when targeting bone loss, as the higher intensity contractions would be desirable. In order to better predict the resultant movement and subsequent hazard from this study's resultant torques, a follow-on study involving a microgravity analog, such as lateral position or a 0-g flight, should be performed.

Our study utilized methods that measured external force and torque production, converted these external forces to internal muscle forces using biomechanical models, and then applied those forces to an FEA model to estimate the strain on the femur. The calculations and assumptions included in these methods have inherent limitations. First, we used an external dynamometer, which could allow for slight movements and subsequent inconsistencies in force measurement between individuals. Additionally, an external measurement was required from the dynamometer to an estimated knee rotation center, which could result in slight errors in the estimated joint torque. We calculated the in-vivo muscle forces with simple biomechanical models that utilized estimated and scaled moment arms and assumed external reaction forces, which may not reflect the true internal biomechanical force transfer.<sup>28,43</sup> We used a single femur FEA model across all 10 subjects, whereas individuals will have varying femur geometry, lengths, and material properties. Last, due to the limitations of the biomechanical model, accurately producing an HRF vector was not possible, and instead we used an identical vector field in the direction of the knee across all subjects. These factors would all contribute to increased variation in peak strains, as well as the locations of peak strains, across each subject.

This study involved comparing the results to those of other strain models from other studies. The studies used here were all comprised of different biomechanical models and finite element models, as well as subject populations. Additionally, the activities modeled had variations between the different studies. For example, walking speeds varied and therefore exact comparisons could not be performed. These limitations necessitated that the current study be limited to a qualitative comparison.

In this study we estimated femoral strains induced by the isometric force from Neuromuscular Electrical Stimulation of the rectus femoris and hamstring complex. By comparing these strain estimates to those previously reported for other activities, we were able to determine the feasibility of using NMES as a countermeasure for bone loss in microgravity. Our results indicated that some, but not all, individuals have sufficiently high muscle forces during NMES to create strains on the femur similar to activities such as walking or stair climbing/descending, with NMES inducing strains comparable to those reported for jumping or resistance exercises in a few individuals. These results suggest that NMES is a promising approach to reduce bone loss in space and provide strong rationale for further investigations, specifically testing whether the use of NMES can prevent bone loss in a bedrest study.

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# Personality Trait Comparison of Pararescue Personnel and Elite Athletes

Anne Shadle; Lennie Waite; Wayne Chappelle

- INTRODUCTION:** Pararescue personnel (PJs) deploy in high-risk environments and perform extraordinary missions under intense conditions, requiring an unusual combination of physical and psychological abilities. The rigorous nature of PJ training and the superior levels of fitness and cognitive functioning to perform challenging physical feats in high-pressure, high-intensity environments have prompted military commanders and embedded health care providers to compare successful performance in the PJ mission with the characteristics required of elite, Olympic-level athletes.
- METHODS:** In the current study, we tested this assumption by comparing the social, emotional, and behavioral functioning of 160 U.S. PJ training candidate graduates and 73 elite, Olympic-level track and field athletes using scores on the NEO Personality Inventory-3.
- RESULTS:** Results from this study suggest that although there are physical and psychological challenges inherent in both the PJ and elite athlete career fields, the emotional, social, and behavioral performance of PJs differs in functional ways from the elite athlete population, with PJs scoring significantly lower in Neuroticism and higher in Extraversion and Conscientiousness.
- DISCUSSION:** The results of this study can be used to improve the delivery of embedded mental health services geared toward improving training and enhancing health, recovery, and performance within operational units.
- KEYWORDS:** pararescue personnel, elite athletes, personality traits, performance enhancement.

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Throughout history, United States Air Force (USAF) pararescue personnel (PJs) have made an immeasurable impact on both military and civil operations. Their exceptional skills in combat search and rescue (CSAR) and trauma medicine provide a distinctive capability for the USAF. The primary duties of a PJ include the ability to deploy in a rapid fashion into friendly, denied, or hostile territories across diverse geographic regions—mountain, desert, arctic, urban, and water—to extract, treat, stabilize, and rescue injured, wounded, isolated, or captured military and civilian personnel. The demands to perform such extraordinary missions require an unusual combination of physical and psychological abilities. Their motto, “That Others May Live,” is the cornerstone of their work and affirms their commitment to not only their self-sacrifice but also their commitment to saving human lives.

Given the rigorous nature of PJ training and CSAR operations, superior levels of physical and psychological aptitudes are essential to adapting to the various stressors and conditions

of operational missions. For example, research regarding physical traits of PJs reveals they must meet exceptional levels of fitness and health standards well above the traditional requirements that most military personnel must demonstrate.<sup>4</sup> Additionally, they possess cognitive (i.e., speed and accuracy of information processing in various visual- and verbal-based aptitudes) abilities that are in the superior range of functioning, well above most military personnel. Further, research assessing personality traits (i.e., a stable and enduring pattern of emotional, social, and behavioral functioning across time

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and settings) reveals that PJs, as a group, when compared with adult peers in the civilian population, are: 1) emotionally less susceptible to experiencing negative emotions, such as fear, worry, apprehension, anger, irritability, sadness, and hopelessness, while simultaneously experiencing higher levels of general stress tolerance, optimism, and happiness; 2) socially higher in levels of self-regard, humility and modesty, gregariousness, assertiveness, interpersonal warmth, altruism, compliance in groups, and interest in forming close interpersonal relationships with others; and 3) behaviorally higher in levels of achievement-striving, dutifulness, flexibility, self-actualization, independence, and impulse control (Chappelle WL, McDonald K, Thompson W. Technical Report No. AFRL-SA-WP-TR-2012-0005; 2012. Available to those with access).<sup>3,4</sup> It is not surprising such traits are consistent with research regarding the importance of emotional “hardiness” in predicting career success for U.S. special operations military personnel.<sup>1,2,14</sup>

When considering the contributing factors to successfully completing the PJ mission, psychological parallels have been drawn between successful performance in combat scenarios and elite performance at the highest level in sporting arenas.<sup>7,16</sup> Both elite athletes and PJs are required to sustain superior levels of fitness and cognitive functioning to perform challenging physical feats in high-pressure, high-intensity environments to achieve victory. Due to these shared characteristics, programming for military personnel is often designed around sport psychology interventions used with elite athletes. For example, studies have investigated the impact of mental skills training programs on performance and stress outcomes for military populations,<sup>5,9</sup> a mindfulness intervention for a military helicopter unit,<sup>12</sup> and the integration of psychological skills training programs during various phases of military training.<sup>11,13,15</sup> Specifically, Meyer<sup>13</sup> studied the impact of a 6-wk sport psychology training program for soldiers and reported that 91% of the participants recognized the importance of the sport psychology skills for Army tasks, such as weapons qualification and combat medic tasks. Overall, the perceived similarities in functioning and high demand performance requirements between PJs and elite athletes have persuaded many military commanders and embedded mental health providers that there are significant similarities in the emotional, social, and behavioral functioning between these two groups.<sup>6</sup>

Although there are enticing, surface-level similarities between the two groups, it is unclear whether these perceptions of overlapping emotional, social, and behavioral traits are correct, given there are no empirically based, objective studies that support this perception. The subjective assumptions about the similarities between PJs and elite athletes are likely based on the high level of physicality, resilience, and mental toughness often noted as prerequisites for success in both communities. Further, the authors' experiences of consulting with USAF line and medical leadership reveal a diverse range of opinions regarding areas of social, emotional, and behavioral functioning that delineate PJs from elite athletes. In sum, there appears to be a lack of consensus between leadership regarding areas of functioning that PJs display that are consistent with elite and Olympic-level

athletes, as well as a lack of objective, empirical data driven studies to support the perceptions regarding the perceived similarities in functioning between PJs and elite athletes.

While elite and Olympic-level athletes perform in large stadiums with cameras following their every movement and millions of fans watching, PJs are performing while their own life is at risk (i.e., under fire, attack). An athlete might step into the competitive battleground like an Olympic stadium, but that is different than a PJ in a Blackhawk helicopter that is flying 15.24 m (50 ft) above the ground, performing banking maneuvers, and under combat fire during a rescue mission that poses risk of significant life-threatening injuries. Considering this description, it is likely the social, emotional, and behavioral traits for successfully adapting and performing under battle-field rescue missions may potentially exceed or be quite different from those who compete in elite athletic events. Combat operations are performed under more highly intense, unexpected, uncontrolled conditions than competitive athletics events in which environmental safety and predictable scheduling are prioritized. However, comparisons remain, as stated by Olympian Alexi Pappas, “There truly is so much overlap between the world of Olympic athletics and the military: we are all elite athletes whose mission is to push ourselves beyond our limits to achieve extraordinary goals” (para. 2).<sup>6</sup> Yet, as mentioned previously, there are no empirical studies assessing where similarities and differences truly exist between elite athletes and military personnel. Senior military leaders who base assumptions solely on anecdotal similarities are missing important insight on how PJs might differ from elite athletes in unique and meaningful ways. Although the physical conditioning and mental skills required to maintain a high level of performance may be similar between the two communities, the variability between these two groups regarding social, emotional, and behavioral functioning remains unknown and may be critical to understanding psychological traits critical to success within the PJ community.

Overall, the aim of this study addresses the gap in the literature by empirically evaluating the similarities and differences in emotional, social, and behavioral functioning between USAF PJs and world-class, Olympic-level athletes. The results of this data-driven study will help provide clear evidence and insight into the strength and direction of specific personality traits universal to those who pursue and excel within physically and psychologically demanding high-performance occupations. Such information can be used to help improve the effective delivery and utilization of services geared toward enhancing health, recovery, and performance within such unique high-risk, high-demand environments.

## METHODS

### Subjects

Subjects included 160 U.S. PJ training candidate graduates between 2014 and 2017 and 73 elite athletes between 2020 and 2021. Although the PJ career field was open to women starting

in 2016, there were no female candidates at the time of data collection. The average age of the PJ training candidates who successfully completed training was 21.7 yr (SD = 2.9). Additional demographic information was not available for this study. The PJ training courses have an 86–90% attrition rate,<sup>4</sup> and those who complete training are considered to be among an elite group of special warfare operators.

The elite athlete sample included world champion and Olympic-level USA track and field (USATF) athletes. The current sample of male elite athletes includes those who have won a total of 43 gold, silver, and bronze medals (**Table I**). The average age of the elite athlete sample is 28.0 yr (SD = 4.9). This study was reviewed by the Air Force Research Laboratory Institutional Review Board at Wright-Patterson AFB, OH, and assigned protocol number FWR20200125H.

The criteria for selection of elite athlete participants included USATF athletes who were: 1) part of the Tiered (1-3) or Talent Protection Program (TPP); 2) a member of a USA World or Olympic Team; or 3) a 2020 Olympic Trials qualifier. These criteria ensured that all participants had experience competing at an elite level or were currently receiving funding because their performances indicated they had the ability to compete in an upcoming Olympic Games and/or World Championships. The criteria for Tiered and TPP athletes focuses on world ranking, marks from the previous season, and medal-winning performances at previous championships such that all Tiered and TPP athletes are deemed to have the potential to medal or compete at a future Olympic Games or World Championships.

## Materials

Personality testing included the administration of a commercially based instrument (i.e., NEO Personality Inventory-3 [NEO-PI-3]). The NEO-PI-3 consists of 240 items and takes about 30 min to complete. Each item has a 5-point response scale, with responses ranging from “strongly disagree” to “strongly agree.” This instrument measures 5 major personality domains—Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness—and 30 different facets in total within all 5 domains. The NEO-PI-3 meets professional psychometric reliability and validity qualities and standards for use as a noncognitive assessment instrument<sup>10</sup> and is used to provide additional information regarding the strengths and vulnerabilities and to assess for potential adaptation problems. In military settings, the NEO-PI-3 is used as part of a battery of tests to identify maladaptive personality traits or maladaptive behavior that could interfere with performance in high-risk, high-demand operational duty positions. Evidence for the reliability and validity has been well established, with reliability coefficients ranging

between 0.91 to 0.93 for the domain scores and 0.62 to 0.92 for the facet scores.<sup>10</sup>

## Procedure

The researchers collaborated with the USATF High-Performance Director to explain the criteria needed to meet the requirements of the study. Eligible participants were notified about the study and connected with the researchers. Additionally, the researchers traveled to key meets in the buildup to the Tokyo Olympic Games to recruit participants in person. The researchers communicated directly with the USATF High-Performance Director to identify critical meets with a high number of Olympians and potential 2020 Olympic Games qualifiers. In-person data collection occurred in Austin, TX, Eugene, OR, Walnut, CA, and Prairie View, TX. After the researchers introduced eligible participants to the study, those interested were sent an email with more study information. The email information included their research identification number and a link to the computerized version of the NEO-PI-3, and provided them with relevant study information so that they understood the purpose and conditions of participating in the assessment. All participants were given information regarding the procedures in place to maintain the confidentiality of their data and maximize self-disclosure. Administration followed a standardized set of instructions, and participants completed testing from their personal computer or mobile-based device (such as a cell phone). Testing was automatically scored via computer upon completion.

The NEO-PI-3 testing was administered to candidates in the first week of basic military training. Testing is administered as part of an aeromedical clinical psychology program for airmen going into high-risk, high-demand career fields and who have to meet enhanced medical standards. Candidates were informed that testing was voluntary, would not affect their training disposition or military status, but would be used as a baseline assessment of their psychological functioning to help improve the delivery of embedded mental health care, if needed, and for research purposes only. They were also informed that test scores were confidential to help maximize self-disclosure. De-identified data were stored on the secure Air Force Research Laboratory database and were accessed by USAF research personnel for inclusion in this study. The researchers used previously published data from a USAF technical report assessing the utility of pretraining personality testing with predicting performance outcomes.<sup>4</sup>

## Statistical Analyses

Descriptive statistics were used to characterize PJs and elite athletes with respect to age and NEO domain and facet scores. Specifically, means and SDs were calculated for domain and facet scores, and two-sample *t*-tests were used to compare scores across domains and facets. Raw scores were used for the analyses and Welch's *t*-test was used to account for unequal sample variance and unequal sample size. This study reported *P*-values, corresponding test statistics, and effect sizes for all comparisons. Due to the uneven sample sizes, Hedges' *g* was reported

**Table I.** Summary of Medal Count for Elite Athletes.

MEDAL	WORLD CHAMPIONSHIPS	OLYMPIC GAMES	WORLD INDOOR CHAMPIONSHIPS
Gold	11	4	4
Silver	5	9	2
Bronze	4	3	1

**Table II.** Internal Consistency for Each Sample of the NEO Domains.

NEO DOMAIN	CRONBACH'S ALPHA	
	ATHLETES (N = 73)	PJs (N = 160)
N: Neuroticism	0.80	0.83
E: Extraversion	0.84	0.76
O: Openness	0.73	0.65
A: Agreeableness	0.71	0.72
C: Conscientiousness	0.87	0.86

for effect sizes. The *P*-values were not adjusted for multiple comparisons across the NEO domains and facets. However, effect sizes of 0.5 or greater were considered to represent statistically significant tests (as defined by Hedges and Olkin<sup>8</sup>), as effect sizes of this magnitude were associated with Bonferroni-adjusted  $\alpha$ -levels of approximately 0.001.

## RESULTS

Cronbach's alpha is presented to assess the internal consistency of the six facet scores that compose each NEO domain across each sample (Table II).

The means and SDs for the NEO-PI-3 domain and facet scores for the total sample of PJs and elite athletes are shown in Table III. The comparison between these two groups revealed several significant differences across domains and facets.

Across NEO-PI-3 domains, results indicated statistically significant differences between PJs and elite athletes on three of the five domains. PJs were lower in Neuroticism [ $t(122.87) = -7.44, P < 0.001$ ] and higher in Extraversion [ $t(106.34) = 5.44, P < 0.001$ ] and Conscientiousness [ $t(116.04) = 6.18, P < 0.001$ ] than elite athletes. Effect sizes greater than or equal to 0.5 were statistically significant. There was not a statistically significant difference between the two groups on Openness to Experience [ $t(125.05) = -1.54, P = 0.13$ ] and Agreeableness, overall [ $t(131.49) = 2.24, P = 0.03$ ].

PJs exhibited significantly lower levels of overall Neuroticism than elite athletes [ $t(122.87) = -7.44, P < 0.001$ ]. There were statistically significant differences across all six facets related to Neuroticism, including anxiety [ $t(124.32) = -5.26, P < 0.001$ ], angry hostility [ $t(131.03) = -4.31, P < 0.001$ ], depression [ $t(112.77) = -6.39, P < 0.001$ ], self-consciousness [ $t(118.92) = -3.95, P < 0.001$ ], impulsiveness [ $t(115.88) = -5.57, P < 0.001$ ], and vulnerability [ $t(109.25) = -6.80, P < 0.001$ ]. Overall, results

**Table III.** Comparison of PJs vs. Elite Athletes.

DOMAIN/FACET	DESCRIPTIVE STATISTIC		COMPARATIVE TEST		
	PJ MEAN (SD)	ATHLETE MEAN (SD)	t-TEST	P-VALUE	EFFECT SIZE
N: Neuroticism	52.08 (18.06)	73.16 (20.92)	-7.44	0.00	1.11
N1: Anxiety	10.16 (4.54)	13.86 (5.18)	-5.26	0.00	0.78
N2: Angry Hostility	8.45 (4.48)	11.32 (4.81)	-4.42	0.00	0.62
N3: Depression	8.56 (3.94)	12.86 (5.11)	-6.39	0.00	0.99
N4: Self-Consciousness	8.86 (4.24)	11.58 (5.12)	-3.95	0.00	0.59
N5: Impulsiveness	11.05 (4.07)	14.82 (5.08)	-5.57	0.00	0.85
N6: Vulnerability	5.01 (3.08)	8.73 (4.17)	-6.80	0.00	1.07
E: Extraversion	132.34 (16.74)	115.69 (23.59)	5.44	0.00	0.87
E1: Warmth	24.46 (4.21)	22.16 (5.42)	3.20	0.00	0.50
E2: Gregariousness	19.16 (4.85)	15.81 (6.06)	4.16	0.00	0.64
E3: Assertiveness	20.88 (3.93)	18.89 (4.98)	3.01	0.00	0.46
E4: Activity	21.39 (3.45)	18.14 (4.64)	5.36	0.00	0.84
E5: Excitement-Seeking	23.73 (3.69)	19.78 (4.70)	6.33	0.00	0.98
E6: Positive Emotions	22.72 (4.46)	20.90 (5.66)	2.42	0.02	0.37
O: Openness to Experience	118.19 (17.01)	122.23 (16.76)	-1.54	0.11	0.23
O1: Fantasy	17.12 (4.90)	20.45 (4.62)	-5.01	0.00	0.69
O2: Aesthetics	17.20 (5.45)	17.80 (6.12)	-0.71	0.48	0.10
O3: Feelings	18.75 (4.83)	20.15 (4.82)	-2.05	0.04	0.29
O4: Actions	20.20 (3.56)	18.00 (3.67)	4.28	0.00	0.61
O5: Ideas	24.18 (5.02)	23.25 (5.71)	-1.20	0.23	0.18
O6: Values	20.74 (4.12)	22.59 (4.33)	-3.07	0.00	0.44
A: Agreeableness	123.90 (16.76)	118.36 (17.91)	2.23	0.02	0.32
A1: Trust	20.09 (4.47)	19.06 (4.75)	1.57	0.12	0.22
A2: Straightforwardness	20.38 (4.61)	19.58 (4.25)	1.30	0.20	0.18
A3: Altruism	25.70 (3.58)	23.45 (4.31)	3.88	0.00	0.59
A4: Compliance	16.07 (4.49)	15.22 (5.10)	1.22	0.22	0.18
A5: Modesty	20.03 (4.59)	18.60 (5.13)	2.02	0.05	0.30
A6: Tendermindedness	21.64 (4.27)	22.45 (4.41)	-1.32	0.19	0.19
C: Conscientiousness	145.56 (17.62)	127.49 (21.95)	6.18	0.00	0.95
C1: Competence	25.15 (3.36)	23.19 (4.00)	3.53	0.00	0.55
C2: Order	21.60 (4.58)	19.43 (5.21)	3.06	0.00	0.45
C3: Dutifulness	25.93 (3.28)	21.78 (4.11)	7.59	0.00	1.16
C4: Achievement-Striving	27.51 (3.18)	24.96 (4.17)	4.64	0.00	0.72
C5: Self-Discipline	25.93 (3.80)	20.29 (5.57)	7.86	0.00	1.27
C6: Deliberation	19.45 (4.42)	17.85 (5.10)	2.31	0.02	0.34



suggest that PJs exhibit lower levels of Neuroticism (i.e., higher levels of emotional stability) than elite athletes.

PJs exhibited significantly higher levels of overall Extraversion than elite athletes [ $t(106.34) = 5.44, P < 0.001$ ]. Namely, PJs demonstrated higher levels of warmth [ $t(113.36) = 3.20, P < 0.001$ ], gregariousness [ $t(115.72) = 4.16, P < 0.001$ ], activity [ $t(109.71) = 5.36, P < 0.001$ ], and excitement-seeking [ $t(114.03) = 6.33, P < 0.001$ ], on average. In addition, self-reported levels of assertiveness [ $t(114.48) = 3.01, P = 0.003$ ] and positive emotions [ $t(114.46) = 2.42, P = 0.02$ ] were higher for PJs, but the effect sizes were not statistically significant.

There was no significant difference in PJs and athletes on the overall domain Openness to Experience [ $t(125.05) = -1.54, P = 0.13$ ]. However, statistically significant differences emerged in two facets—fantasy [ $t(147.25) = -5.01, P < 0.001$ ] and actions [ $t(135.65) = 4.29, P < 0.001$ —with PJs reporting lower scores on fantasy and higher scores on actions. There were no statistically significant differences on aesthetics [ $t(126.01) = -0.71, P = 0.48$ ], feelings [ $t(139.66) = -2.05, P = 0.04$ ], ideas [ $t(124.71) = -1.20, P = 0.23$ ], and values [ $t(133.51) = -3.07, P = 0.002$ ], although PJs' scores did trend lower on these facets, on average, than elite athletes'.

PJs exhibited significantly higher levels of overall Conscientiousness than elite athletes [ $t(116.04) = 6.18, P < 0.001$ ]. Notably, results indicated that PJs had statistically significant higher levels of competence [ $t(120.21) = 3.64, P < 0.001$ ], dutifulness [ $t(115.68) = 7.59, P < 0.001$ ], achievement-striving [ $t(111.59) = 4.64, P < 0.001$ ], and self-discipline [ $t(103.61) = 7.86, P < 0.001$ ] compared to elite athletes. The two remaining facets, including order [ $t(124.74) = 3.07, P = 0.003$ ] and deliberation [ $t(123.17) = 2.31, P = 0.02$ ], demonstrated a similar positive trend, but were not statistically significant.

The overarching domain of Agreeableness did not demonstrate significant differences between PJs and elite athletes [ $t(131.49) = 2.24, P = 0.03$ ]. However, one facet within the domain emerged as statistically significant, with PJs demonstrating higher levels of altruism when compared to elite athletes [ $t(118.93) = 3.88, P < 0.001$ ].

## DISCUSSION

Results from this study suggest that although there are physical and psychological challenges inherent in both the PJ and elite athlete career field, the emotional, social, and behavioral functioning of PJs differs significantly and in functional ways from the elite athlete population. In the sections below, we summarize these differences, discuss applied implications within the PJ career field, address future areas of research, and note the limitations related to the current study.

The results of this study found, when compared with elite and Olympic-level track and field athletes, PJs are less susceptible to experiencing negative emotional states in general (i.e., neuroticism), as well as the more specific states of fear, worry, apprehension (anxiety), irritability, frustration (angry hostility), sadness, and helplessness (depression). The findings also

revealed PJs are less susceptible to feelings of awkwardness and embarrassment (self-consciousness), as well as less susceptible to reacting impulsively (impulsiveness). Overall, the results of this study suggest PJs possess greater levels of emotional resilience and stamina when compared with elite and Olympic-level track and field athletes.

The finding that PJs possess greater levels of emotional stamina appears consistent with the requirements of adapting and performing in highly intense, life-threatening conditions with many unknown and uncontrollable factors. Given the conditions that PJs must operate within, the greater levels of emotional stamina appear logical. As a result, military leadership may consider the reality that operating within CSAR operations requires a level of emotional stamina exceeding that of elite and Olympic-level athletes.

The difference in emotional functioning may also shed light on the different pressures that world class athletes experience when compared to PJs. Athletes must perform in the moment, on demand, and in the spotlight while, at times, millions are watching. The pressure to perform from media influence, sponsor expectations, contractual obligations with financial impact depending on the result of the performance, expectations from family, coaches, and other stakeholders such as national governing bodies, or even the internal pressure they place on themselves adds to the emotional burden athletes carry. The embarrassment of a poor performance or sensitivity to public ridicule that elite athletes often experience can also be a significant emotional stressor. Regardless of such challenges, the emotional pressures of athletes do not reflect the life and death conditions in which PJs must operate.

The between-group differences in susceptibility to negative emotional states might also speak to the level of emotional stamina needed to adapt to extreme CSAR missions and the types of personalities drawn to the career field. The environment elite athletes compete in could be perceived as more of a controlled and safe environment that is accompanied by predictable environmental conditions and governed by competition rules. The higher level of emotional stamina likely serves as an important and adaptive function within PJs given the type of operational missions in which they must perform. The higher levels of emotional stamina in PJs likely plays an important role in performing in uncontrolled, unsafe, and unpredictable environments where the possibilities of being injured, disfigured, disabled, or killed are very real.

Another contributing factor to PJs' higher levels of emotional stamina may be influenced by extensive screening for mental health issues prior to entering and remaining in the career field. Only those who have fully recovered, have low susceptibility to recurrence, pose minimal safety risk, or have no history of mental health issues are allowed into the training pipeline. Those same standards do not apply to elite athletes. In fact, many elite athletes, including Michael Phelps, the most decorated Olympian of all time, and USATF World Champion and Olympic Medalist Noah Lyles, have openly discussed their own mental health struggles prior to competing in events.

Results suggest that PJs tend to be overall more socially outgoing than elite athletes. The results suggest that PJs are more affectionate, friendly (warmth), and outgoing (gregariousness). These social preferences may support the PJ team aspect of training as well as the job requirements of working within a Special Operations Command team across military branches and with specific joint North Atlantic Treaty Organization missions. Higher levels of occupational tempo (activity) and the tendency to seek out excitement and stimulation (excitement-seeking) serve as functional aspects given the job duties. For example, deploying into restricted, hostile, and politically sensitive environments and parachuting out of a plane to save a life are not the best career choice for highly introverted, risk-averse individuals, who prefer a slower paced social lifestyle. Being comfortable with a rapid tempo while continuously operating in groups and fluctuations in routine appears to be a characteristic of successful PJs.

On the other hand, the road to being an elite and Olympic-level track and field athlete can be lonely. Many athletes can spend significant time training in isolation from others to achieve their goals. For example, track and field athletes are often depicted alone in commercials, whether on a deserted road training before sunrise or an empty track at sunset. Allyson Felix, the most decorated track and field athlete of all time, winning 11 Olympic medals and breaking Carl Lewis's record, has shared stories of her sacrifices throughout her career, including missing her high school prom and adding in additional training alone to make sure she was ready to compete to the best of her ability. The extra time and energy athletes put into being elite often leaves them disconnected from their peer groups.

PJs' mission outcomes depend on team collaboration and team success. PJs deploy as a unit, and the importance of the team is highly valued. For PJs, the social functioning of the team could impact a life-or-death outcome. For elite athletes in both team and individual sports, individual statistics are often viewed as an indicator of successful performance above and beyond team performance. Furthermore, the same life or death outcomes do not apply to team performance, and athletes can often walk away from a team loss with fans praising them for their impressive individual performance.

The results of this study also indicate that PJs have higher levels of consideration for others (altruism) when compared to elite and Olympic-level track and field athletes. This difference may likely be attributed to the PJ career field motto "That Others May Live." The commitment of PJs to assisting others in need of help is a core component of their job. The higher the score on altruism, the more compelled one feels to rescue others, whereas the lower the score on altruism, the less compelled one feels to help others. While PJs are focused on saving the lives of others, elite athletes perform more for the glory of the medal and distinguishing themselves from others. Elite athletes do not have the freedom or luxury to pursue or show interest in other people's problems because of their desire for individual glory. Emotionally, athletes can relate to others (sympathy), but perhaps engage in self-preservation by limiting the energy

required to engage in the act of helping because of the physical and emotional drain.

PJs and elite and Olympic-level track and field athletes have similar levels of openness to experience. Of note, however, such elite athletes have a more active and vivid imagination than PJs (fantasy). As a group, the elite athletes are likely to spend more time using visualization techniques and engaging in creative and innovative thinking. As a result, they are often more likely to be open to thinking about strategies and ideas that are unique, original, and distinct from conventional methods. This is in sharp contrast to the reality that PJs must face in their day-to-day work. For PJs, their thinking must be grounded in reality, conventional wisdom, and proven methods. The severity and readiness to respond to life and death situations depend on where they choose to keep their mind focused on the practical and conventional. Their lower scores on fantasy suggest that as a group, PJs tend to focus their thoughts on what they consider to be objective and realistic.

Behaviorally, PJs are more open to going new places and trying new activities (actions). PJs must operate in a variety of environments, whether that be on land and sea or within extreme heat or cold. Because they operate in such unique environments, their openness to experiences is likely associated with a PJ's willingness to adapt. Having an openness to trying new and innovative techniques is also important to saving a life while in combat. A PJ's willingness to take risks and think "outside the box" likely serves as a functional difference when compared to elite and Olympic-level track and field athletes. In contrast, such athletes often find a routine that works for them, and they do not deviate from that performance routine. Such athletes may cling to rituals, routines, and even superstitions to achieve desired outcomes. The elite athlete is less likely to experience the chaotic environmental and situational changes PJs experience, especially when deployed. The demands to adapt are likely more constant for PJs than elite athletes. An emphasis is also placed on maximizing rest and recovery between training and competitions for elite athletes. The differences measured in the Openness to Experience domain support both groups of high performers in novel ways.

PJs also reported higher levels of confidence in their abilities (competence). PJ personnel deploy into unpredictable, challenging environments and provide emergency trauma and field medical care, which likely require high levels of perceived self-competence across a wide range of settings. A moment of self-doubt for a PJ could have dire consequences, such as the loss of life. Elite athletes' skills are domain specific to their sport in a much more predictable track and field arena. Although elite athletes might have a high level of self-competence within the arena they compete in, that self-competence may not extend into other areas of their life. Overall, PJs perform many skills with an extreme level of proficiency, while elite athletes are only required to be exceptional at one skill.

PJs' higher level of sense of responsibility and commitment to others (dutifulness) may be reflected by their dedication to rescue/recovery missions and their willingness to sacrifice their

own life for the prosperity of their country. PJs are making a commitment to the very people who are part of their job (i.e., their fellow PJs). If they do not execute their job duties perfectly, it could cost the life of the people they are trying to rescue and the lives of the PJs who are part of their group. They likely have a higher commitment to others because they operate in a group environment and the consequences of a commitment failure are likely higher. Athletes may feel more justified in letting commitments to others slip because they are focused on giving priority to the single mission of enhancing personal performance and earning a medal.

PJs report a higher need to achieve (achievement-striving) than elite and Olympic-level track and field athletes. Such elite athletes already have high levels of achievement when compared to the general population, but PJs have a significantly higher level. This finding may come as a surprise because the core perception of elite athletes is their ability to work hard to achieve their Olympic dreams. However, PJs report a stronger drive in this domain than elite athletes, highlighting the importance of high aspirations and work ethic to handle the PJ career field. The standards PJs set for themselves are extraordinarily high and are adaptive for their career demands. PJs are exposed to extremely dangerous situations, and their achievement-striving mentality provides them with the belief they will complete the mission with success.

PJs report higher levels of discipline to complete tasks (self-discipline) than elite athletes, suggesting they are less vulnerable to procrastinating or quitting before their job is complete. Elite athletes may choose to take a season off or have a hiatus from the competitive arena, but PJs are not afforded this luxury of exiting the career field and reentering when they feel more motivated. Along these same lines, PJs must exhibit high levels of self-discipline and motivation under intensely distracting environments to carry out their missions, whereas elite athletes are often encouraged to take a break, recover, and commence their training another day. Additionally, elite athletes have the infrastructure of their coach, trainers, and other support staff members to motivate them when they lack self-discipline and motivation.

There are three limitations of this study worth noting. First, the results of this study may not generalize to other special warfare career fields. Additionally, we focused on track and field athletes for the comparison group in this study, and the unique characteristics of the individual sport may impact the generalizability of our findings. For example, athletes from team sports may exhibit higher levels of extraversion and consideration for their teammates and therefore may be more like PJs rather than track and field athletes. Replicating this study with an additional group of elite athletes from a team sport may shed light on the drivers of personality differences between elite track and field athletes and PJs. Second, the NEO-PI-3 is a self-report assessment, and thus impression management and lack of full disclosure could impact the results. Although all participants were assured of the confidentiality of their results, some may have answered the questions in a more desirable way than others. Third, the lack of

demographic data available for this study prevented the researchers from matching participants on age, education, and other demographic variables that may impact similarities and differences between the two groups. Future studies may investigate groups with similar demographic variables such as race, age, marital status, and education.

The results of this study illuminate quantitative data measures on personality characteristics to assist leadership, embedded clinical psychologists, and performance psychology professionals with appropriate interpretation of psychological test scores assessing multiple areas of emotional, social, and behavioral functioning when evaluating PJs and elite track and field athletes. The data obtained from this research may help to improve readiness evaluations, as well as develop performance enhancement interventions. The results of the study may also provide insight into the strength and direction of specific personality traits universal to those who pursue and excel within physically and psychologically demanding high-performance occupations. Job duties of military personnel in high-risk, high-demand communities as well as elite athlete requirements require adaptation to highly strenuous, physically and psychologically demanding conditions. Although this study is exploratory in nature, it will help inform key personnel on the characteristics that may enhance or undermine performance.

Over the last decade, the military has increased attention on providing psychological skills training to help warfighters handle stress, thereby increasing performance.<sup>14–16</sup> Whether you are a PJ or elite athlete, it is clear: optimizing human performance in the competitive arena is the key to success. Although there are obvious differences in job duties, career demands, and performance conditions, both groups are striving for excellence under intense conditions. Even considering the differences in social, emotional, and behavioral functioning highlighted in this research, there are many avenues of collaboration between sport and military psychology worth pursuing because of the common goal of achieving peak performance under stressful and adverse conditions.<sup>16</sup>

Implementation of nontraditional and innovative embedded care strategies to help manage the demands placed on this population is becoming more of the norm. These strategies include embedding psychologists and performance enhancement professionals within special operations units to support mission readiness, recovery, and peak performance. This research may provide additional insight into how psychologists and performance enhancement professionals embedded in these units may leverage personality data to improve performance readiness and overall mission success. The results of this study can be used to improve the delivery of embedded mental health services geared toward improving training and enhancing health, recovery, and performance within operational units. By better understanding the psychological traits of PJs, the Air Force can improve selection, training, employment, and reconstitution of such a unique group of military personnel in a way that maximizes human and monetary capital.



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# Attention Network Changes of High-Altitude Migrants

Xin An; Getong Tao; Xinjuan Zhang; Hailin Ma; Yan Wang

- INTRODUCTION:** The present study aimed to explore whether there are changes in the alerting, orienting, and executive network efficiencies of attention function between high altitude immigrants and low altitude residents.
- METHODS:** Event-related potentials (ERP) were acquired during an attention network test (ANT). The high-altitude (HA) group comprised 22 college student immigrants who were born and raised at low altitudes and had lived at a HA (11,975 ft/3650 m) for 26 mo (tests were conducted when they returned to HA for 3 mo). The low-altitude (LA) group comprised 23 college students who had never visited HA areas before.
- RESULTS:** Compared with the LA group, the HA group had a higher pulse rate, lower oxygen saturation level, and decreased alerting and orienting effects in the behavioral results. The ERP results of the HA group showed a smaller P1 in the occipital area, a larger N1 both in the parietal and occipital areas of the alerting network, and a smaller P1 and larger N1 in the orienting network than the LA group. In the executive control network, the N2 amplitude of the HA group was more negative and the P3 amplitude of the HA group decreased in incongruent conditions.
- DISCUSSION:** Together, these findings suggest that high-altitude migrants are less effective at alerting and orienting than low-altitude residents. For executive control function, changes in the P3 amplitudes of incongruent conditions indicated a decrease in conflict inhibition underlying the executive-control network.
- KEYWORDS:** high altitude hypoxia, attention network, event-related potential, alerting, orienting, executive control.

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The Tibet Autonomous Region, located on the Qinghai-Tibet Plateau, or “the roof of the world,” has an average altitude of more than 13,123 ft (4000 m).<sup>4</sup> The average partial pressure of oxygen in this region is only 60–65% that at sea level.<sup>26</sup> In recent years, studies using neuroimaging technology have found that long-term repeated exposure to hypoxia causes a decrease in gray matter volume in the bilateral prefrontal lobes, right cingulate gyrus and left precentral gyrus, etc.<sup>32,33</sup> This impairs mental functions such as perception, attention, memory, decision making, and emotions, as well as social adaptation.<sup>3,24,34</sup>

Attention is the orientation and concentration of psychological activities on certain objects. Posner suggested that attention involves voluntary (endogenous) and involuntary (exogenous) systems.<sup>17</sup> Voluntary attention is a volitionally controlled, top-down process that is usually related to central symbolic cues. In contrast, involuntary attention is an automatic reflexive, bottom-up process elicited by abrupt peripheral cues. Furthermore, the attention network is composed of three functionally distinct neural networks: alerting, orienting, and executive control.<sup>18</sup> Alerting is defined as physically increasing response preparation

in reaction to an external warning stimulus. Orienting refers to the ability to prioritize sensory input by selecting a modality or location and shifting attention; for example, by distracting and refocusing attention. Finally, the executive control network involves conflict control and resolution during habitual response inhibition, decision making, and error detection.<sup>18</sup> Based on Posner's theory, Fan designed the attention network test (ANT), which can effectively measure the functions of the three attention networks.<sup>6</sup> The frontal and parietal lobes of the right hemisphere of the brain are involved in the alerting process.<sup>6,22</sup> In the orienting process, the dorsal and ventral attention systems are involved.<sup>5</sup> The former, responsible for top-down visuospatial orientation, consists of the frontal eye field (FEF), intraparietal

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sulcus, and superior parietal lobe. The latter, responsible for bottom-up reorientation, consists of the temporoparietal junction (TPJ) and the ventral frontal cortex (VFC).<sup>17</sup> In the executive control process, the anterior cingulate cortex (ACC) and dorsolateral prefrontal cortex play an important role in monitoring and resolving conflict.<sup>27</sup>

Event-related potentials (ERP) are special brain potentials evoked by stimuli, and ERP components reflecting specific cognitive functions can be extracted by using the fixed stimulus-response time-lock relationship and the computer's average superposition processing. These brainwave components are typically named using a combination of letters and numbers. P and N indicate the positive and negative trends of the waveform, respectively, whereas the numbers indicate the position of the peak in the waveform.<sup>11</sup> Studies examining ERP have found that P1 and N1 components in the parietal and occipital regions appear after 80–200 ms of stimulus presentation, which are related to alerting and orienting functions in the attention network.<sup>35</sup> The P1 is generally thought to be the earliest influence of spatial attention on visual processing.<sup>15</sup> The attended stimulus can also elicit a larger N1 amplitude. The increased amplitudes of P1 and N1 reflect a sensory-gain control mechanism that results in the enhanced perceptual processing of the attended stimulus.<sup>35</sup> The N2 component, which is associated with conflict monitoring in executive control function, occurs between 200–350 ms after stimulus presentation. The ACC is an anatomical region of the brain that affects the N2, which recruits top-down resources to improve stimulus evaluation when conflict is detected.<sup>10</sup> Many studies with flanker tasks have indicated that incongruent flanker conditions elicit a more negative N2 than congruent conditions.<sup>19,20</sup>

P3 is another component that is frequently measured in studies of executive control.<sup>29</sup> Its subcomponents, P3a and P3b, are often elicited about 300–600 ms after the stimulus.<sup>29</sup> The frontally generated P3a reflects involuntary and transient allocation of attention to distractors or novel stimuli. Parietal-generated P3b is a task-related activity regarded as related to the control of cognitive attention and the stimulus evaluation process.<sup>29</sup> In the present study, we focus on P3b, the traditional P3, in the ANT. However, there is controversy over in which condition P3 amplitude was larger.<sup>15</sup> Some of the authors have concluded that there was a larger P3 amplitude in the incongruent target and suggested that P3 amplitude was enhanced by response inhibition,<sup>9</sup> while others argue that reduction in amplitude may be related to greater response inhibition.<sup>20</sup>

Various studies have investigated the effects of high altitude on attention. Studies using visual search tasks and the digit symbol substitution test have found that people exposed to high altitude environments for 8 h had reduced attention capacity and decreased scores in visual search tasks.<sup>21</sup> Additionally, a neuroimaging study has shown that high altitude influences brain areas related to attention processing (frontoparietal network), with a decreased volume of gray matter in the bilateral prefrontal area, right cingulate gyrus, and precentral gyrus among members of the Han ethnic group who were born and grew up (more than 20 yr) in high-altitude environments.<sup>32</sup> Previous research has also indicated that high-altitude subjects

[individuals who were born and grew up in low-altitude areas but migrated to 11,975 ft (3650 m) in adulthood and have lived at high altitude for at least 3 yr] had longer reaction times and lower accuracy in spatial attention tasks compared to low-altitude subjects (individuals who have only lived in low-altitude areas). In high perceptual load conditions, the high-altitude subjects had a smaller N1 and P3 compared to the low-altitude subjects.<sup>28</sup> Furthermore, their bilateral occipital regions were activated and the lateralization effects of the attention process disappeared.<sup>28</sup> It has been suggested that long-term exposure to high altitude may influence spatial attention and the brain adapts to compensate for high-altitude environments.<sup>28</sup>

High altitude affects attention network functions. Our 2-yr longitudinal study using the ANT explored the temporal effects of high-altitude environments and showed that Han students who entered the 11,975-ft (3650-m) high-altitude area for the first time after adulthood experienced a significant decline in executive control network function after staying at high altitude for a week. Recovery occurred after 1 mo but declined again after 2 yr of living at high altitude.<sup>1</sup> This result suggested that high-altitude environments affect attention and the extent of the effect varies with the duration of residence.<sup>1</sup> However, the neural mechanisms of the effect of high altitude on attention network functions are still unclear. Previous studies have found that long-term high-altitude exposure influences executive control function.<sup>12,13</sup> Using the flanker task and go/no-go task, studies showed decreases in the conflict monitoring and conflict control abilities of Han students who migrated to high altitudes and stayed there for more than 3 yr.<sup>12,14</sup> However, evidence for the influence of high altitudes on alerting and orienting is still inconclusive. In addition, our previous work examined the neural mechanisms of high altitudes on Tibetans' attention network functions.<sup>35</sup> We found that young Tibetans who grew up at an altitude of 13,780 ft (4200 m) had decreased orienting function but increased executive control function.<sup>35</sup> Due to long-term adaptation to high-altitude environments, the genetic and physiological structures of indigenous residents are different from those of immigrants.<sup>1</sup> Therefore, results in indigenous residents cannot be extended to immigrants. In recent years, an increasing number of immigrants have visited high-altitude areas for work or travel. Thus, it is important to study the influence of exposure to high altitudes on attention function in immigrants from low-altitude areas.

In the current study, ANT was used and ERP was recorded to systematically explore the changes in attentional function of high-altitude migrants. Based on existing studies, due to high-altitude, exposure can damage the brain areas related to attention such as the bilateral prefrontal area, right cingulate gyrus, and precentral gyrus;<sup>3,31,32</sup> it also causes changes in ERP, such as the larger N1, N2, and smaller P1, P3.<sup>12,14,28</sup> We hypothesized that high altitude would affect attention networks, indicated by decreased scores on behavioral tests measuring alerting, orienting, and executive control. In the ERP results, we hypothesized that there would be a decreased P1 and increased N1 amplitude in both alerting and orienting networks, and increased N2 amplitude and decreased P3 amplitude of incongruent conditions in the executive control network.



## METHODS

### Subjects

A total of 49 healthy Han college students (age range: 19–26 yr old; 25 men) participated in our experiment. We used G\*Power 3.1<sup>7</sup> to calculate the required sample size ( $F = 0.25$ ,  $\alpha = 0.05$ ,  $1 - \beta = 0.80$ ). The results showed that a total of 24 subjects were adequate for detecting an effect of altitude on N1 and P1 amplitude in the alerting and orienting networks, and 34 subjects were adequate for detecting an effect of altitude on N2 and P3 amplitude in the executive control network. Here, we sought to collect data from 49 participants in total. They were all right-handed and had normal or corrected-to-normal vision without psychiatric or neurological disorders. They had no stress-inducing activities, such as college examinations, for a month before taking the test. In addition, they were required to get adequate sleep the day before the test and to not take drugs, drink coffee, or engage in other behaviors that might interfere with the test. All participants were born and raised in low-altitude areas (<3281 ft or 1000 m). The 25 students in the high-altitude (HA) group were from Tibet University and had lived in Lhasa (11,975 ft/3650 m) for 26 mo. They were third-year college students who studied at high altitudes from March to July and September to December (9 mo in total), all returning to low altitudes (<1000 m) during the rest of the year. The 24 students in the low-altitude (LA) group had never been in a high-altitude environment before. Because of excessive eye movements and artifacts, two subjects from the HA group and two subjects from the LA group were excluded. Finally, 22 subjects in the HA group ( $21.88 \pm 1.33$  yr; 11 men) and 23 subjects in the LA group ( $21.36 \pm 1.60$  yr; 11 men) were included in the final analysis of behavioral and EEG data. The two groups were matched in terms of age, sex, education, and scores on national college admission examinations. This study followed the Declaration of Helsinki and was approved by the Health Science Research Ethics Board of the Institute of Psychology, Chinese Academy of Sciences (No. H16037). Written informed consent was obtained from all participants, who received compensation for their participation. The HA group was tested at an altitude of 11,975 ft (3650 m) when they returned to high altitude for 3 mo. The LA group was tested at an altitude of 131 ft (40 m). To avoid test differences caused by changes in equipment, we brought the equipment from the LA lab to the HA lab. Therefore, the same laboratory equipment was used for both tests.  $S_{pO_2}$  and pulse rate were measured with a warmed hand in a resting condition using a pulse oximeter (DEDAKJ-CMS50D, Shenzhen City, China) before completing the ANT to obtain information regarding the degree of hypoxia in the two groups.  $S_{pO_2}$  was significantly lower in the HA group than in the LA group ( $P < 0.01$ ), while pulse rate was significantly higher in the HA group ( $P < 0.001$ ) (Table I).

### Procedure

All the stimulus presentation for the ANT and behavioral response collection were conducted using software package

**Table I.** Age, Education, Pulse Rate, and  $S_{pO_2}$  of Each Group [Mean (SD)].

	LA (N = 23)	HA (N = 22)	t	P
Age (yr)	21.4 (1.6)	21.9 (1.3)	-1.3	0.22
Education (yr)	15.3 (1.5)	15.8 (1.2)	-1.4	0.16
Pulse rate (bpm)	74.0 (11.3)	82.0 (9.7)	-2.7*	0.01
$S_{pO_2}$ (%)	97.4 (1.1)	90.7 (2.8)	10.7**	0.001

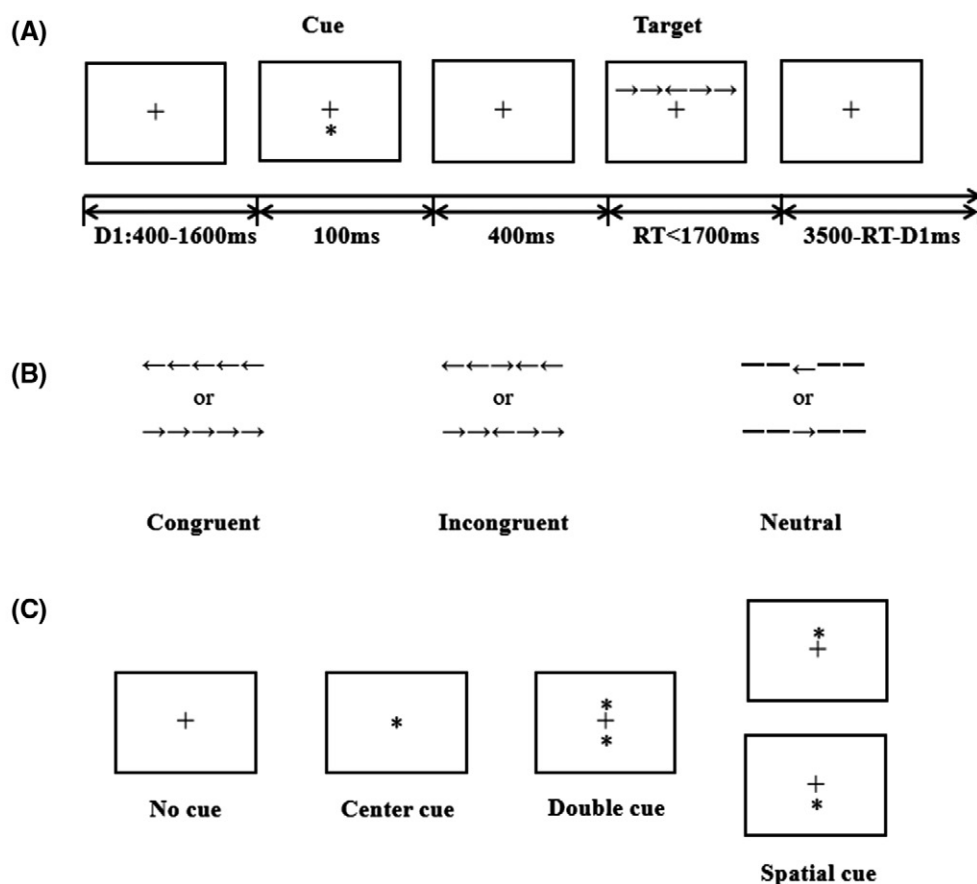
HA = high altitude group; LA = low altitude group. \* $P < 0.05$ , \*\* $P < 0.01$ .

E-prime 2.0 (Psychology Software Tools, Inc., Pittsburgh, PA). The procedure is illustrated in Fig. 1.

Subjects were seated in a comfortable chair at a viewing distance of 50–60 cm in front of the computer monitor in a quiet room. A fixation cross (+) 0.5 cm  $\times$  0.5 cm displayed on the center of the screen was maintained for a variable duration between 400 and 1600 ms, followed by a cue that lasted 100 ms. Subsequently, the target array appeared 500 ms after cue onset. There were four types of cue conditions: no cue, center cue, double cue, and spatial cue. Of note, the no cue was the condition without any cue after the fixation cross. The center cue was the condition when a “+” symbol of 0.5 cm  $\times$  0.5 cm briefly replaced the center fixation cross. The double cue condition referred to simultaneous “+” symbols of 0.5 cm  $\times$  0.5 cm appearing both above and below the fixation cross, and the spatial cue was the condition when an “+” appeared either above or below the fixation cross and thereby cued the location where the target array would appear. The target array consisted of five horizontally arranged arrows 1.0 cm in length, including one central target arrow and four flankers, and displayed 1.06° above or below the fixation cross. The target conditions could be congruent (flanker arrows had the same direction as the center arrow), incongruent (flanker arrows pointed to the opposite direction), or neutral (a central arrow with four horizontal lines). The congruent targets and incongruent targets were equal in number and presented randomly.

For each trial, responses were recorded by pressing the left mouse button with the right hand when the target arrow pointed to the left and the right mouse button when the arrow pointed to the right. Subjects were instructed to respond rapidly and accurately. Target stimulus were presented 400 ms after the cue interval and maintained on the screen until a response was made by the participant, or until a maximum of 1700 ms had elapsed. The task began with a complete practice block of 20 trials, followed by three experimental blocks of 96 trials, lasting about 20 min. The reaction time (RT), accuracy rate, and ERP were recorded during the task.

According to previous research, based on both congruent and incongruent correct response trials RT, the three attention networks were defined as follows: alerting effect =  $RT_{no\ cue} - RT_{center\ cue}$ —the larger difference indicated a greater alerting effect because attention will focus on the cue where the target stimulus will appear, thereby reducing the RT; orienting effect =  $RT_{center\ cue} - RT_{spatial\ cue}$ —the location of the spatial cue was the position where the target would later occur, so a greater difference meant a better orienting effect; and conflict effect =  $RT_{incongruent} - RT_{congruent}$ —in the incongruent condition, the executive control network plays an important role in suppressing the interference stimulus to effectively process the target



**Fig. 1.** Materials and procedure. A) The sequence of events for the ANT used in the present study; B) the three target conditions; and C) the four cue conditions.

stimulus, resulting in a longer RT than the congruent condition. Hence, the smaller the difference, the better the executive control effect.<sup>5</sup>

Electroencephalogram (EEG) data were recorded during the ANT task with a 64-channel amplifier (SynAmps2, NeuroScan Inc., Herndon, VA, USA) and data acquisition software (Scan4.5, Neuroscan). The 64 Ag-AgCl electrodes were placed on the scalp by means of a head cap (NeuroScan Inc.), according to the 10-20 International System. Electrodes were online referenced to a reference site in the middle of the Cz and CPz locations, and an electrode placed between Fpz and Pz was used as the ground. Electrode impedance were maintained at 5 k $\Omega$  or less. Horizontal and vertical eye movements were recorded from tin electrodes placed at the outer canthi of both eyes, and above and below the left eye, respectively. EEG and electro-oculogram (EOG) signals were continuously acquired and sampled at a rate of 500 Hz, applying a 0.05–100 Hz band-pass.

### Statistical Analysis

All statistical analyses were conducted with SPSS (SPSS, Inc., Chicago, IL, USA) for Windows, with a significance level set at 0.05. The Student's *t*-test was conducted to analyze the score of the three network effects, with the altitude group as the independent variable.

EEG data were re-referenced to the average of bilateral mastoid electrodes. The EEG and EOG data were digitally filtered

with a 0.1–30 Hz bandpass filter. Trials with eye blink/eye movements or muscle activity were excluded from further analysis. A regression procedure implemented in Neuroscan software (Neuroscan Inc.) was used to identify vertical and horizontal ocular artifacts and this study further removed them from the signal; trials with various artifacts were rejected with a criterion of  $\pm 75 \mu V$ . Epochs were computed for the 1000 ms after the onset of the target stimulus relative to a 200-ms pre-stimulus baseline. Each participant's average waveform of each of the four conditions was calculated and the incorrect response trials were excluded in the average ERP calculations.

The time frames of posterior target P1 were defined as the most positive peak at 80 to 150 ms and N1 were defined as the most negative peak at 150 to 250 ms after the onset of target stimulus. On the basis of previous studies, the posterior target P1 and N1 component was determined over three sites at the parietal area (P3, Pz, and P4) and three sites at the occipital area (O1, Oz, and O2), respectively.<sup>15,35</sup> A mixed factors ANOVA was adopted to the different network effects. A group (HA and LA)  $\times$  cue condition (no cue and double cue)  $\times$  brain area (the parietal area and the occipital area) ANOVA was carried out for the P1 and N1 mean components to analyze the alerting network effect. Three-way mixed design repeated measures analysis of variance was conducted with two within-subject factors, cue condition (center cue and spatial cue) and brain area (the parietal area and the occipital area), and one between-subject

**Table II.** Mean Reaction Times (ms) Based on Both Congruent and Incongruent Correct Response Trials of Each Experimental Condition for the Two Groups [Mean (SD)].

GROUP	NO CUE		DOUBLE CUE		SPATIAL CUE		CENTER CUE	
	CO	IC	CO	IC	CO	IC	CO	IC
LA	559 (52)	658 (74)	508 (55)	608 (66)	476 (54)	563 (68)	529 (61)	630 (71)
HA	591 (63)	681 (78)	537 (60)	647 (74)	518 (75)	602 (81)	550 (77)	670 (86)

CO: congruent; IC: incongruent; LA: low altitude; HA: high altitude.

factor, group (HA and LA), on mean amplitude of the P1 and N1 components to evaluate the orienting network effect.

In previous studies, the amplitudes of N2 and P3 were always largest at the midline electrode sites along the anterior to posterior axis, including FCz, Cz, CPz, and Pz.<sup>8,16</sup> Thus, in the current study, we analyzed N2 and P3 components from these electrode sites. The N2 and P3 components were analyzed for the time frame from 280 to 500 ms and 450 to 700 ms, respectively, following the presentation of target stimulus. We examined the mean amplitude of these two components for statistical analysis. We conducted a target condition (congruent and incongruent)  $\times$  group (HA and LA) mixed-model ANOVA to analyze the N2 and P3 components. Simple effect analyses were adopted to further investigate interaction effects.

## RESULTS

**Table II** summarizes the mean RT based on both congruent and incongruent correct response trials of each experimental condition between groups. Furthermore, **Table III** displays the calculation of the network scores. Since the average accuracy rate of both groups was over 99% and there was no significant difference, the accuracy results are no longer presented.

With respect to the alerting network, *t*-testing indicates a significant effect of group [ $t(43) = 2.65, P < 0.01$ ]. The alerting scores of the HA group were lower than those of the LA group. As for the orienting network, there was a significant effect of group, with a larger orienting score in the LA group than in the HA group [ $t(43) = 2.90, P < 0.01$ ]. However, there were no differences between the executive control score in either group [ $t(43) = -1.04, P > 0.05$ ], but there was also a downward trend in executive control efficiency (90.9 vs. 98.4). The scores of the attention network are shown in **Fig. 2** and **Table III**.

### Posterior Target P1 Amplitude

We observed a significant main effect of the cue condition [ $F(1,43) = 49.84, P < 0.001, \eta^2 = 0.54$ ], showing that the P1 amplitude of the no cue condition was increased compared with that of the double cue condition. The interaction between

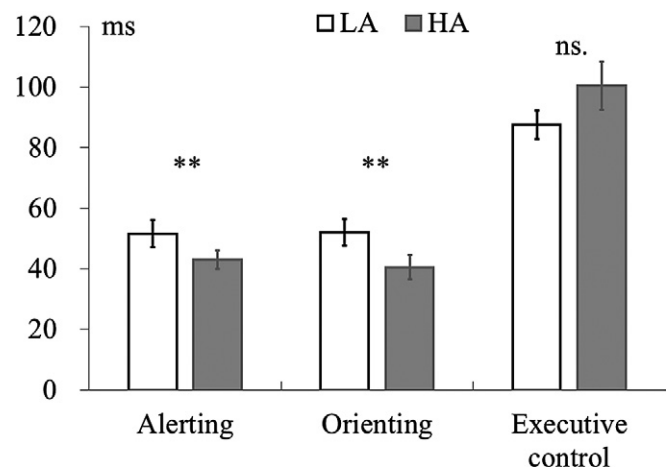
the cue condition, brain area, and group were significant [ $F(5, 39) = 3.65, P < 0.01, \eta^2 = 0.32$ ], with increased P1 amplitude in the occipital area of the LA group compared with the HA group in the no cue condition ( $P < 0.05$ ) (see alerting in **Fig. 3**). There were no other main effects or interactions.

### Posterior Target N1 Amplitude

The main effect of cue condition was significant [ $F(1,43) = 119.63, P < 0.001, \eta^2 = 0.74$ ], indicating that the N1 amplitude of the double cue condition was more negative than that of the no cue condition. The main effect of group was significant [ $F(1,43) = 5.14, P < 0.05, \eta^2 = 0.11$ ]. The N1 amplitude of the HA group was more negative than that of the LA group. The interaction between the cue condition, brain area, and group were significant [ $F(5, 39) = 5.42, P < 0.01, \eta^2 = 0.41$ ]. In the double cue condition, the N1 amplitude in the occipital area of the HA was more negative than that of the LA group ( $P < 0.05$ ). In the no cue condition, the N1 amplitude in both the parietal and occipital area of the HA were more negative than that of LA group ( $P < 0.05$ ). There were no other main effects or interactions.

### Posterior Target P1 Amplitude

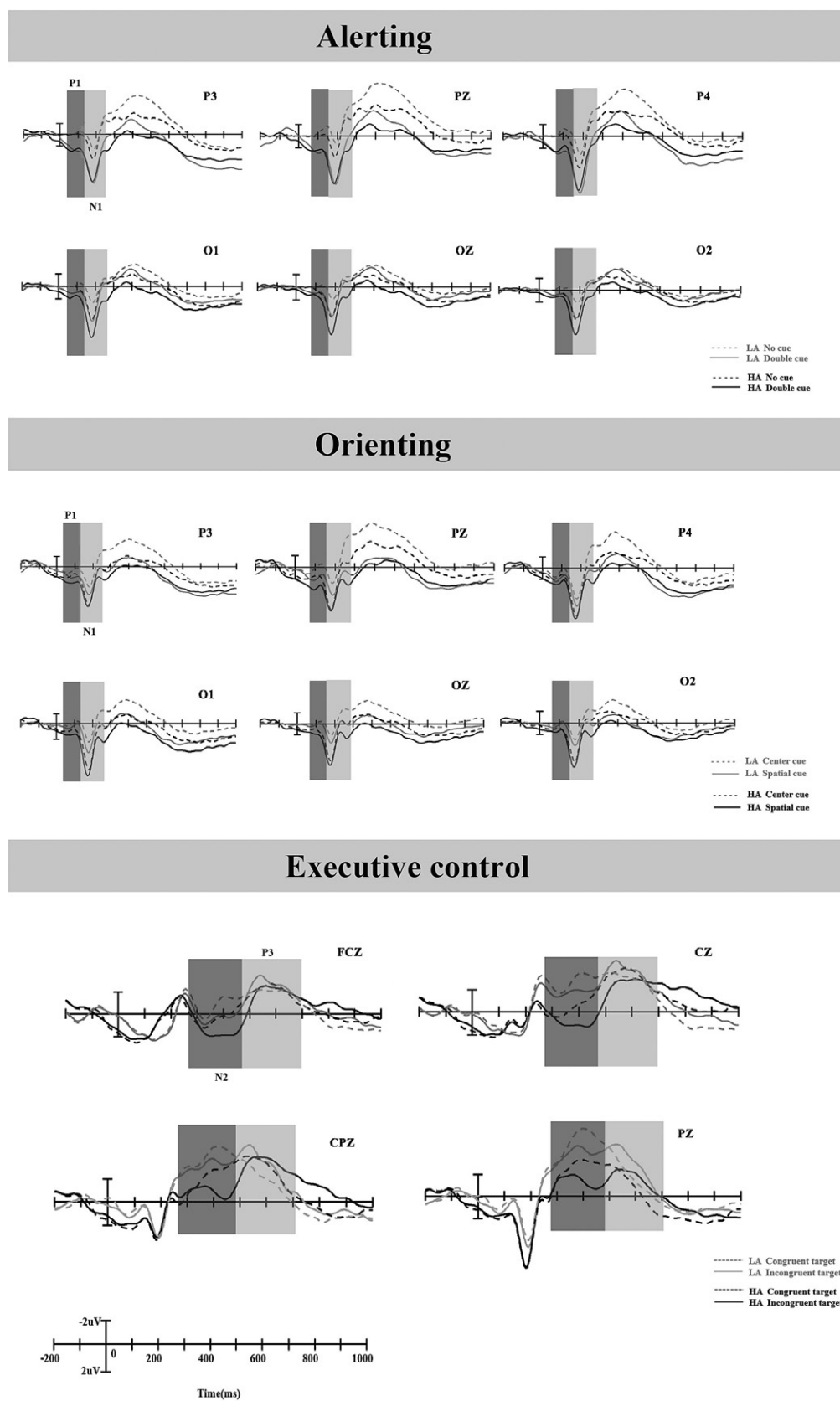
We found a significant main effect of cue condition [ $F(1,43) = 21.37, P < 0.001, \eta^2 = 0.33$ ], indicating that the P1 amplitude of the center cue condition was increased compared with that of the spatial cue condition. The main effect of group was significant [ $F(1,43) = 11.44, P < 0.01, \eta^2 = 0.21$ ]. The P1 amplitude of the LA group was more positive than that of the HA group (see orienting in **Fig. 3**). There were no other main effects or interactions.

**Fig. 2.** Attention network scores based on the RTs of the two groups (Mean  $\pm$  SEs). \*\* $P < 0.01$ .**Table III.** Attention Network Scores Based on the RTs of the Two Groups [Mean (SD)].

	LA (N = 23)	HA (N = 22)	t	P
Alerting	55.79 (19.67)	42.36 (13.65)	2.7	0.011
Orienting	59.42 (17.54)	44.85 (16.12)	2.9	0.006
Executive control	90.88 (24.96)	98.43 (23.61)	-1	0.304

RT: reaction time; LA: low-altitude group; HA: high-altitude group.





**Fig. 3.** ERP waveforms of alerting effect, orienting effect, and executive control in the two groups. The P1 and N1 waveforms were located in the parietal areas (P3, Pz, P4) and occipital areas (O1, Oz, O2) at 80 to 150 ms and 150 to 250 ms. The N2 and P3 waveforms were located in the anterior to posterior axis (FCz, Cz, CPz, Pz) at 280 to 500 ms and 450 to 700 ms.

### Posterior Target N1 Amplitude

Regarding the target N1 amplitude, the main effect of cue condition was significant [ $F(1,43) = 32.44, P < 0.001, \eta^2 = 0.43$ ], with more negative N1 amplitude in the spatial cue condition compared with that of the center cue condition. The main effect of group was significant [ $F(1,43) = 14.90, P < 0.001, \eta^2 = 0.26$ ], demonstrating that the N1 amplitude of the HA group was more negative than that of the LA group (see orienting in Fig. 3). There were no other main effects or interactions.

### Target N2 Amplitude

With respect to the target N2 amplitude, the main effect of target condition was significant [ $F(1,43) = 24, P < 0.001, \eta^2 = 0.36$ ], with larger N2 amplitudes in incongruent conditions than in congruent conditions. The main effect of group was significant [ $F(1,43) = 4.80, P = 0.040, \eta^2 = 0.10$ ] and the N2 amplitude of the HA group was more negative than that of the LA group (see executive control in Fig. 3). There were no other main effects or interactions.

### Target P3 Amplitude

With respect to the target P3 amplitude, we observed a significant interaction between target condition and group [ $F(1,43) = 3.60, P = 0.036, \eta^2 = 0.18$ ], with smaller P3 amplitude in the HA group than in the LA group under incongruent conditions [ $F(1,43) = 3.12, P = 0.041, \eta^2 = 0.13$ ] (see executive control in Fig. 3). There were no other main effects or interactions.

## DISCUSSION

This study was designed to explore whether there are changes in attention network between high altitude immigrants and low altitude residents. Behavioral data showed a decrease in alerting and orienting efficiency scores in the HA group. There was also a downward trend in executive control efficiency. The higher pulse rates and lower blood oxygen saturation of the HA group are responsible for these effects. Correspondingly, in the alerting network, the P1 amplitude of the HA group was smaller than the LA group in the occipital area in the no cue condition, and the N1 amplitude of the HA group was larger in the double cue condition in the occipital area and larger in the no cue condition in both the parietal and occipital areas. In the orienting network, the P1 amplitude of the HA group was smaller and the N1 amplitude of the HA group was larger. Compared with the LA group, the N2 amplitude of the HA group was larger in the incongruent condition, and the P3 amplitude of the HA group was smaller in the executive control function. These results suggest that the attention networks for alerting, orienting, and executive control of high-altitude migrants was more decreased than those of low-altitude residents, which may be caused by high altitude hypoxia exposure.

Behavioral performance revealed a high-altitude effect on alerting and orienting functions. The efficiency of alerting and orienting in the HA group was lower than that in the LA group. The decreased alerting efficiency in the HA group indicated

that they needed more time to focus on cue location. The lower orienting network efficiency suggests that the HA group did not benefit as much as the LA group from physical or symbolic cues that direct attention to the likely location or identity of upcoming target information. We inferred that the decline in these two functions might result from changes in the neural systems that support these functions.

Of note, the ERP results greatly corresponded with behavioral performance in alerting and orienting efficiency. Specifically, concerning the post-target P1, the amplitude of the alerting-related post-target P1 of the HA group was smaller than that of the LA group in the no-cue condition. P1, an early component of the attention process, was enhanced by increasing attention load, reflecting the early processing of stimuli. The decreased P1 amplitude in the HA group indicated weak perceptual processing of target onset, reflecting poor alerting. In addition, the HA group had a smaller orienting related P1 amplitude, which is similar to the results of a previous aging study. This suggests that there may be a correlation between the effects of high altitude and aging through common neural mechanisms. Furthermore, in the orienting function, a center cue showed a greater positive P1 than those following a spatial cue in both the HA and LA groups. This is a common finding that invalid cues elicit a larger P1 than valid cues.<sup>30</sup> The decreased P1 amplitude in the HA group indicated that they were not as sensitive to less informative cues (invalid cues like center cues in our study) as the LA group.

The amplitude of post-target N1 was greater for the HA group than for the LA group both in the alerting and orienting functions, similar to the previous study.<sup>26</sup> The N1 amplitude reflects the difficulty of target discrimination.<sup>25</sup> The increased N1 amplitude of the HA group demonstrated that a high-altitude environment might affect the early perceptual processing of attended stimuli, resulting in the HA group showing a stronger engagement with the target properties and experiencing greater difficulty in target discrimination than the LA group. Compared with residents in lower-altitude areas, previous researchers using ANT also demonstrated that residents of higher altitude regions had more negative N1 amplitudes in their orienting network.<sup>35</sup> This indicated that mental resources were limited in HA residents for the alerting and orienting networks. In addition, consistent with previous research, the post-target N1 was more negative in the double-cue condition than in the no-cue condition in the alerting function and more negative following spatial cues compared to center cues in the orienting function.<sup>30</sup> This suggested that post-target N1 reflects the characteristics of the stimulus and may be related to top-down modulation of a visual discriminative process at attended locations.

In incongruent trials, the HA group had a smaller P3 amplitude than the LA group, suggesting that high-altitude environments influence the conflict-resolving stage in the executive control process, meaning that the conflict-resolving ability of the HA group was decreased. The P3 amplitude is associated with attentional resources used to improve cognitive control.<sup>29</sup> The smaller the amplitude, the less attentional resources are

available. A decrease in the P3 amplitude was observed in the HA group. A possible explanation is that, compared to the LA group, the HA group required more attentional resources to overcome conflict when performing the same task, which was regarded as a dysfunction of attentional resource allocation and inhibition control in patients with neurotrauma.<sup>2</sup> This means that, with their limited attentional resources, the HA group always has a high cognitive demand to overcome conflict control. Similarly, our previous study found that P3 amplitude was smaller in the HA group, indicating that long-term exposure to high altitudes consumes attentional resources.<sup>26</sup> In addition, we examined the effects of high altitude on executive control using the flanker task.<sup>14</sup> The results showed that the HA group had a smaller P3 amplitude than the LA group in incongruent conditions, and incongruent P3 components were localized in the parietal cortex. The parietal cortex, which plays a key role in conflict resolution, was affected by long-term high-altitude exposure.<sup>3</sup> This explains the decrease in the incongruent P3 amplitude in the HA group. Therefore, we conclude that executive control function is altered after exposure to high-altitude areas as a consequence of the affected cognitive process in the conflict-resolution stage.

For the behavioral results, the executive control function scores between the two groups were not significant; however, the results still showed a declining trend at high altitudes. The disappearance of behavioral effects may be due to the lower sensitivity of the behavioral tests. The ANT detects executive control mainly by judging the direction of an arrow. It is relatively simple for our test subjects, with an average correct rate of over 99%, though there may be a ceiling effect. Behavioral effects may be more obvious with a more difficult task. After the ANT task, we asked the subjects to complete a more difficult Stroop color word task, which specifically detects executive control function, and found that the behavioral RT of the HA and LA groups were significantly different, as reported in another paper.<sup>23</sup>

There were some limitations to the current study. First, although the subjects lived at high altitude for a total of 26 mo, they returned to low altitude several times to rest. Previous studies have shown that the adaptation period for living at or above 11,975 ft (3650 m) can be divided into three stages. The first stage is the acute adaptation period (3 d after entering the high-altitude environment), during which individuals are prone to acute mountain sickness. The second stage is subacute adaptation (within 6 mo after entering the high-altitude environment). Most people can compensate during this stage through compensatory mechanisms with the extension of exposure time and gradually adapt to the hypoxic environment. The third stage is chronic adaptation or complete hematocrit adaptation, in which chronic altitude sickness may occur and manifest as excess red blood cells and severe reversible tissue hypoxia.<sup>36,37</sup> These physiological conditions also affect mental functioning. The test used in this study was conducted when the subjects had just returned to high altitude after spending 3 mo in a low-altitude area. They may have been experiencing both acute and chronic hypoxia. To better illustrate the impact

of high-altitude exposure on the attention network in future research, we will strictly control the duration of the subjects' stay at high altitude.

For the second limitation, the subjects were distributed across 13 provinces in China before they were admitted to Tibet University. We were unable to gather data for the baseline test before the participants entered high altitude. Therefore, it was not possible to conduct a longitudinal study, which is another limitation of this study. In future research, we will consider selecting army soldiers as test subjects for a longitudinal study, since they are assembled first at low altitude before entering Tibet.

For the third limitation, the advantage of ERP is its high temporal resolution; however, its spatial resolution is insufficient. In the future, various technical methods, such as fMRI, could be used to explore this effect collaboratively. In addition, we investigated the effects of high altitude on cognitive function by comprehensively considering the many factors that make up a high-altitude environment, including special natural and cultural environments such as hypobaric hypoxia, low temperatures, intensive ultraviolet radiation, and unique living customs. Future studies should independently examine these factors.

Finally, can these altered cognitive functions recover after returning to low altitude? How long does recovery take? Can cognitive training be used to maintain a good cognitive level in high-altitude environments? These issues should be explored further in future studies.

In conclusion, the current study indicates that the attentional network was decreased in high-altitude immigrants compared with low-altitude residents. The changes in attention function were due to the influence of high-altitude exposure on attention-related areas of the brain.

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# Head-Mounted Dynamic Visual Acuity for G-Transition Effects During Interplanetary Spaceflight: Technology Development and Results from an Early Validation Study

Ethan Waisberg; Joshua Ong; Nasif Zaman; Sharif Amit Kamran; Andrew G. Lee; Alireza Tavakkoli

- INTRODUCTION:** Dynamic visual acuity (DVA) refers to the ability of the eye to discern detail in a moving object and plays an important role whenever rapid physical responses to environmental changes are required, such as while performing tasks onboard a space shuttle. A significant decrease in DVA has previously been noted after astronauts returned from long-duration spaceflight (0.75 eye chart lines, 24 h after returning from space). As part of a NASA-funded, head-mounted multimodal visual assessment system for monitoring vision changes in spaceflight, we elaborate upon the technical development and engineering of dynamic visual acuity assessments with virtual reality (VR) technology as the first step in assessing astronaut performance when undergoing G-transitional effects. We also report results from an early validation study comparing VR DVA assessment with traditional computer based DVA assessment.
- METHODS:** Various VR/AR headsets have been utilized to implement DVA tests. These headsets include HTC Vive Pro Eye system. Epic's game engine UnrealEngine 4 Version 4.24 was used to build the framework and SteamVR was used to experience virtual reality content. Eye tracking technology was used to maintain fixation of the participant. An early validation study with five participants was conducted comparing this technology versus traditional DVA with a laptop.
- RESULTS:** The head-mounted technology developed for assessing DVA changes during G-transitions is fully functional. The results from the early validation study demonstrated that the two DVA tests (laptop-based and VR) indicated a strong association between both methods (Pearson correlation coefficient of 0.91). A Bland-Altman plot was employed to assess levels of agreement, with all data points falling within the limits of agreement.
- DISCUSSION:** The results from this early validation study indicate that head-mounted DVA assessment performs similarly to traditional laptop-based methods and is a promising method for assessing DVA during spaceflight, particularly in G-transitions. Future studies are required for further assessment of validation and reliability of this technology. With its ease of use, accessibility, and portable design, VR DVA has the potential in the near-future to replace conventional methods of assessing DVA. The technology will likely be an important aspect to help monitor functionality and safety during interplanetary missions where astronauts are exposed to G-transitions.
- KEYWORDS:** dynamic visual acuity assessment, long duration spaceflight, ocular monitoring.

Waisberg E, Ong J, Zaman N, Kamran SA, Lee AG, Tavakkoli A. Head-mounted dynamic visual acuity for G-transition effects during interplanetary spaceflight: technology development and results from an early validation study. *Aerosp Med Hum Perform.* 2022; 93(11):800–805.

Dynamic visual acuity (DVA) refers to the ability of the eye to visually discern detail in a moving object. DVA plays an important role whenever rapid physical responses to environmental changes are required, from playing sports to performing tasks onboard a space shuttle. DVA depends on several factors including: the vestibulo-ocular reflex (Fig. 1), catch-up saccades, and possibly visual motion processing.<sup>13</sup> One day after astronauts returned from long-duration spaceflight, a decrease in DVA of approximately 0.75

eyechart lines has been observed, with some astronauts having a reduction in DVA similar to a group of vestibular-impaired

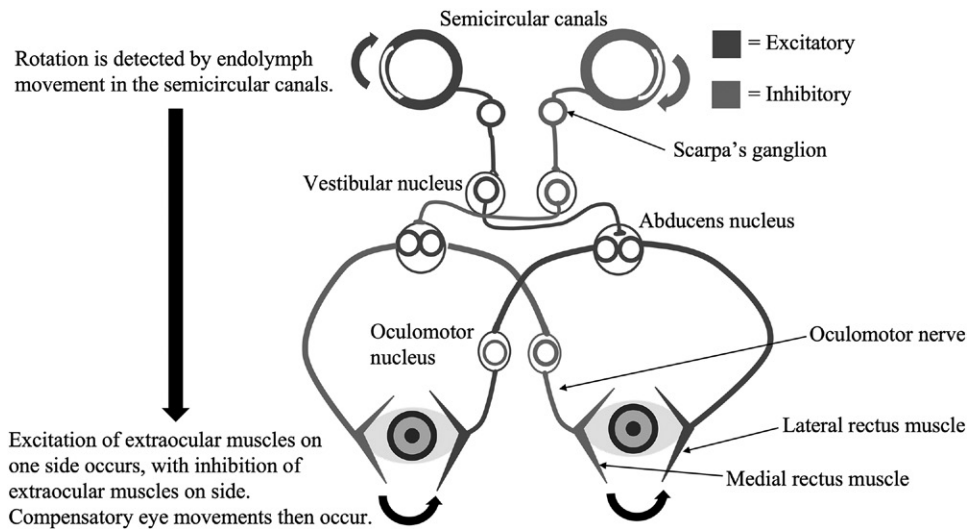
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**Fig. 1.** The vestibulo-ocular reflex uses eye movement to stabilize images on the retina when movement of the head is detected about any axis (vertical, horizontal, torsional). Otoliths detect translation of the head, while semicircular canals detect rotation. Movement of the eyes then occurs from excitatory signals to extraocular muscles on one side, and inhibitory signals to extraocular muscles on the other side.

patients.<sup>11</sup> Although these results are significant, they may underestimate the impact of G-transitions on DVA as they were collected 24 h after landing. This decrease in DVA was believed to have occurred as a result of altered gaze control after exposure to microgravity.

During interplanetary space travel, multiple transitions between gravity levels will be anticipated, including transitions between microgravity, hypogravity, and hypergravity (e.g., upon re-entry to Earth). These gravitational transitions initiate compensatory physiological adaptations which can lead to space motion sickness, altered blood pressure regulation, and altered sensorimotor control.<sup>4</sup> Although many studies demonstrated that the sensorimotor function of humans can eventually adapt to hypogravity and hypergravity, the process of adaptation when transitioning to a new level of gravity is not fully understood. This is particularly concerning as gravitational transitions occur during the most critical phases of space missions, such as while approaching a new planet, in which peak astronaut performance of complex tasks is required. Potential inability to perform these tasks correctly may lead to mission failure.

Assessment of DVA traditionally involves moving the participant's head from left to right at a target velocity of 100°/s while the participant maintains their gaze on a screen.<sup>12</sup> Following correct responses, the optotypes shown on the screen become progressively smaller, and following incorrect responses, the optotypes become larger. Although this traditional method of assessing DVA is accurate, it is currently not performed in space. To perform this traditional DVA assessment during spaceflight would be relatively time-consuming process and requires specialized hardware that is bulky.

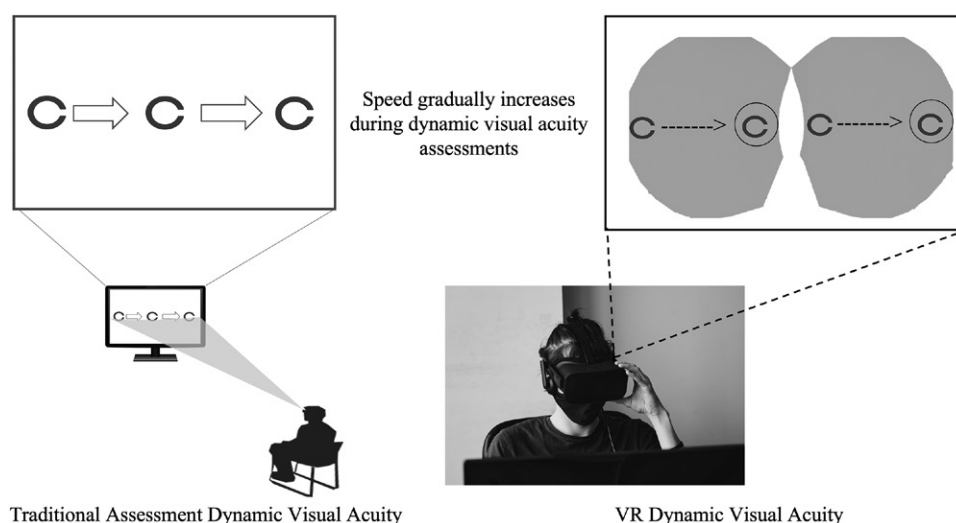
This lack of knowledge about DVA during spaceflight is due to the current difficulties in collecting data on astronauts in real time while entering new gravitational environments.<sup>4</sup> The terrestrial assessment of DVA has been largely conducted on stationary platforms with a laptop. While assessments of DVA

have not occurred during spaceflight, this set-up may likely be optimized in time-sensitive moments such as immediately after landing in a new gravitational environment. The National Aeronautics and Space Administration (NASA) has identified altered sensorimotor/vestibular function as a potential risk for affecting critical mission tasks and has assigned this risk an elevated "Likelihood and Consequence" rating.<sup>14</sup> One of the tasks listed for this risk in the NASA Human Research Program is to develop and test countermeasures for symptoms during and following G-transitions to help crewmembers perform critical tasks (SM-202).<sup>14</sup> As part of a NASA-funded, head-mounted multimodal visual assessment system for monitoring vision changes in spaceflight, we report the development and engineering of dynamic visual acuity assessments with virtual reality (VR) technology as the first step in assessing astronaut performance when undergoing G-transitional effects (**Fig. 2**). We further discuss the current assessment design for terrestrial testing of this technology and future considerations.

Traditional forms of assessing DVA require extensive instrumentation and equipment that would likely be prohibitive on the International Space Station (ISS). This VR-based method of assessing DVA overcomes these limitations and provides a portable, lightweight technique to monitor these changes. This assessment is one aspect of a NASA-funded head-mounted display, multimodal visual assessment system for long duration spaceflight. This novel mixed reality device will integrate static and DVA, contrast sensitivity, visual field, and metamorphopsia data to closely monitor functional vision.<sup>9</sup>

Assessment of visual function using VR tests has grown quickly in the past several years. To our knowledge, only two previous studies assessed dynamic visual acuity using a head-mounted device, and the first study required the head of the participant to be oscillated manually.<sup>3</sup> The second study involved testing DVA in vertical, horizontal, and no head motion conditions.<sup>6</sup> In this manuscript, we report the overarching





**Fig. 2.** Image illustration comparing between laptop and virtual reality dynamic visual acuity.

features of the head-mounted, multimodal assessment system and the DVA component for spaceflight and how it compares to a laptop-based method of DVA assessment.

## METHODS

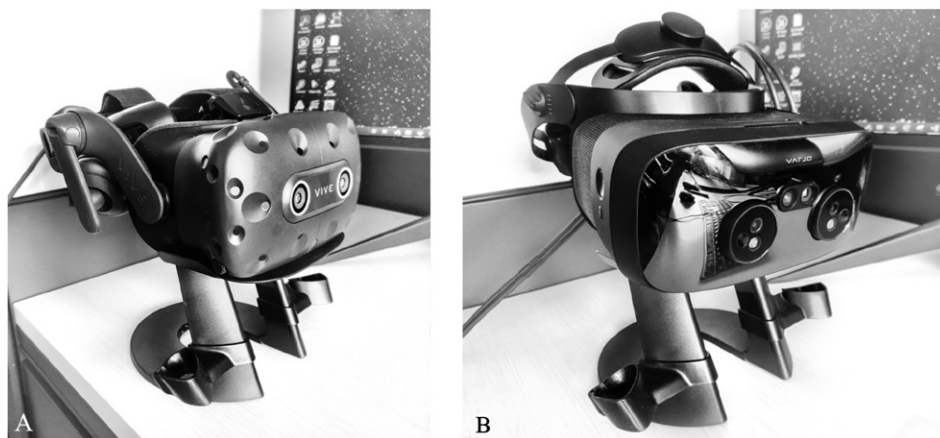
### Equipment

Various VR/AR headsets have been utilized to implement DVA testing. These headsets include HTC Vive Pro Eye system (HTC, Xindian District, New Taipei City, Taiwan), which has a pixel density of 615 pixels per inch, per eye, and a field of view of 110°. The headset weighs only 555 grams and consists of an AMOLED screen with a band to fit comfortably over the head of a subject. Epic's game engine Unreal Engine 4 Version 4.24 (Epic Games, Cary, NC) was used to build the framework and Steam VR was used to experience virtual reality content (Fig. 3). Eye tracking technology was used to maintain fixation of the participant. If the gaze of the participant deviated significantly from the stimuli, the response was then discarded. Eye

tracking accuracy was assessed on each participant in advance using an Unreal Engine plugin called "SRanipal" to determine if eye tracking was reliable. In the VR headset, text was displayed to help participants focus. Participants were assisted with calibration of the VR headset to ensure an appropriate pupil distance, focus distance, and to avoid lens rim artifact. The individualized adjustments made were then noted for each participant.

### Procedure

In our experiment design, DVA is measured binocularly. A single Landolt C is displayed at a fixed distance of 6 m from the observer and moved horizontally across from left to right and right to left at an angular speed of 30°/s. In each presentation, the Landolt C can be oriented at any of the eight directions. The participants use the numpad keys to respond to the direction of the gap in the Landolt C. A staircase method is used to vary the size of the Landolt C after each response. If the participant responds correctly for the same-sized stimuli, the subsequent character size will be decreased logarithmically. Otherwise, it will be increased



**Fig. 3.** Virtual reality headsets used for the current experiments in dynamic visual acuity assessment. Compared to the A) HTC Vive Pro Eye, the B) Varjo XR-3 has significantly higher pixel density and, therefore, can be more effective in detecting changes in dynamic visual acuity.

along the same logarithmic scale. This procedure was approved by the University of Nevada, Reno, Institutional Review Board and was in accordance with the tenets of the Declaration of Helsinki.

### Subjects

An early validation study with five participants was conducted comparing this technology versus traditional DVA with a laptop. The laptop-based test was assessed on a 23-in monitor connected to a PC with Nvidia RTX 2080 GPU, 32 GB RAM and Intel Core-i7 8700. To minimize bias, both tests were conducted during the same session, on the same day, with Landolt ring optotypes.

### Statistical Analysis

Descriptive statistical analysis was primarily conducted due to the nature of the early validation study with a relatively small number of participants. Future studies will likely have comparative statistics.

## RESULTS

The mean age of participants in our study was  $26.4 \pm 1.5$  yr and 4 of the 5 participants were men. All participants had a best correctable visual acuity of 20/20. Further information of participant demographics can be seen in **Table I**. DVA was plotted graphically using Excel version 16.44 (**Fig. 4A**). The Pearson correlation was greater than 0.9 (0.911), indicating a strong, positive association between both methods of DVA measurement. A Bland-Altman plot was also used to examine the level of agreement (**Fig. 4B**). All data points were within the limits of agreement, indicating that our head-mounted system is a promising method to assess DVA.

## DISCUSSION

NASA's Human Research Program (HRP) identified "Risk of Altered Sensorimotor/Vestibular Function" as a potentially significant biomedical risk, with the greatest risk during and following gravitational transitions.<sup>5</sup> Gravitational transitions are a critical time for astronauts as they occur while entering

and landing on a new planet, which is one of the most difficult spaceflight tasks. Risks during landing include potential loss of life, vehicular damage, or damage to other assets. Although all piloted spacecraft landings to date have been successful, the risk of failure during Mars missions is significantly higher due to the prolonged period in microgravity (6 mo), which will lead to more significant sensorimotor adaptations, and thus likely lead to a larger physiological response to the gravitational transition on entry to Mars.<sup>1</sup> The ability for astronauts to control complex systems in space requires a combination of cognitive function, visual acuity and spatial orientation perception, all of which have been shown to be impacted in microgravity.<sup>1</sup>

It has previously been shown that DVA can be enhanced after participating in specialized training involving distinct eye movement patterns.<sup>10</sup> Currently, pre-spaceflight training and post-spaceflight rehabilitation protocols are not optimized to attenuate the changes on sensorimotor function and DVA after gravitational transitions.<sup>4</sup> Our VR dynamic visual framework can potentially serve as a countermeasure for astronauts entering another gravitational environment.

Developing a countermeasure for loss of DVA may be important as the inability to focus an image on the retina can create sensory conflict and cause motion sickness. Motion sickness is currently experienced by 60–80% of astronauts during their first 2 to 3 d in microgravity, which may impact their ability to perform critical tasks during gravitational transitions.<sup>5</sup> Although symptoms such as nausea and vomiting may seem relatively innocuous in a terrestrial environment, vomiting in an extra vehicular activity (EVA) suit could potentially be a life-threatening situation.<sup>2</sup>

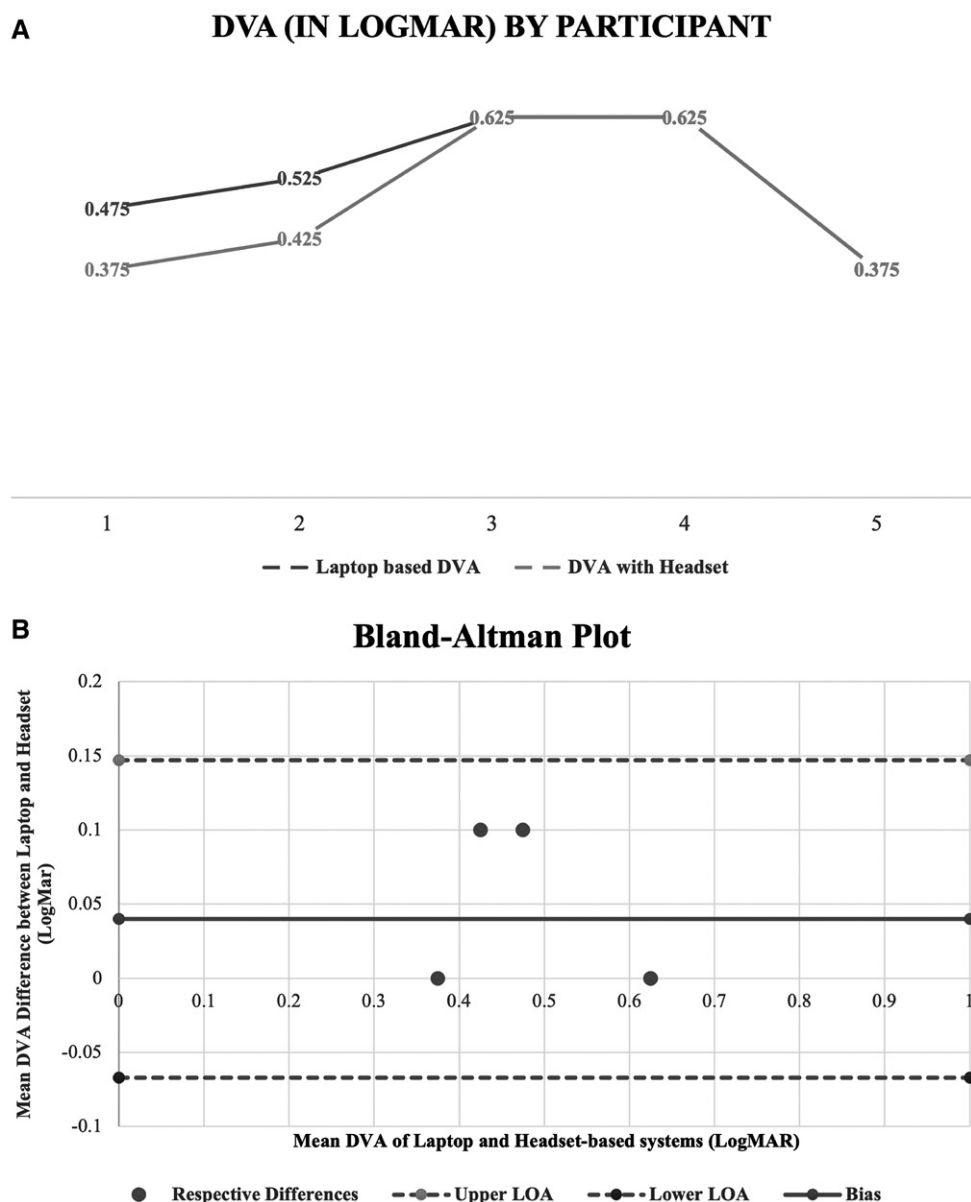
Potential drawbacks of our study include not assessing the diagnostic utility of our proposed system as well as not determining the test-retest variability. In future studies, we plan on using a higher resolution VR headset, which will likely improve DVA values. The speed and direction of the stimuli may be varied in future studies to holistically quantify the nature of the deterioration in DVA.

Our early validation study showed that DVA can be measured in virtual reality with a similar level of accuracy as the traditional laptop-based method. There are several limitations to this technology and study. The main study limitation is the small sample size of this early validation study. Future studies will aim to test a larger sample size to increase reliability of this technology when compared to laptop-based methods. There are also technology limitations that can be improved upon. Future improvements from current developments include minimizing motion blur, which commonly occurs in OLED displays and can negatively impact dynamic visual acuity results. Our studies may also be limited by the VR device resolution of 13.09 pixels per degree, as well as minor variations in VR screen brightness at different battery levels. These limitations have been taken into consideration during this ongoing development and are actively being optimized as technological capabilities continue to expand.

In conclusion, with increased portability and accessibility, VR-based DVA assessment has promising potential to replace

**Table I.** Subject Demographics and Results.

CHARACTERISTIC	SUBJECTS
Age (yr)	$26.4 \pm 1.5$
Gender	
Male	4
Female	1
Ocular history	None
Best correctable visual acuity	20/20
History of seizures or vertigo	None
Any neurological or balancing disorder	None
Standard deviation (logMAR)	0.114
Average DVA (with laptop)	0.525
Average DVA (with headset)	0.485
Pearson correlation	0.911



**Fig. 4.** A) Graphical comparison of our headset vs. a laptop-based DVA test. Note for the last three participants that the last three laptop-based test results cannot be seen as they were equal to the headset-based results. B) Bland-Altman plot showing a good correlation between our headset-based DVA assessment system with a laptop-based method. LOA: limits of agreement.

traditional laptop-based methods of assessing DVA. This technological advancement will be particularly important for astronauts undergoing G-transitions during interplanetary spaceflight missions.

Our group plans to conduct future studies with various other visual function assessments to map a multimodal assessment of visual function during spaceflight.<sup>9</sup> These forms of assessment include visual acuity, contrast sensitivity, Amsler grid metamorphopsia, foveal rendering and simulated daylight reading visual acuity.<sup>8</sup> These assessments are built around the various risks that astronauts may face during spaceflight including G-transitions and Spaceflight Associated Neuro-Ocular Syndrome (SANS), a group of neuro-ophthalmic findings observed in astronauts after long-duration spaceflight.<sup>9</sup> As a

potential barrier to spaceflight, close monitoring SANS with consistent functional testing and imaging is of utmost importance for visual health during spaceflight.<sup>7</sup> Accurate extraterrestrial assessment of DVA will provide an additional metric for close monitoring of microgravity-induced visual acuity. Future directions of this research will also involve training using our VR-based DVA system to serve as a countermeasure for gravitational transitions during interplanetary travel. Our pilot study demonstrated the effectiveness of measuring DVA using a VR headset. Future studies are needed to evaluate for test-retest reliability, improve the accuracy of our DVA assessment framework and determine if training using our VR-based system can serve as a countermeasure during future long duration manned missions.



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# Genetic Markers of Atopic Dermatitis Risk for Screening Aviation Applicants

Ian D. Gregory; Jacob Collie; Richard R. Chapleau

**INTRODUCTION:** Atopic dermatitis (AD) is a skin condition with many genetic risk factors. In this review, we summarize the different genetic variants for AD from the perspective of screening purposes within the U.S. Air Force aviation community. Using a PRISMA-informed systematic review approach, we found 13 papers reporting genetic associations with AD. We report 98 genetic associations with AD, of which 4 had a greater than twofold increased odds of developing the condition when present. These 98 variants were found in 45 associated genes, including LRRC32, OVOL1, and IL13, which were each replicated in 3 studies; as well as RTEL1 and ZNF365, which were each replicated in 2 studies. A polygenic risk model created based upon these variants or genes could contribute to a risk screening protocol for military aviation candidates, potentially helping minimize risk for candidates at increased genetic risk for AD or other atopic diseases (e.g., asthma, allergic rhinitis).

**KEYWORDS:** eczema, genetic variants, aviation risk assessments, flight physicals, medical evaluations.

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Atopic dermatitis is an inflammatory, chronic, recurrent, and relapsing skin disorder. It falls under the eczematous family of skin presentations, with multiple underlying causes, including environmental factors, a disrupted skin barrier, and a significant genetic predisposition.<sup>4</sup> Atopic dermatitis is a part of the “atopic triad,” which also includes asthma and allergic rhinitis, which are different presentations of conditions with related underlying causes (IgE mediated response to environmental conditions). When atopic dermatitis flares up, lesions can cause disruptive irritation, pruritis, cracks in the skin, and even secondary infections. While most of the time proper skin hydration and topical anti-inflammatory medications can prevent and treat the condition, uncontrolled atopic dermatitis can cause a significant disruption to quality of life for patients, and even distract from mission completion for aviators. It is estimated that about 15% of people within industrialized nations have atopic dermatitis;<sup>20</sup> therefore, it is highly likely that a small but not insignificant portion of the aviation community also suffers from the condition. According to the Air Force Medical Standards Directory, which outlines those conditions which are not compatible with special duties (such as aviation), “atopic dermatitis that requires chronic topical steroids for control” does not meet aviation standards and would

require a waiver for continued flying duties.<sup>1</sup> Multiple studies, including a twins study,<sup>16</sup> have shown that the genetic component of atopic dermatitis is significant.<sup>3</sup>

Ongoing research attempts to isolate the specific variations within the genome that are associated with increased risk of developing atopic dermatitis. Reviewing different studies from Genome Wide Association Studies (GWAS), researchers look through cases of atopic dermatitis and analyze whether any specific genetic variations (specifically single-nucleotide polymorphisms – SNPs) stand out as leading to an increased risk of the condition.<sup>11</sup> Several larger GWAS studies have specifically looked at which possible genetic variations lead to atopic dermatitis.<sup>8,10,19</sup>

Eczema in and of itself is a concern for the U.S. Air Force (USAF) aviation community, but it is generally a minimally

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problematic condition. A recent look into the Aeromedical Information Management Waiver Tracking System showed that in the last 20 yr (dating back to 2001), there were 202 applications for aviation waivers for atopic dermatitis in the USAF. Of those applications, 178 were granted. Of the 24 that were disqualified for the condition, all of them were for initial applicants. All trained aviators who developed the condition and had adequate control received a waiver. While atopic dermatitis is not a widespread problem within the USAF aviation community, asthma is definitely a significant concern (along with allergic rhinitis to a lesser degree). Both of these diagnoses can prevent mission completion while flying, which is a problem for the safety of the member and the mission. Atopic march has been described as a common progression of the “atopic triad,” where patients diagnosed with atopic dermatitis go on to develop asthma and allergic rhinitis.<sup>7,17</sup> Understanding the genetic predisposition for one condition of relatively minimal aeromedical significance can help understand and anticipate the risk for other conditions of greater aeromedical significance. One study has already specifically used a GWAS to identify specific genetic variations which lead to the “atopic march,” where members with eczema who then developed asthma had their genomes analyzed to look for common anomalies.<sup>14</sup> The genetic connection among the diseases is already known and a genetic link to the progression within the disease has now been verified.

Since atopic dermatitis is a condition for which genetic variants have already been analyzed and identified, this condition is a candidate for the creation of a screening protocol for aviation applicants. Once established, this protocol could be used as a model for development of screening protocols for other conditions.

## METHODS

The same methods were used here as in a recent review of the genetic markers associated with obstructive sleep apnea and the possible role of genetic health screening in aerospace medicine.<sup>6</sup> In order to make it easier for the reader, the methods section was reproduced here. No human subjects or human subjects data were used in this literature review and assessment, therefore no IRB review was obtained. The concepts outlined in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement were followed while developing the study<sup>15</sup> and the Begg's and Egger's test for characterization bias was not performed.

### Publication Search

The authors identified eligible studies from two GWAS databases (the NHGRI-EBI GWAS Catalog<sup>5</sup> and the Atlas of GWAS Summary Statistics<sup>21</sup>) and from keyword searches using PubMed and Google Scholar. Keywords used for searching were “eczema” and (“SNP” or “allele” or “variant” or “polymorphism” or “gene”) and (“GWAS” or “genomics” or “genetic” or “gene” or “meta-analysis” or “review”). These GWAS and

publication database searches were supplemented with citations contained within identified studies reporting additional genetic associations with atopic dermatitis.

### Inclusion and Exclusion Criteria

Studies were included that met the following conditions: 1) published in peer-reviewed journals; 2) reported data about genetic associations with atopic dermatitis or eczema risk; and 3) were case-control or cohort design studies. Reviews were included in this study for background knowledge, as a meta-analysis was not performed. Additional genetic markers from reviews that included meta-analyses that met statistical significance were included as a part of the research. Studies with sufficient sample sizes to identify associations yet still reporting null results (lack of an association) were included. Studies were excluded for the following reasons: 1) lacked participants in the cohort with dermatitis; 2) did not report data; or 3) associations were contradictory within the study. Studies reporting results contradictory to prior literature reports were included. For articles not published in English, the English language abstract was used for identifying genetic associations. English abstracts of non-English papers that did not include *P*-values for associations were excluded.

## RESULTS

### Search Results

In total, 16 studies were identified using the established search criteria. After screening for inclusion and exclusion criteria and duplicate removal, 12 remained for review.

### Study Characteristics

The earliest study was published in 2009 and the most recent, at the time of the search in the summer of 2021, was published in 2019. The geographic sources of the studies included Europe, Asia, North America, and Australia/Oceania. The populations studied included children and adults, a range of bodyweights including healthy weight and overweight participants, and multiple ethnicities. All of the papers reported effect sizes using odds ratios.

### Variant and Gene Characteristics

There were 90 variant associations reported with the risk of developing atopic dermatitis from 12 published genome-wide association studies found. There were no duplicated variants, however, several variants were in close proximity to each other and are in linkage disequilibrium (LD). LD is a measure of how often two variants are associated with each other in a nonrandom manner.<sup>18</sup> This is in contrast to conventional Mendelian genetics, where the assumption of inheritance relies upon every genetic location being independently assorted. Therefore, LD can only occur when two genetic locations are on the same chromosome and, the closer they are to each other, the more likely it is that they will be co-inherited. For the purposes of our discussion, since the ability to sequence every base on the

genome has only recently come about, we use LD blocks to suggest that the specific genetic mutation increasing eczema risk exists in a localized region of the genome (termed an “LD block”). To that end, variant associations with eczema risk were identified on 13 chromosomes, 6 of which did not have LD blocks.<sup>13</sup> Of the seven chromosomes with LD blocks, chromosomes 5 and 11 had three LD blocks each; chromosomes 1 and 6 had two LD blocks each; and chromosomes 2, 19, and 20 each had one LD block (Table I). These LD blocks account for 61% ( $N = 43$ ) of the variants on chromosomes with LD blocks ( $N = 70$ ) and 48% of the cumulative variant associations.

The 90 variants identified were found in 45 genes and the remainder were within intergenic regions. Similar to the variant associations, the majority (37, 79%) of genes were only represented once. Of the nine genes with at least one association, four genes had two associations, one gene had three associations, two genes had four associations, and a single gene had five variant associations (Table II).

Association strength effect size was compared by using the reported odds ratios that represent a doubling of the odds of decreased ( $OR \leq 0.5$ ) or increased risk ( $OR \geq 2.0$ ).<sup>6</sup> The observations identified four variants associated with significant increased risk (rs13403179,  $OR = 2.95$ ,  $P = 8.1 \times 10^{-8}$ ; rs9540294,  $OR = 2.66$ ,  $P = 1.0 \times 10^{-8}$ ; rs675531,  $OR = 2.19$ ,  $P = 6.8 \times 10^{-7}$ ; and rs3099143,  $OR = 2.13$ ,  $P = 3.0 \times 10^{-7}$ ) and none associated with decreased risk of developing eczema.

**Table I.** Linkage Disequilibrium Analysis of Variants Associated with Eczema Risk.

CHROMOSOME	VARIANTS IN LD BLOCKS	VARIANTS NOT IN LD BLOCKS
1	9	5
2	2	3
5	13	2
6	6	13
11	9	2
19	2	1
20	2	1
Total	43 (61%)	27 (39%)

LD = linkage disequilibrium.

**Table II.** Genes with More Than One Association.

GENE NAME	NUMBER OF ASSOCIATIONS	ASSOCIATED VARIANTS
FLG	2	rs11204971 rs3126085
IL13	2	rs1295686 rs20541
OVOL1	2	rs10791824 rs479844
ZNF365	2	rs2393903 rs2944542
TNXB	3	rs12198173 rs12211410 rs13199524
LRR32	4	rs7130588 rs2155219 rs2155219 rs2212434
TMEM232/ SLC25A46	4	rs10067777 rs13360927 rs13361382 rs7701890
RAD50	5	rs2897443 rs6871536 rs3091307 rs12188917 rs2158177

## DISCUSSION

Within the 13 articles that were reviewed (and the 12 that were used in the study), 90 genetic variants were found to be associated with atopic dermatitis. All of the studies reviewed were case controls of some sort, except one (a cross-sectional study of an ongoing prospective cohort study). Of the articles, 5 conducted straight case control studies, while 4 articles were meta-analyses of multiple other case control studies, ranging from 3 to 30 in number. Two articles were considered cohort case control studies. Ages of the cases within the studies ranged from infants (less than 3 yr old) up to adults, with a majority of the cases being children since eczema frequently presents during childhood and sometimes resolves before adulthood. The study sizes ranged from 797 cases and controls in one of the single case control studies up to 459,000 in the large meta-analysis study. An average of 82,868 and a median of 6163 cases/controls were included in the articles. Study participants came from different countries, with European countries, Germany in particular, being the most numerous. Other countries involved in the studies included Ireland, Scotland, The United Kingdom, China, Japan, Czech Republic, Poland, Sweden, and unspecified African countries.

There is still much to learn about polygenic risk scores (PRS), including their usefulness in the aerospace medicine environment. The full utility is still to be determined, but genetic testing in the medical field in general is still in its infancy. As scientists and clinicians learn more about the use of genetic testing to evaluate risk, determine the most effective medications and other treatments, the efficient use of PRS in the aerospace medicine setting will naturally evolve. Currently, genetic testing is most frequently used for diagnosis, screening, prognosis, and treatment of conditions with known underlying genetic causes, and no fewer than 16 organizations have resources or practice guidelines for genetic testing.<sup>2,9</sup> However, none of these organizations currently have clinical practice guidelines incorporating PRS.

In aerospace medicine, the main advantage of incorporating PRS is recognizing the risk of developing a condition and taking steps to minimize that risk or instituting early interventions. Every single pilot applicant in the USAF comes to one of two places for their medical evaluation and/or certification (U.S. Air Force Academy, Colorado Springs, CO, USA; or U.S. Air Force School of Aerospace Medicine, Wright-Patterson Air Force Base, OH, USA). During this medical evaluation to clear the pilot applicant for flying duties, saliva samples could be taken to obtain genetic information. Through the PRS described above, the genetic material could be evaluated for any one of the variants outlined in this article. If the member were to have any of the variants, measures could be taken to minimize the impact of those variants. To prevent clinically significant atopic dermatitis, members could be counseled on the need to ensure proper skin hydration. Education could be provided on what to look for with the early stages of atopic dermatitis eruption so care and treatment of the condition could be obtained before it disrupts quality of life or job performance.



Additionally, as noted, atopic dermatitis is often an early precursor to asthma, which is very disruptive in the aviation environment, especially in a high-G environment. With increases in altitude, a decrease in atmospheric pressure of oxygen in the ambient air can lead to decreased oxygen delivery to tissue. Any disease that inhibits efficient oxygen exchange from the air into the blood stream will be exacerbated by the decrease in available oxygen molecules in the air. Asthma, where inflammation around airways is combined with muscular constriction of airways, inherently decreases efficient oxygen exchange. Asthma can be a chronic condition with insidious onset where an aviator may not recognize a decrease in oxygen delivery and, therefore, a decrease in performance, or it may present as an acute attack leading to sudden incapacitation. In the high altitude and high-g environments of military fighter aircraft, conditions such as asthma which exacerbate ventilation-perfusion mismatches have a higher impact on performance compared to at the terrestrial level. Aviation is an occupational environment that is susceptible to hypoxia that people without asthma or other respiratory diseases can cope with, but when an aviator has asthma, then the ability to overcome subtle decreases in oxygen levels may not be present.

Pilot applicants with the noted genetic variants can undergo more frequent pulmonary evaluations to monitor for early lung function changes that are indicative of asthma. Counseling on environmental precautions could be given to minimize the atopic reactions which may lead to asthma as well. If indicated, medical treatment could be instituted as well. A waiver would be needed to continue flying duties if a member is diagnosed with asthma, but they are frequently granted in the trained aviator if the condition is well controlled on appropriate medication. In fiscal year 2021 within the U.S. Air Force, there were 148 total requests for an initial waiver to start training as an aviator because of a history of asthma. Of those, 92 members received the waiver, 50 were disqualified from flying, 4 were qualified (found to not actually have the diagnosis of asthma), and 2 requests were incomplete (did not follow through on waiver request).

More generally, asthma poses an additional problem for military recruits and presents management challenges to military medical staff for service members in any career field, especially considering the Department of Defense's recent policy requiring the separation of any soldier, sailor, or airman who has not been able to deploy for 12 consecutive months.<sup>12</sup> With this in mind, asthma relapse and deployment waivers can pose significant roadblocks to mission readiness and directly conflict with this newer deployment policy by the Department of Defense. Given the impact on mission readiness, as well as the career ramifications for military personnel, further studies on genetic predictors of relapse and/or pharmacogenetic predictors of response are worthwhile endeavors. Such information could help optimize asthma management for personnel, as well as provide additional parameters for waiver considerations during military medical evaluations.

For this information to be useful when screening USAF pilot applicants and other service members, an algorithm will need

to be developed which can help predict who might be affected by atopic dermatitis within the population if they have the genetic variants of concern. Creating this algorithm will be the next step in the process and will be accomplished by analyzing the genetic material of USAF aviators who were found to have atopic dermatitis and comparing those genes to the genetic material of controls without atopic dermatitis. The algorithm could then be applied to applicants who provide their genetic material for analysis.

In conclusion, while atopic dermatitis is not seen as a significant risk to aviation safety, in some instances severe cases can interfere with mission completion and aviator quality of life. Additionally, since atopic dermatitis is a part of the atopic triad, development of this condition can be a part of progression to the more concerning condition of asthma. Screening for atopic dermatitis can be a part of a greater program of screening within the aviator medical evaluation process. Development of a polygenic risk score using the information already obtained from prior research is an efficient way to determine risk for multiple diseases, including atopic conditions. The identification of specific genetic variants associated with atopic dermatitis allows for improved awareness and monitoring of aviation applicants who are at higher risk for developing atopic dermatitis or other atopic diseases. When these individuals are identified, efforts to minimize development of these conditions can be implemented, thereby decreasing risk for aviation mishaps and medical disqualifications.

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# Mitigating Risks of Altitude Chamber Training

Idan Nakdimon; Oded Ben-Ari

- INTRODUCTION:** Altitude chambers are used for training aircrews in a hypobaric hypoxic environment to better prepare them for pressurization and oxygen malfunction incidents during flights. However, adverse effects may occur during training sessions, with decompression sickness (DCS) being a major concern. The aim of this study was to examine the risks of different adverse effects during altitude chamber trainings (ACT) in the Israeli Air Force (IAF) facility and to compare them to other training facilities.
- METHODS:** We retrospectively reviewed the records of 1627 individuals in the IAF who were trained in the altitude chamber between 2015 and 2019. Data regarding adverse effects and training safety were extracted. Literature review of altitude chamber trainings was performed and adverse effects rates were compared.
- RESULTS:** There were a total of 91 adverse effects cases in the IAF during the study period. The overall risk rate for an adverse effect was 5.59%. The most common adverse effect was middle ear and sinus barotrauma (69.3% of adverse effects cases), followed by breathing problems (14.3%) and DCS cases (9.9%).
- CONCLUSIONS:** Mitigating the risk for DCS should be major concern during ACT. We recommend setting a standard protocol for an ACT which includes a 45-min preoxygenation period, a maximal ascent rate of  $3000 \text{ ft} \cdot \text{min}^{-1}$  ( $914 \text{ m} \cdot \text{min}^{-1}$ ), and setting a maximum altitude of 25,000 ft (7620 m) for fixed-wing trainees.
- KEYWORDS:** altitude chamber, barotrauma, decompression sickness, denitrogenation, hypobaric chamber, pre-oxygenation.

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Altitude chamber training (ACT), also known as hypobaric chamber training, for military aircrew is important for flight safety.<sup>11</sup> Therefore, this training is a mandatory part of the aviation physiology training syllabus for aircrew and auxiliary aircrew in the Israeli Air Force (IAF) and among other air forces. In this training, trainees are exposed to hypoxic and hypobaric environments.

ACT has several goals. The main goal of this training is to familiarize the trainees with their own combination of signs and symptoms of hypoxia. The second goal is to instruct trainees about the correct use of oxygen delivery equipment and its function of positive pressure breathing.<sup>2</sup> Other goals of this training are recognizing the pressure changes in hollow body organs involving trapped gases and the ability to equalize pressure in the middle ear.<sup>5</sup>

An altitude chamber is not free of risks and it may cause several medical adverse effects. Adverse effects during ACT can be classified as effects which result from either a change in atmospheric pressure or due to hypoxia.<sup>7</sup> A major adverse risk of atmospheric pressure changes during ACT is decompression sickness (DCS), which is a condition caused by the reduction in

barometric pressure along with a subsequent release of nitrogen gas bubbles. DCS can cause limb or joint pain, lymph node enlargement, and cutaneous manifestations such as pruritus, tingling, or rash. These symptoms are classified as DCS Type 1. Some of the less common symptoms include the appearance of neurological (headache, visual deficit, cognitive impairment, mental status changes, sensory or motor deficit), cardiopulmonary (cough, chest pain, tachypnea, and cardiac involvement), or inner ear symptoms. These are classified as DCS Type 2.<sup>15</sup> Another adverse effect related to pressure changes is barotrauma, which can manifest as either middle ear pain (barotitis media), sinus pain (barosinusitis), or toothache (barodontalgia).

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Hypoxia related adverse effects include hyperventilation and delayed recovery from hypoxia.

Due to the major adverse effects related with pressure changes which can generate criticism over the safety of this training, it is possible to induce hypoxic conditions in which to train aircrew, but without pressure changes (normobaric environment), using the Reduced Oxygen Breathing Device (ROBD).<sup>10</sup> However, ACT is still considered to be the golden standard for simulation of flight conditions.

The goal of this study was to investigate the risks for adverse effects during ACT in the IAF and to compare them with previous published data from other facilities around the world. We hypothesize that the risk rate for an adverse effect in IAF ACT would be similar to the risk rate of other facilities around the world.

## METHODS

In this retrospective study we reviewed our database of ACT sessions from January 2015 to December 2019.

### Subjects

The subjects of this study were all aircrew and auxiliary aircrew personnel from the IAF who trained in the altitude chamber as part of the IAF standard physiology training program between 2015 and 2019. Additional subjects were the physiology instructors (PI), who supervised the trainees in the chamber.

### Equipment

All training sessions were conducted in the altitude chamber of the aviation physiology section in the Israeli Aeromedical

Center (AMC). The altitude chamber was built by Vacudyne Corporation (model 9A9, Chicago Heights, IL, USA), and was reconstructed by Environmental Tectonics Corporation (ETC; Southampton, PA, USA) in 2009. The chamber is located at a height of 213.3 ft (65.0 m). Capillary oxygen hemoglobin saturation level ( $S_{pO_2}$ ) was monitored using a standard Nonin pulse oximeter.

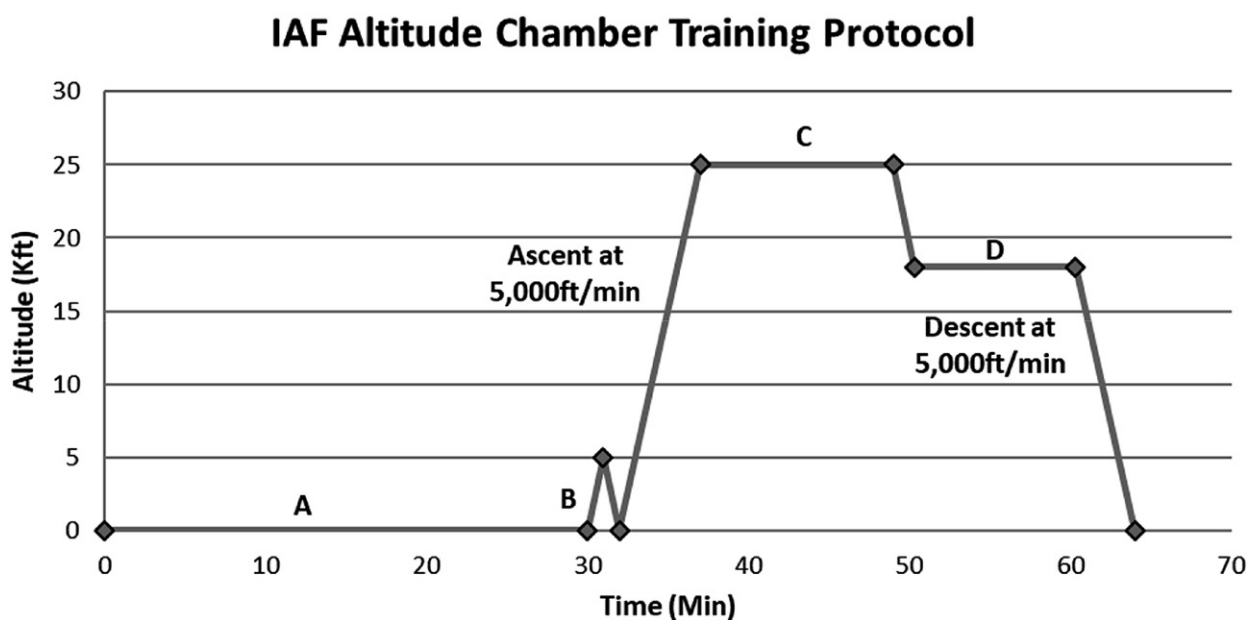
### Procedure

All individuals who participated in the training sessions were medically qualified for all flight duties by the Israeli AMC and specifically for the training in the chamber. The IAF protocol for ACTs is presented in Fig. 1. The maximal altitude for the training is 25,000 ft (7620 m), with ascent and descent rates of 5000 ft · min<sup>-1</sup> (1524 m · min<sup>-1</sup>). Preceding the training is a 30-min preoxygenation period (also called denitrogenation) of 100% oxygen breathing.

### Statistical Analysis

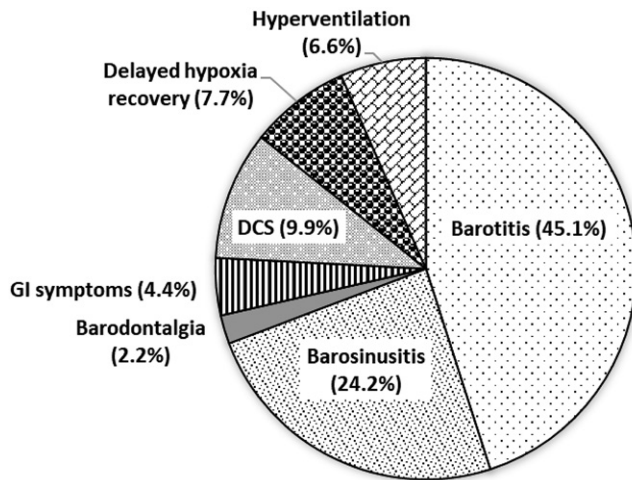
Cases defined by the physician supervising the training as DCS, barotrauma, hyperventilation, or delayed recovery from hypoxia were considered adverse effects. PI were not exposed to hypoxic conditions during the ACT and were, therefore, excluded from the study cohort for calculation of risk for hyperventilation and delayed recovery from hypoxia.

Total risk rate for the ACT and specific risk rates for each adverse effect were calculated. Graphs were conducted using MS-Excel ver. 2016. Significance was calculated using Chi-squared and Fisher's exact tests for comparisons between the different study groups. All statistical tests were performed using SPSS version 22 (IBM, Armonk, NY, USA). *P*-values < 0.05 were considered statistically significant.



**Fig. 1.** Israeli Air Force altitude chamber training protocol. A) Pre-oxygenation time; B) ears and sinus pressure equalization check; C) hypoxic exposure at 25,000 ft (7620 m); D) night vision drill at 18,000 ft (5486 m).





**Fig. 2.** The distribution of adverse effects during IAF altitude chamber training.

## RESULTS

During the study period, 185 training sessions were performed with a total of 1627 individuals. A total of 91 adverse effects were recorded. The distribution of adverse effects is shown in **Fig. 2**. Barotitis was the most common adverse effect (45.1%).

The overall risk rate for an adverse effect in our facility was 5.59%. The majority of trainees were aircrew and auxiliary aircrew personnel (1263, 77.6%), and the overall risk rate for this group was 6.57%. However, the overall risk rate for an adverse effect in the PI group (364, 22.4%) was significantly lower (2.20%,  $P = 0.001$ ). The specific risk rate for barotitis was significantly lower among PIs (0.55%) in comparison to trainees (3.09%,  $P = 0.004$ ). The specific risk rate for DCS was equal between the two groups (0.55%). The specific risk rates for other adverse effects are presented in **Table I**.

A literature review of altitude chamber protocols and adverse effects is shown in **Table II**.<sup>1–14</sup> Maximum altitude in the different protocols ranged between 25,000 to 43,000 ft (7620 to 13,106 m). Rate of ascent ranged between 2000 to

5000 ft · min<sup>-1</sup> (610 to 1524 m · min<sup>-1</sup>). Descent rate, for the majority of the facilities, was equal or lower than the ascent rate in the same facility. The overall adverse effect risk rate varied dramatically between facilities and ranged between 1.37–11.37%. The most common adverse effect in all facilities was barotitis, with a specific risk rate ranging from 0.93 to 11.11%. DCS risk rate was less than 1% in all facilities. Overall risk rate was found to be significantly higher among our trainees in comparison to the calculated data from previous studies ( $P = 0.000$ ), especially due to the higher risk rate for DCS in our facility ( $P = 0.000$ ).

## DISCUSSION

ACT is an important physiological training for aircrew, but nevertheless it is not risk free. In this study we analyzed our adverse effects data in a 5-yr time frame (2015–2019). We found the risk rate for an adverse effect to be 5.59%, with the most common manifestation being barotitis.

A literature review of different ACT protocols revealed substantial differences. The three parameters which dictate the risk for adverse effects are maximal altitude (ranging from 25,000 to 43,000 ft), ascent rate (ranging from 2000 to 5000 ft · min<sup>-1</sup>), and descent rate [ranging from 2000 to 10,000 ft · min<sup>-1</sup> (610 to 3048 m · min<sup>-1</sup>)]. Maximal altitude and ascent rate are related to the risk for DCS. Another parameter which may influence the risk for DCS is preoxygenation time. The standard duration is 30 min and it is usually identical throughout training facilities. Descent rate is a risk factor for barotitis and barosinusitis. The review we conducted showed a wide range of overall risk rate for an adverse effect, ranging from 1.37 to 11.37%, with the weighted average being 1.59%.<sup>7,14</sup>

The IAF ACT protocol is moderate regarding the maximal altitude reached (25,000 ft); however, it is relatively challenging with regard to both ascent and descent rates (5000 ft · min<sup>-1</sup>). This might explain our relatively high overall risk rate for an adverse effect (5.59%).

Equalization of pressure on both sides of the tympanic membrane is needed in order to prevent barotitis. The technique improves with training and experience. Our data indeed

**Table I.** Risk Rates for Different Adverse Effects.

RISK RATE (%)	OVERALL RISK (N = 1627)	TRAINEES (N = 1263)	PHYSIOLOGY INSTRUCTORS (N = 364)	P-VALUE
Total	5.59	6.57	2.20	0.001
Barotrauma	4.24	4.99	1.65	
Barotitis	2.52	3.09	0.55	0.004
Barosinusitis	1.35	1.42	1.10	0.799
Barodontalgia	0.12	0.16	0	1.000
GI symptoms	0.25	0.32	0	0.581
DCS	0.55	0.55	0.55	1.000
Breathing problems	—	1.03	—	—
Delayed hypoxia recovery	—	0.55	—	—
Hyperventilation	—	0.48	—	—

GI, gastrointestinal; DCS, decompression sickness.

P-values compare trainees to physiology instructors.

**Table II.** Altitude Chamber Protocols and Adverse Effects in the Literature.

AUTHOR	HYPOBARIC CHAMBER PROTOCOLS				ADVERSE EFFECTS RISK RATE (%)							DELAYED RECOVERY FROM HYPOXIA	HYP
	NUMBER OF PARTICIPANTS	MAXIMUM ALTITUDE (Kft)	RATE OF ASCENT TO 15,000 ft (ft/min)	RATE OF DESCENT FROM 15,000 ft (ft/min)	OVERALL	BAROTITIS	BAROSINUSITIS	BARODONTALGIA	GI SYMPTOMS	DCS			
al-Wedyan <sup>1</sup>	705	25-32	4000	4000	6.10	3.97	1.70	0	0	0	0.28	0.14	
Bason <sup>2</sup>	88,520	25-40								0.09			
Bason <sup>3</sup>	136,696	25	5000	2500						0.10			
Cheok <sup>4</sup>	3259	25	4000-RD	2000-4000						0.12			
Crowell <sup>5</sup>	21,423	25-43		10,000	7.87	5.75	1.12	0.12	0.06	0.32	0.42		
Davenport <sup>6</sup>	5851	25	5000	2500	3.30	2.31	0.43	0.05		0.21	0.05		
DeGroot <sup>7</sup>	23,656	29	2000	2000	1.37	0.93	0.16	0.03	0.01	0.12	0.01		
Ercan <sup>8</sup>	7272									0.11			
Morgagni <sup>10</sup>	1241	25-43	4000	2500	2.60	1.53	0	0	0.16	0.08			
Morgagni <sup>9</sup>	314	25-35	4000	2500		11.10							
Ohrui <sup>11</sup>	58,454	43		5000	6.29	4.79	0.86	0.03	0.34	0.05	0.08	0.08	
Piwinski <sup>12</sup>	12,408	25								0.10			
	1380	35								0.36			
	757	45								0.40			
Rice <sup>13</sup>	28,094	25	5000	2500						0.26			
	8823	35	5000	2500						0.19			
Valdez <sup>14</sup>	1725	25	2000	2000	7.71	6.14	1.10	0	0.06	0	0.17		
	3034	29	3000	2000	11.37	8.17	2.67	0.20	0.16	0	0.10		
Weighted risk rate					1.59	4.12	0.79	0.05	0.19	0.13	0.17		
Current study	1627	25	5000	5000	5.59	2.52	1.35	0.12	0.25	0.55	0.55	0.47	

GI, gastrointestinal; DCS, decompression sickness; HYP, hyperventilation; RD, rapid decompression.

show lower risk for barotitis in the PI group, who are more trained and experienced in the technique of pressure equalization. In spite of our relatively high descent rate, our risk rate for barotitis is low (2.52%) compared with the literature weighted risk rate for barotitis (4.12%).

No doubt DCS is a major concern of ACTs and may even lead to fatalities. The risk for DCS was found to be less than 1% (weighted average of 0.13%) in all the facilities we reviewed. Our risk for DCS was found to be 0.55%, which was the highest in this series. We explain this high risk rate by the fact that the diagnosis of DCS (especially Type 1), is clinical by nature and, to some extent, subjective (as opposed to barotitis, for example). A high index of suspicion is warranted, in our opinion, due to the risks posed by this syndrome. The proximity of a hyperbaric chamber facility may be another consideration, leading to possible over-diagnosis.

In light of our relatively high risk rate for DCS, we have decided to implement some precautionary measures in order to mitigate this risk. We started extending the preoxygenation time from 30 to 45 min. Additionally, we decreased the ascent rate from 5000 ft · min<sup>-1</sup> (1524 m · min<sup>-1</sup>) to 3000 ft · min<sup>-1</sup> (914 m · min<sup>-1</sup>). We also lowered the maximum altitude of an ACT for rotary-wing platform trainees (both aircrew and auxiliary aircrew) from 25,000 ft (7620 m) to 13,000 ft (3962 m), as there is no operational scenario in which this platform reaches 25,000 ft. We did not change our descent rate (which is relatively high), due to the fact that no excessive risk rate for barotitis was noticed. We also started monitoring our trainees using pulse-oximetry throughout the hypoxic exposure. Following the implementation of these precautionary measures, we experienced no DCS events in trainees over the last 18 mo.

The limitations of this study are the relatively small cohort size, the lack of objective criteria for the diagnosis of some of the above mentioned adverse effects, and the absence of a standard protocol for ACT, which makes comparison between risk rate ratios more difficult.

In conclusion, mitigating the risk for DCS should be a major concern during ACT. This goal can be achieved by extending the preoxygenation period, reducing the ascent rate, and limiting the maximum altitude of the training where possible. We recommend setting a standard protocol for an ACT which includes a 45-min preoxygenation, a maximal ascent rate of 3000 ft · min<sup>-1</sup>, and limiting the maximum altitude to 25,000 ft for fixed-wing trainees.

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# Time Cost of Provider Skill: A Pilot Study of Medical Officer Occupied Time By Knowledge, Skill, and Ability Level

Dana R. Levin; Margaret Siu; Kristina Kramer; Edward Kelly; Reginald Alouidor; Gladys Fernandez; Tovy Kamine

- INTRODUCTION:** On space missions one must consider the operating cost of the medical system on crew time. Medical Officer Occupied Time (MOOT) may vary significantly depending on provider skill. This pilot study assessed the MOOT Skill Effect (MOOTSke).
- METHODS:** An expert surgeon (ES), fifth year surgical resident (PGY5), second year surgical resident (PGY2), and an expert Emergency Physician (EP) with only 4 mo direct surgical training each performed two simulated appendectomies. The completion times for endotracheal intubation, appendectomy, and two subprocedures (multilayer tissue repair and single layer tissue repair) were recorded.
- RESULTS:** The ES performed the appendectomy in 410 s, the PGY-5 in 498 s, the PGY-2 in 645 s, and the EP in 973 s on average. The PGY-2 and EP time difference was significant compared to the expert. The PGY-5 was not. The EP's time was significantly longer for the appendectomy and the multilayer repair than either surgical resident. For the single layer repair, only the EP-ES difference was significant. A single intubation attempt by the PGY-2 took 73 s while the EP averaged 27 s. The average recorded MOOTSke between novice and expert was 2.5 (SD 0.34).
- DISCUSSION:** This pilot study demonstrates MOOTSke can be captured using simulated procedures. It showed the magnitude of the MOOTSke is likely substantial, suggesting that a more highly trained provider may save substantial crew time. Limitations included small sample size, limited number of procedures, a simulation that may not reflect real world conditions, and suboptimal camera angles.
- KEYWORDS:** knowledge, skills, and abilities, crew medical officer, procedure skills, training, space.

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This pilot study was designed to assess the time to completion required by providers of different knowledge, skills, and abilities (KSA) performing the same procedure. Since medicine aims to reduce patient risk and improve quality of life, expedition medical kits and space medical systems are designed to minimize risks such as death, need for evacuation, and disability.<sup>3,9</sup> Similarly, provider KSA is evaluated through expected skills obtained at various points in standardized training curricula and assessed through testing, simulation, or educator written skills evaluations. These baseline skills are readily available through publications such as national guidelines for Emergency Medical Technicians and ACGME milestones for physicians.<sup>1,12</sup> However, on missions with small crews, limited resources, and tight timelines, one

must also consider the operating cost of the medical system on aspects of the mission itself, such as crew time.<sup>3,13</sup> Patient downtime is often accounted for since time for recovery is expected and, by rendering care, the unavoidable time cost of injury or illness is minimized.<sup>13</sup> Medical Officer Occupied Time (MOOT), however, is not typically considered and may

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vary significantly depending on provider KSAs. This MOOT skill effect (MOOTSke) can be combined with estimations of medical event frequency to better understand how much crew time is spent on unplanned medical events and if/how the onboard KSA can mitigate the cost.

The purpose of this study was to evaluate: 1) if there is a difference in time taken to perform medical tasks as a function of skill level; and 2) if simulation can detect and quantify the potential time difference. The methods used in this study were meant to be applied to any medical procedure. For the purposes of this trial, simulated open appendectomy was chosen due to the easily marked starting and ending points, the commonality of the illness, and the ability to capture time for multiple procedures (e.g., intubation, appendectomy, multilayer tissue repair, and single layer tissue repair) in a single testing session.<sup>2,8,11</sup> Additionally, while laparoscopic surgery is certainly possible in microgravity, laparoscopic equipment requires much more mass and volume and is more challenging for a novice to perform.<sup>5</sup>

The authors acknowledge that this and other surgical emergencies are not likely to occur or be managed in spaceflight, but with the exponential increase in crew time spent in orbit over the last 5 yr (Fig. 1) and increased focus on long duration exploration missions, the risk of a mission critical surgical problem occurring in flight is significant and it is worth considering how such events would be managed.<sup>4,6,7</sup>

## METHODS

### Subjects

An expert Surgeon board certified in General Surgery and Surgical Critical Care (ES), a Surgical Chief Resident (PGY-5), a second year Surgical Resident (PGY-2), and an Emergency Medicine Physician board certified in Emergency Medicine and Aerospace Medicine (EP) were tasked to perform an open appendectomy on a simulator. The EP served as the “novice.” Participants were chosen from a convenience sample for their training level, interest, and availability for the pilot study.

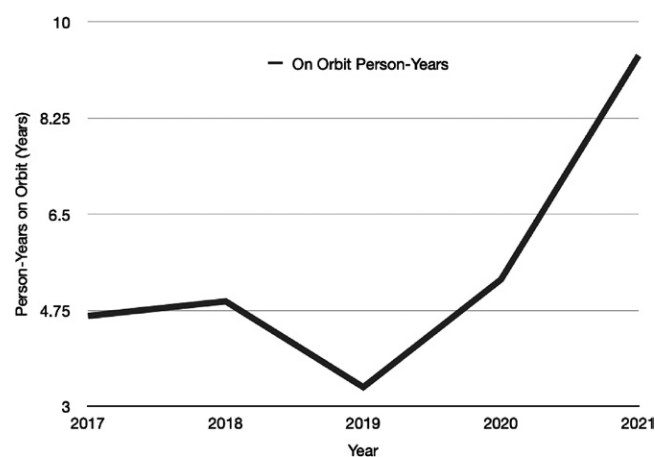


Fig. 1. On orbit person-years by mission launch year.

### Equipment

The Baystate Simulation Center and Goldberg Surgical Skills Laboratory (Springfield, MA, USA) were used to simulate a spacecraft. Operating room (OR) table and arm board dimensions were measured in centimeters from an OR approved by The Joint Commission. The operating room table measured 194 cm × 58 cm, and 194 cm × 124 cm with one arm extended. Standard hospital tables were used to represent an operating table. A trauma back board was used to stabilize the simulated patient when performing appendectomies in kneeling fashion. A standard intubation training head-and-lungs mannequin was secured at the head of the backboard and a surgical trainer abdominal cavity was secured in the appropriate position on the backboard. The Ambu bag, face mask, endotracheal tube, and a laryngoscope with a MAC 3 blade were placed on a tray near the head of the bed.

A set of surgical instruments considered essential in performing an open appendectomy was gathered. Instruments included a disposable 10-blade scalpel, a Jacobson mosquito forceps, a standard Kelly clamp, sutures, a needle driver, a set of pick-ups, a pair of scissors, and appropriate 3-0 and 4-0 sutures. A simulated inflamed appendix was forged using a tubular-shaped foam, measuring 2" long and 1 cm wide, adhered to soft rubber tubing that mimicked the cecum. The simulated appendix was placed deep into a hollow mannequin to represent appendicitis.

### Procedure

Internal review board (IRB) approval was obtained from the Baystate Health IRB. This pilot study used a simulated open appendectomy to assess the MOOTSke for selected components of the procedure, estimate its magnitude for various training levels, and identify areas for study design improvement. Times were captured by defining the beginning and ending as follows.

- 1) Endotracheal intubation begins: laryngoscope picked up. Endotracheal intubation ends: delivery of first breath via Bag Valve Mask.
- 2) Appendectomy begins: scalpel picked up. Appendectomy ends: needle driver placed on surgical tray after skin closure.
- 3) Multilayer Repair of a 12-cm abdominal cavity incision begins: suture material picked up from tray at start of fascial repair. Multilayer Repair ends: scissors replaced on tray after final deep suture placed.
- 4) Single Layer Repair of a 12-cm abdominal cavity incision begins: suture material picked up from tray at start of skin closure. Single Layer Repair ends: needle driver replaced on tray after final skin suture placed.

Since the novice (EP) had only 4 mo of direct surgical training, their initial appendectomy was performed under in-room guidance from the ES. The EP's second appendectomy was done with telemedical guidance from the ES using a camera placed over the surgical field.

Video cameras were used to record the procedure. The video was then analyzed to capture time data using the start/stop

points in **Table I** and **Table II**. Data from the EP's second procedure was not captured due to technical difficulties.

### Statistical Analysis

The small sample size limited statistical analysis. The reported results were obtained by averaging the two procedure attempts of each participant and comparing the results with a two-tailed, two-sample homoscedastic Student's *t*-Test. Significance was set at  $P < 0.05$ . No analysis was possible for the intubation procedure in this pilot study as only a single data point from the initial attempt by the PGY-2 was available for comparison to the expert EP.

## RESULTS

The average time to perform an appendectomy by KSA level fits a logarithmic curve with a correlation coefficient of 0.99. Similar curves can be seen for the multilayer repair and the single layer repair (**Fig. 2**), both with a correlation coefficient of 0.91.

Table I and Table II present the average time each KSA provider took to complete each procedure and the statistical significance of their time compared to the expert reference. The difference between the PGY-5 and the ES was not significant for any procedure. The PGY-2 was only significantly different for overall appendectomy time while the EP took significantly longer than the ES for the appendectomy, the multilayer repair, and the single layer repair. The magnitude of this difference was 2.4 times greater for the appendectomy, 2.6 times greater for the multilayer tissue repair, and 2.8 times greater for the single layer repair.

A significant difference between surgeon and nonsurgeon was also present with both the PGY-5 and the PGY-2 compared to the EP for the appendectomy and the multilayer repair. However, the magnitude of this difference decreased by 19% for the appendectomy, 16% for the multilayer repair, and 32% for the single layer repair when comparing to the PGY-5, and 37%, 27%, and 31% when compared with the PGY-2. The difference in single layer repair time was not significant between the EP, the PGY-5, nor the PGY-2.

For intubation, only a single value for the nonexpert PGY-2 was captured so no statistical analysis could be run. However, the PGY-2 (novice) took twice as long as the EP to intubate the simulated patient. Actual times taken for the surgical procedures are presented in **Table III** along with the effect size for each procedure. The MOOTSke average was 2.59 with a standard deviation of 0.34.

## DISCUSSION

The results suggest the potential for a strong correlation between years of training and time to complete an appendectomy (**Fig. 2**). This correlation fits a logarithmic curve with a 58% time reduction occurring by year 2 and 84% by year 5, meaning that the MOOTSke in this study is a factor of 2

**Table I.** Average Time by KSA and Significance by *P*-Value from Student's *t*-Test.

	EXPERT	PGY-5 TO EXPERT			PGY-2 TO EXPERT			NSP COMPARED TO EXPERT		
		TIME	DF	<i>t</i> -STAT	<i>P</i> -VALUE	TIME	DF	<i>t</i> -STAT	TIME	<i>P</i> -VALUE
Appendectomy	410 s	498 s	1	-2.06	0.176	645 s*	1	-24.65	973 s*	0.002
Multilayer 12-cm repair	299 s	351 s	1	-0.71	0.549	405 s	1	-1.39	766 s*	0.010
Single layer 12-cm repair	132 s	193.5 s	1	-1.4	0.296	193 s	1	-1.24	370 s*	0.025
Endotracheal intubation†	38 s					73 s				

KSA = knowledge, skills, and abilities; PGY-5 = 5<sup>th</sup>-year surgical resident; PGY-2 = 2<sup>nd</sup>-year surgical resident; DF = degrees of freedom; NSP = nonsurgeon physician.

\*Significant difference ( $P < 0.05$ ); †reference time is Emergency Medicine doctor's mean.

**Table II.** Comparison of Non-Surgeon Physician (NSP) to Non-Expert Surgeons.

	NSP COMPARED TO PGY-5			NSP COMPARED TO PGY-2		
	DF	t-STAT	P-VALUE	DF	t-STAT	P-VALUE
Appendectomy	1	-9.86	0.010*	1	-13.92	0.005*
Multilayer 12-cm Repair	1	-7.26	0.018*	1	-5.96	0.027*
Single layer 12-cm Repair	1	-3.06	0.092	1	-2.6	0.102

PGY-5 = 5<sup>th</sup> year surgical resident; PGY-2 = 2<sup>nd</sup> year surgical resident; DF = degrees of freedom; NSP = nonsurgeon physician (EP).

\*Significant difference ( $P < 0.05$ ).

between a novice and an expert. The intubation data may also support this given the similar magnitude of the effect, though we urge caution in drawing conclusions based on the single point of comparison.

However, the small sample size and number of simulations means that this value should not be taken as a definitive answer. This study is more valuable for its demonstration of the ability to detect a difference than its conclusion of the magnitude of this difference, though the magnitude may be useful for future studies when conducting a power analysis to determine sample size and/or number of simulations.

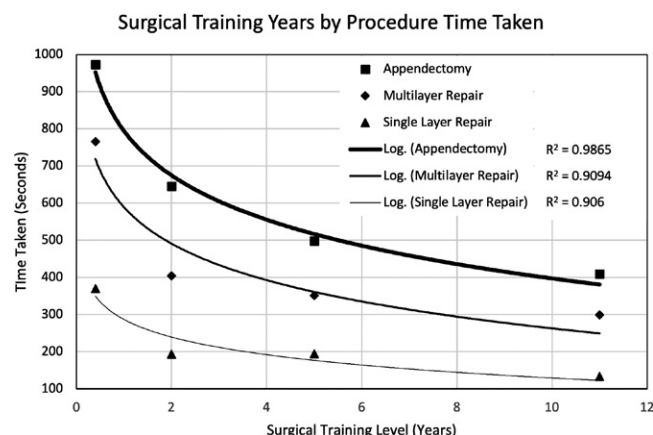
It is also worth noting that an attending Emergency Physician is not naïve to surgical methods. Lower KSA providers, such as physicians who have not completed Emergency Medicine residency or nonphysician crew medical officers, may take significantly longer to perform this procedure.

Another interesting finding is the lack of a significant MOOTSke between the EP and the surgical residents for the single layer repair while the MOOTSke with the ES was significant. Single layer tissue repair is a common procedure for both specialties. However, surgeons perform the procedure multiple times a day at the close of surgeries in the operating room, while Emergency Physicians perform it regularly for patients with skin lacerations in the Emergency Department. Given this, one might expect that there would be no time difference between attending physicians from either specialty. However, the regularity of the procedure for surgeons compared to the episodic nature of it for Emergency Physicians may provide a clue. A logarithmic learning curve predicts that the greatest learning effect will appear early in training, with subsequent MOOTSke reductions taking progressively longer to manifest. Based on

this, one would expect to see progressively shorter times based on number of times the procedure is performed and, indeed, when the single layer repair times are plotted on a graph against years of surgical training, they neatly fit a logarithmic curve, with the  $R^2$  value slightly lower than in the other curves (Fig. 2). This supports the conclusion that the confusing significance pattern may be a result of insufficient power from the miniscule sample size. It is also possible that the EP is simply not as skilled with suturing and additional training and or experience will decrease their procedure times.

Taken as a whole, this pilot study suggests that MOOTSke is likely to have a substantial effect on procedure time. Thus, MOOTSke may have a considerably negative impact on available crew time during a mission. Our average measured effect was that a novice took an average of 2.5 times longer to perform a procedure under ideal circumstances and in a familiar environment. This difference is likely to increase when the circumstances are less than ideal and the environment unfamiliar, as they would be during a medical emergency in space. The silver lining is that the converse is also true: an experienced medical provider could cut the time spent on medical operations by more than half. This is particularly true if the MOOTSke holds up for other aspects of medical care such as interpretation of clinical data, medical management decisions, and patient assessments. These tasks are harder to evaluate, but represent a critical part of all medical care and may be just as costly in terms of crew time.

One other aspect worth noting is that the EP in this study would not have been able to complete the procedure without expert guidance. While real-time, telemedical support was sufficient for the second EP appendectomy, the initial run was done in person. This is not surprising, given that emergency medicine and surgery are different specialties with vastly different training, but it does raise an important issue. While all physicians are highly trained, that training is not equal. Physicians trained in different specialties have different skillsets that may not have much overlap. Terrestrial medicine has long required a team approach which may be limited or even unavailable in space.<sup>3</sup> Furthermore, the distances at which exploration class missions operate mean they will not have access to real time telemedical guidance.<sup>9,10</sup> This may degrade many procedure outcome metrics, including MOOTSke. These points make it unlikely that the skillset required by a true deep space exploration medical officer will fall neatly into any single terrestrial training paradigm. Determining the optimal training curriculum for such a practitioner will require substantial additional study.



**Fig. 2.** Years of surgical training (x-axis) by time required to perform procedure.

**Table III.** Time Taken for Surgical Procedures by KSA Level and Novice to Expert Effect Size.

	EXPERT	PGY-5	PGY-2	NSP	EFFECT SIZE NSP TO EXPERT
Years of practice	11	5	2	0.4	
Appendectomy 1	419	540	646	949	2.26
Appendectomy 2	400	456	644	996	2.49
12-cm multilayer repair 1	345	408	344	762	2.21
12-cm multilayer repair 2	252	294	465	770	3.06
12-cm single layer repair 1	126	237	144	332	2.63
12-cm single layer repair 2	138	150	241	407	2.9
Average effect size					2.59 SD, 0.34

KSA = knowledge, skills, and abilities; PGY-5 = 5<sup>th</sup> year surgical resident; PGY-2 = 2<sup>nd</sup> year surgical resident; NSP = nonsurgeon physician (EP).

As a pilot study, the primary goals were to test the feasibility of our simulation method for capturing time data, estimate effect size, and identify areas for further study. Our method for capturing procedure time through low-cost procedure simulation and subprocedure analysis was successful. We were able to identify a potentially large effect of training level on procedure time that appears to follow a logarithmic curve. However, this study is limited in many ways.

First and foremost, it consists of a small sample size with participants only completing two simulations. Therefore, it is not possible to draw definitive conclusions about effect size without substantially increasing the number of participants and/or trials. Furthermore, the EP could not perform the procedure without guidance from an expert surgeon. This means that the time taken for the “novice” reflects the required time with real time instruction. The EP’s second attempt was done with remote guidance via a telemedicine set up and, anecdotally, required less instruction, but this too reveals a limitation of the study. Two appendectomies done in relatively quick succession by the same provider may demonstrate a training effect on time to complete the procedure. While the authors believe it unlikely that this effect would be substantial, and the magnitude seen in the experiment despite the small sample size argues against this, the potential cannot be entirely discounted and may affect the accuracy of our results.

Secondly, it is worth noting that the skills required for a successful appendectomy require KSA from at least two different terrestrial specialties: anesthesia and surgery. These specialties do not overlap in skillsets and, even in this study, the KSA required for intubation and surgery are not often present in the same provider without substantial additional training and practice. Therefore, MOOTSke may be best evaluated by comparing experts on individual capabilities rather than tying it to terrestrial specialty expertise and potentially combining all aspects of a procedure together (as was done with skin closure and appendectomy) rather than measuring each individually (as was done with intubation and appendectomy).

Third, this study did not account for the time required to set up equipment, prep the patient, monitor the patient for recovery, nor any other associated medical tasks. This means that the operational cost of medical procedures is likely to be far greater than the procedure itself and this time should be investigated in future studies to ensure accurate time values and evaluate the operational significance (or lack thereof) for the MOOTSke.

Finally, the study was conducted in a 1-G, nonspacecraft environment. It is unable to account for the effect of environmental differences on MOOTSke. The comparison of procedure time between environments, however, may be an interesting follow-on study.

Future studies should seek to increase the simulation fidelity and address these limitations. Additionally, future studies would benefit from optimizing camera angles for the specific procedure and simulating a more continuous procedure, starting with equipment set up, patient prep, IV insertion, rapid sequence induction, surgery, and recovery. This will enable more accurate estimation of the procedure time cost. It is also worth devising a method for assessing the nonprocedural MOOTSke skills alluded to above (clinical data interpretation, management decisions, and patient assessment). These skills could be tested for various KSA levels with and without clinical decision aids to assess both the MOOTSke magnitude and methods for mitigating it.

In conclusion, this pilot study demonstrated a method for capturing the medical officer procedure time cost of a simulated appendectomy and several sub-procedures by provider experience level and suggests that the magnitude of the Medical Officer Occupied Time Skill Effect (MOOTSke) on this procedure follows a logarithmic curve. It also suggests that provider skill level may have a substantial effect on available crew time which may be mitigated by flying higher skill level providers or through targeted training of crew medical officers.

This study is limited in many ways, including small sample size, limited number of tested medical capabilities, a simulation set up that may not accurately reflect mission conditions, and suboptimal camera angles. Future studies should seek to improve on these limitations.

## ACKNOWLEDGMENTS

*Financial Disclosure Statement:* The authors have no competing interests to declare.

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Springfield, MA, USA, and Tovy Kamine, Department of Healthcare Policy and Population Science, University of Massachusetts Chan School of Medicine, Worcester, MA, USA.

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## Erratum

Erneston CG, Fass RD, Ritschel JD, Cox AM. A preliminary analysis of the costs and benefits of physical therapy and strength training for fighter pilots. *Aerosp Med Hum Perform.* 2022; 93(8):637–642.

DOI: <https://doi.org/10.3357/AMHP.6086.2022>

In the above article, Tables III and IV should have been updated to show that the first column heading should be SUMMARY. BENEFITS should be a sub-heading beneath the column heading.

Below are the corrected tables. We apologize to the authors and subscribers for this error and the inconvenience it has caused.

**Table III.** Equivalent Annual Worth Summary Table (OHWS Replaces Up to 100% of Outpatient Costs; 0% of Work Loss Costs).

SUMMARY	EAW 0%	EAW 2%	EAW 4%	EAW 6%	EAW 8%
<b>Benefits (B)</b>					
Outpatient	\$530,838	\$530,665	\$530,506	\$530,360	\$530,228
Work Loss (WL) is considered a wash cost					
1 Pilot Training Year	\$1,644,000	\$1,778,821	\$1,958,698	\$2,194,246	\$2,500,156
<b>Costs (C)</b>					
OHWS Contract	\$ 4,980,263	\$ 5,009,310	\$ 5,039,099	\$ 5,069,606	\$ 5,100,807
<b>Net (B – C)</b>					
Best Case 100%	\$(4,449,425)	\$(4,478,645)	\$(4,508,593)	\$(4,539,245)	\$(4,570,579)
Optimistic 90%	\$(4,502,509)	\$(4,531,712)	\$(4,561,644)	\$(4,592,281)	\$(4,623,602)
Moderate 50%	\$(4,714,844)	\$(4,743,978)	\$(4,773,846)	\$(4,804,425)	\$(4,835,693)
Pessimistic 10%	\$(4,927,180)	\$(4,956,244)	\$(4,986,048)	\$(5,016,569)	\$(5,047,784)
Worst Case 0%	\$(4,980,263)	\$(5,009,311)	\$(5,039,099)	\$(5,069,606)	\$(5,100,807)
<b>Breakeven*</b>					
Best Case	2.71	2.52	2.30	2.07	1.83
Optimistic	2.74	2.55	2.33	2.09	1.85
Moderate	2.87	2.67	2.44	2.19	1.93
Pessimistic	3.00	2.79	2.55	2.29	2.02
Worst Case	3.03	2.82	2.57	2.31	2.04

OHWS: Optimizing the Human Weapon System; EAW: equivalent annual worth.

\*Represents the improvement in pilot retention (# pilots) required for EAW to equal \$0.

**Table IV.** Equivalent Annual Worth Summary Table (OHWS Replaces Up to 100% of Outpatient and Work Loss Costs).

SUMMARY	EAW 0%	EAW 2%	EAW 4%	EAW 6%	EAW 8%
<b>Benefits (B)</b>					
Outpatient	\$530,838	\$530,665	\$530,506	\$530,360	\$530,228
Work Loss (WL)	\$4,686,474	\$4,685,180	\$4,683,894	\$4,682,617	\$4,681,349
Total	\$5,217,312	\$5,215,845	\$5,214,401	\$5,212,978	\$5,211,577
1 Pilot Training Year	\$1,644,000	\$1,778,821	\$1,958,698	\$2,194,246	\$2,500,156
<b>Costs (C)</b>					
OHWS Contract	\$4,980,263	\$5,009,310	\$5,039,099	\$5,069,606	\$5,100,807
<b>Net (B – C)</b>					
Best Case 100%	\$237,048	\$206,535	\$175,302	\$143,372	\$110,770
Optimistic 90%	\$(284,683)	\$(315,050)	\$(346,139)	\$(377,926)	\$(410,388)
Moderate 50%	\$(2,371,607)	\$(2,401,388)	\$(2,431,899)	\$(2,463,117)	\$(2,495,018)
Pessimistic 10%	\$(4,458,532)	\$(4,487,726)	\$(4,517,659)	\$(4,548,308)	\$(4,579,649)
Worst Case 0%	\$(4,980,263)	\$(5,009,311)	\$(5,039,099)	\$(5,069,606)	\$(5,100,807)
<b>Breakeven*</b>					
Best Case	–	–	–	–	–
Optimistic	0.17	0.18	0.18	0.17	0.16
Moderate	1.44	1.35	1.24	1.12	1.00
Pessimistic	2.71	2.52	2.31	2.07	1.83
Worst Case	3.03	2.82	2.57	2.31	2.04

OHWS: Optimizing the Human Weapon System; EAW: equivalent annual worth.

\*Represents the required improvement in pilot retention (# pilots) required for EAW to equal \$0.

## Erratum

Wingelaar-Jagt YQ, Wingelaar TT, Riedel WJ, Ramaekers JG. *Subjective effects of modafinil in military fighter pilots during deployment.* *Aerosp Med Hum Perform.* 2022; 93(10):739–745.

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In the above article, the authors made an error in Table II. In the sixth column, labeled 'Mood', third and fourth lines down, the 4 should be a 3 and the 73 should be a 72. Below is the corrected table with apologies for the inconvenience.

**Table II.** Side Effects Encountered During Ground Tests.

	HEADACHES	DIZZINESS	NAUSEA	SLEEPINESS	MOOD	OTHER
Severe	1	0	0	0	0	0
Moderate	0	0	1	0	0	0
Mild	7	0	1	4	3	5
None	67	75	73	71	72	70
Total	75	75	75	75	75	75

### STATEMENT OF OWNERSHIP, MANAGEMENT AND CIRCULATION (Required by 39 U.S.C. 3685)

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### 15. Extent and Nature of Circulation:

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1. Paid/requested outside county mail subscriptions	748	86
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4. Other classes mailed through USPS	0	0
c. Total paid/requested circulation	1153	141
d. Free distribution:		
1. Outside county	0	0
2. In-county	0	0
3. Other classes mailed through USPS	0	0
4. Free distribution outs	35	50
f. Total free distribution	35	50
g. Total distribution	1188	191
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i. TOTAL	1359	211
Percent Paid and/or Requested Circulation	97.03%	73.82%

## Aerospace Medicine Clinic

This article was prepared by Ian D. Gregory, D.O.

You are seeing patients in the Flight and Operational Medicine Clinic of a U.S. Air Force base when your next patient presents with a recent history of a seizure. He is a 33-yr-old male C-17 pilot who first sought care about 7 wk ago after having a “syncopal episode” where he fell and hit his face, suffering a nasal fracture that required surgical repair. About 6 wk later, he had a witnessed loss of consciousness, with generalized tonic-clonic movements of his body. Clinical suspicion in the emergency room after this visit was high for diagnosis of seizure. He has no past medical history and does not take any medications regularly (including over the counter or supplements). He denies a family history of seizures or any other significant condition. He also denies tobacco or illicit drug use and infrequently drinks alcohol.

On examination, he is 71 in tall, 173 lb, and has normal speech and comprehension. Heart and lung exam is normal. His nasal fracture (from 1 mo ago) is healing normally. Basic neurological exam (including cranial nerves, mental status exam, motor and sensory exam, reflexes, cerebellar testing) is normal. Vital signs are normal.

1. A differential diagnosis for a seizure includes all of the following except:
  - A. Early stage dementia.
  - B. Syncope.
  - C. Migraine headache.
  - D. Paroxysmal movement disorders.
  - E. Psychogenic nonepileptic seizures (PNES).

### ANSWER/DISCUSSION

1. **A.** Seizures are common throughout the world, with an estimated 50 million people affected with epilepsy (seizure disorder).<sup>22</sup> It is also estimated that the incidence of all seizures, whether a part of epilepsy or not, is 29–39 per 100,000 per year, or affecting up to 10% of the population over their lifespan.<sup>8</sup> There are several presentations for seizures, with most being divided into the classifications of either focal or

generalized. Focal seizures have electrical activity start in only a specific part of the brain and then may spread (secondarily generalized). A larger area (both sides) of the brain is affected in generalized seizures, which can present as just staring spells, myoclonic jerks, or generalized tonic-clonic movements. In addition to the location of brain involvement, seizure types are divided into categories based on the type of or absence of motor activity.<sup>8,16</sup> Main categories of seizure type include focal onset, generalized onset, and unknown onset. Within these categories, seizures are further subdivided based on motor or nonmotor onset.<sup>7</sup>

Since the presentations of seizures can vary, there are multiple different conditions that can also mimic seizure activities. Depending on the presentation of the seizure and the presence of any potential comorbidities, syncope, migraine headaches, or paroxysmal movement disorders can all present similarly to different types of seizures. Syncopes specifically can have tonic-clonic type motor movements and can very much mimic generalized motor seizures. Additionally, PNES, also known as nonepileptic seizures, psychogenic seizures, or pseudo-seizures, can be the actual cause of up to 30% of patients admitted to epilepsy centers for evaluation and up to 60% of military members with a new diagnosis of seizure.<sup>2,14</sup> These patients have seizure-like motor movements, but do not have the epileptic brain activity causing the movements. Psychiatric/psychological underlying stressors are found in these members, and it is thought the PNES is a dissociation defense mechanism. Because of the multitude of seizure mimicking conditions, a good history of the event (from an observer) and past medical history are very important for determining where to focus the evaluation and subsequent treatment.

Upon review of the initial diagnostic studies for the patient, both from the emergency room (after the witnessed tonic-clonic event) and subsequent neurology evaluation, the diagnosis of epilepsy (seizure disorder) was given.

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2. Which of the following is not an appropriate study to obtain in the workup of a patient with a suspected seizure?
- Magnetic resonance imaging (MRI).
  - Computed tomography (CT).
  - Electroencephalogram (EEG).
  - Electromyography.
  - Complete blood count (CBC).

## ANSWER/DISCUSSION

2. **D.** The evaluation for suspected seizures consists of many different modalities. An MRI is recommended for the evaluation of all initial seizures, as it is effective at identifying structural findings associated with seizures. The timing of when the MRI should be performed is often debated, but most agree it can be done in an outpatient setting if the patient is clinically stable.<sup>3,13</sup> A CT of the head should be strongly considered in all patients with acute seizure if there is a clinical history of trauma, risk of bleeding, or other urgent matters that require evaluation.<sup>10</sup> An EEG, if it can be obtained during an actual seizure, is the gold standard for diagnosis to identify specific brain wave activity during a seizure. EEGs can generally be performed in an outpatient setting, but should be considered more urgently if a patient has not returned to baseline status after noticeable seizure activity has stopped.<sup>13,18</sup> Currently, electromyography has no role in the routine evaluation for seizures. Routine blood work, including comprehensive metabolic panel, CBC, glucose, pregnancy testing, and potentially cerebrospinal fluid evaluation, should be performed on all initial seizures to evaluate for any underlying abnormalities.<sup>1</sup>

The blood work from the emergency room showed a normal CBC and comprehensive metabolic panel (including glucose level). The CT of the head confirmed the nasal fracture, but was otherwise normal. Cerebrospinal fluid evaluation from lumbar puncture was normal except notable only for a protein level at the upper limits of normal at  $56 \text{ mg} \cdot \text{dL}^{-1}$ . MRI of the brain was normal, and the EEG showed bifrontal intermittent rhythmic delta waves, consistent with significant brain dysfunction, probably postictal in this case.

3. Which of the following is incorrect regarding the initial stages of evaluating/managing a patient with a new onset suspected seizure?
- EEGs are very useful for the diagnosis of seizures, but their utility decreases the farther out from the reported activity the EEG is performed.
  - History and risk factor evaluation are very important for making the correct diagnosis.
  - A normal EEG and MRI rule out an epileptic seizure.
  - For someone with an obvious acute/reversible cause of the seizure (such as hypoglycemia, eclampsia, or impact seizures from mild to moderate traumatic brain injury), antiepileptic drug therapy is generally not indicated for treatment.

## ANSWER/DISCUSSION

3. **C.** Individuals with seizure disorders will not always have abnormal findings on EEG. The timing of conducting the diagnostic EEG after an initial seizure is important, with the best time to conduct the EEG being at the time of the actual seizure. Within 24 h is generally considered acceptable to do the EEG, but studies have shown that 50% of people will show no abnormal wave forms on EEG 24 h after a seizure, and 75–80% will have no abnormalities 48 h later.<sup>4</sup> A proper history is always an important part of making any diagnosis, including seizure disorder. Information from a witness can provide diagnostic clues to help make the diagnosis, particularly in the setting of someone who has risk factors for seizures (increased age, head trauma, family history, alcohol withdrawal, etc.). As described, EEGs and MRIs are very important for confirming the diagnosis of a seizure, but frequently they will not show any abnormalities, depending on the timing of the study or type of seizure. Since most people with a seizure have no identifiable underlying cause, and the risk of developing a second seizure is high (21–45% in the first 2 yr), some patients with an initial seizure get started on antiepileptic medication immediately following diagnosis, particularly those with a nocturnal seizure or EEG or MRI that portends a higher risk.<sup>12</sup> However, for those with an underlying treatable cause, most are not started on medication and instead obtain treatment of the underlying issue.<sup>11</sup>

Upon further questioning, the patient states that for 1–2 yr he has been having episodes lasting 15–20 s described as trouble perceiving speech. He knew that something was not quite right, but didn't think it was anything serious, as he was still able to function at home and work quite well.

4. Neurologically normal adults (particularly in a screened population) who experience an initial seizure most commonly have which of the following risk factors?
- Head injury.
  - Infection.
  - Cerebral tumor.
  - Family history of seizure disorder.
  - None of the above.

## ANSWER/DISCUSSION

4. **E.** There are multiple risk factors for seizure, a common one being a history of a prior seizure. Head injury/trauma often can lead to a cerebral hemorrhage, which can lead to a seizure acutely or over time. Infection can cause inflammation of the brain tissue, which can lead to seizure activity. Tumors, with focal dysfunction from a variety of mechanisms, are a common cause of seizure. Individuals with epileptic seizures may be up to three times more likely to have a family member with epilepsy.<sup>1</sup> In the 35–64 age range, 15% of seizures are thought to be from cerebrovascular causes, 7% are posttraumatic, and 7% are

from tumors.<sup>11</sup> However, up to 60% of all patients with seizures have no known risk factors.<sup>11,17,19</sup>

Now that a seizure has been confirmed in your patient, he has many questions about seizure types. He is confused because he thought that all seizures involved convulsing of the body. You explain to him that the periods of amnesia he was having earlier likely were actually seizures as well. He wants to know more about the different types of seizures.

5. What is the most likely seizure type that neurologically normal adults will have as their first seizure (not necessarily the first seizure type for which they first seek medical care)?
  - A. Generalized tonic-clonic.
  - B. Focal impaired awareness (formerly known as complex partial seizure).
  - C. Generalized nonmotor (absence).
  - D. Generalized myoclonic.
  - E. Focal atonic.

## ANSWER/DISCUSSION

5. **B.** While the classic clinical presentation of a generalized tonic-clonic seizure tends to be more obvious, where the patient has usually less than a minute of full body jerking and shaking with loss of consciousness and/or confusion, many seizures have different presentations and may occur for an extended period of time before a diagnosis is made. In focal impaired awareness seizures (formally known as complex partial seizures), only part of the brain is affected, and often-times no dramatic tonic-clonic activity is seen. However, small, subtle, stereotyped automatisms are common. In these seizures, the patient may have brief periods of confusion and amnesia and present with or without muscle tension. Often-times these patients report needing to have conversations repeated back to them because they frequently don't remember what was happening to them in the prior few minutes (which is also common in generalized nonmotor seizures). Amnesia is common in complex partial seizure types, making the diagnosis challenging.<sup>5</sup> This may happen for a long time before it is recognized, by the patients or someone close to them, or a new seizure type occurs, and medical attention is sought.

As a U.S. Air Force pilot, the member is very concerned about his ability to resume his flying career in the future. He realizes he has a serious medical condition, but also knows that waivers are granted regularly to experienced pilots such as himself for many different medical conditions.

6. Based on this member's clinical presentation, workup, and treatment, the likelihood of this member returning to flying duties in the U.S. Air Force is:
  - A. Zero chance. Seizures are not compatible with flying duties, and there is no chance for waiver potential, as

there have never been any waivers granted for aviators who have had a seizure.

- B. Minimal chance. Seizures are not compatible with flying duties. Few waivers have been granted in situations where risk of recurrence and risk to mission and human life were thought to be low, but they were rare situations.
- C. Pretty good chance. While the Medical Standards Directory states that seizures are not compatible with flying duties, if a member can stay seizure free for multiple years on appropriate treatment, a waiver is likely to be granted.<sup>20</sup>
- D. Excellent chance. As long as a pilot can demonstrate stability on appropriate treatment, then he or she should be returned to flying duties.

## ANSWER/DISCUSSION

6. **B.** According to the U.S. Air Force Medical Standards Directory, the accompanying medical standards document to Department of the Air Force Manual 48-123, Medical Examinations and Standards, seizures are not compatible with flying duties. (Waivers can be considered on a case-by-case basis when a single seizure was obviously provoked by trauma or an extrinsic factor.)<sup>20</sup> Because the risk of recurrence for unprovoked initial seizures is so high (greater than 40% over 5 yr), waivers for these types of seizures are rare. In 2019, a search of the Air Force waiver tracking system showed that of the seizure waivers approved for flying duties, the large majority were for initial applicants who had a history of childhood febrile seizure (which does not portray a higher risk for future seizures as an adult). A few waivers were granted for provoked seizures where the member had shown subsequent stability. The high risk for recurrent seizures in unprovoked initial seizures is the primary reason that waivers are usually not recommended for continued flying duties.<sup>9,20</sup> The U.S. Army and U.S. Navy have similar standards for waivers among aviators. Any seizure is disqualifying for aviation duties.<sup>15,21</sup> According to the Federal Aviation Administration, an aviator with epilepsy, or any seizure that cannot be explained by an underlying cause, may not be approved for flying by a local Aviation Medical Examiner. All cases must be deferred for Federal Aviation Administration disposition and are considered on a case-by-case basis.<sup>6</sup> However, for a Special Issuance to be considered, historically, the pilot must be at least 4 yr removed from the seizure and 2 yr off medications. Generally, for a pilot with multiple seizures (or a diagnosis of epilepsy), the pilot must be at least 10 yr seizure free and 3 yr off medications (Hesselbrock R. Personal communication; 2021. Murphy R. Personal communication; 2021).

After 2 yr of treatment, your pilot had yet to obtain clinical stability. He had tried and failed different treatment regimens and was still having breakthrough seizures. He was given a medical disqualification from flying with the U.S. Air Force.

Gregory ID. *Aerospace medicine clinic: epilepsy (seizure disorder) diagnosis in an aviator*. *Aerosp Med Hum Perform*. 2022; 93(11):824–827.

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**NOVEMBER 1997**

*Gender differences in parachuting injuries* (U.S. Army Research Institute for Environmental Medicine, Natick, MA; Social Sectors Development Strategies, Inc., Natick, MA; U.S. Army Center for Health Promotion and Preventive Medicine, Aberdeen Proving Grounds, MD): "While military parachuting injuries have been well studied, the relationship between gender and risk of injury has not. Injuries among women may be different due to anatomic and physiologic differences, or due to exposure to different jump conditions. Training methods and equipment developed for men may not be as effective in preventing injuries among women... This descriptive retrospective study used 10 yr of parachute injury data reported to the U.S. Army Safety Center at Fort Rucker, AL, and exposure data obtained from the Defense Manpower Data Center, Monterey, CA... Women appear to jump under less hazardous conditions (jump more often than men in daylight and in static-line, non-tactical environments), yet appear to be at greater risk of serious injury, particularly lower extremity fractures. Injured male parachutists are more likely to experience upper extremity injury. Women's injuries are more likely to be the result of an improper parachute landing fall or parachute malfunction, while men are more likely to be injured due to ground hazards... There are some provocative gender differences in patterns of injury. Further research is indicated starting with a comprehensive, prospective study, controlling for physical fitness and exposure differences, as well as for potential reporting bias, in order to better understand the apparent differences in reported injuries."<sup>2</sup>

**NOVEMBER 1972**

*Mishaps among waived aviators* (Air Force Inspection and Safety Center, Norton AFB, CA): "During past years thousands of United States Air Force (USAF) airmen have been granted medical waivers for a great variety of conditions in order that they could continue flying. Although these waivers have been granted with reasonable assurance that flying safety has not been compromised, there may still be an element of doubt in some cases. In order to eliminate this doubt (or possibly to confirm it) the author reviewed the final reports of all USAF aircraft accidents/incidents which occurred during the period 1 January 1962-31 December 1970 in which the pilot or navigator was flying with a medical waiver... Only 33 such cases were identified in which the pilot or navigator was flying with a waiver for an ophthalmologic (17), neurologic (8), cardiopulmonary (5) psychiatric (2) or otolaryngologic (1) disorder which could have been a contributing cause. Perhaps this is an indication that the USAF waiver policy through the years has been prudent and consistent with flying safety."<sup>4</sup>

*Pulling G and the EKG* (USAF School of Aerospace Medicine, Brooks AFB, TX): "Electrocardiograms were recorded during 45-sec. exposures to +6.5 to +9.0 G<sub>z</sub> of 14 human subjects on the USAF School of Aerospace Medicine human centrifuge. Maximum heart rate (HR) reached by each subject ranged from 155 to 205 beats/min. Four subjects developed a slowing of HR at 16 to 38 seconds into the run due to slowing of the sinus pacemaker, sometimes the escape of an A-V junctional or ventricular pacemaker. Similar escape rhythms also occurred during the sinus slowing with deceleration. Ventricular premature beats (VPBs) occurred frequently in

7 subjects, occasionally in 6, and not at all in one. When frequent, the number increased markedly in the latter part of the 45-sec. runs. These VPBs were frequently multiform and occasionally occurred in runs of 2 or 3 with a few runs of 4 to 7. In no case did any serious arrhythmia persist after deceleration, nor did G tolerance appear to be affected. The etiology and significance of these arrhythmias remain unclear."<sup>5</sup>

**NOVEMBER 1947**

*Air evacuation success record* (Chief, Air Evacuation Department, School of Aviation Medicine, Randolph Field, TX): "The pioneer advocates of air transportation of casualties in the various Air Forces, United States and foreign, visualized the rapid, safe, and logistically economical transportation of war casualties by airplane. The development of air evacuation of casualties has necessarily been dependent on the growth of modern aviation and an opportunity such as afforded by the recent war to prove its feasibility. The judgment of the pioneers in air evacuation has been vindicated by its highly successful operation in World War II.

"Air evacuation today is supported by military authorities because of its logistic and strategic advantages. Medical personnel endorse and favor it since it provides casualties with comfortable transportation to definitive medical care in the shortest possible time. In addition, it is of great value in stimulating morale, and consequently hastening the recovery of the sick, injured and wounded."<sup>3</sup>

*Preparation for ejection* (Aero Medical Laboratory, Wright Field, Dayton, OH): "In service use, it is evident that a thorough indoctrination should be given all pilots of aircraft equipped with ejection seats so that they may become conditioned to the sequence of events prior to ejection and appreciate the necessity of assuming the proper body position. This indoctrination should consist of a demonstration of the equipment, movies of actual live ejections, such as the two made in August, 1946, at Wright Field, and an ejection on the 100-foot ejection seat test tower."<sup>1</sup>

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# Aerospace Medicine and Human Performance

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