Comparison of an Intermittent Hypoxic Exposure Acclimatization Program to Staging at Moderate Altitude on Endurance Performance at 4300 m

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ABSTRACT

Endurance performance decreases upon initial exposure to altitude but improves following acclimatization induced by continuous altitude residence. For low-altitude residents, acclimatization to a target altitude can be induced by temporarily residing (staging) at moderate altitudes. However, staging may not be available or logistically practical for low altitude-based Warfighters needing to rapidly ascend to high altitude. An alternative method for inducing altitude acclimatization, termed intermittent hypoxic exposure (IHE), may provide an acceptable alternative for minimizing endurance performance decrements at altitude following rapid ascent. ***PURPOSE:*** *The purpose of this study was to compare the effects of one week of normobaric IHE to one week of staging (STG) at 2,200 m on endurance performance at 4,300 m altitude in healthy male lowlanders.* ***METHODS:*** *Two studies were conducted using the same facilities, test equipment and investigators. IHE study: 11 male lowlanders (Mean±S.E., age: 22±1 yr, VO_2peak: 47±5 $ml•kg^{-1}•min^{-1}$) were initially (Pre-T) exposed to 4,300 m, followed by ~12 days of sea level residence to deacclimatize, then 6-7 days of normobaric IHE (hypoxia room: 2 h PIO_2=90 mmHg sedentary & 1 h PIO_2 =110 mmHg exercising at 80% peak heart rate) followed by a 60 hour delay at sea level and a second exposure (Post-T) to 4,300 m. STG study: 10 male lowlanders (age: 21 ± 1 yrs, VO_2peak: 51±7 $ml•kg^{-1}•min^{-1}$) were initially exposed to 4300 m before (Pre-T) and after (Post-T) staging for 6 d at 2,200 m. In both studies, subjects were tested on a cycle ergometer during 40 min steady-state exercise followed immediately by a 360 kJ maximum effort Time-Trial (TT) at sea level, and again beginning within 3 hrs of high altitude (HA) exposure to 4,300 m. During the TT, the men freely adjusted power output. Arterial oxygen saturation (SaO_2), heart rate (HR), and ratings of perceived exertion (RPE) were measured every 5 min during exercise.* ***RESULTS:*** *From Pre-T to Post-T at 4,300 m resting SaO_2 increased ($p<0.05$) from 81±1% to 82±1% in the IHE group, and increased ($p<0.05$) from 80±1% to 83±1% in the STG group. Pre-T sea level TT duration was 38.9±1.9 and 40.8±1.3 min, in the IHE and STG groups, respectively. In the IHE group, from Pre-T to Post-T at 4,300 m there was no improvement in TT performance (62.0±4.8 to 63.7±5.2 min), exercise SaO_2, HR or RPE. In contrast, in the STG group from Pre-T to Post-T at 4,300 m TT performance improved ($p<0.05$) from 65.2±6.7 to 51.0±6.8 min, RPE was lower (16±1 vs. 13±1, $p<0.01$), but SaO_2 and HR were unchanged despite a higher exercise intensity.* ***CONCLUSION:*** *Whereas staging at moderate altitude for 6 days effectively improved endurance performance at 4,300 m, 6-7 days of normobaric IHE did not improve endurance performance in lowlanders. One week of normobaric IHE, therefore, is not an efficacious alternative to actual altitude exposure to induce acclimatization.*

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14. ABSTRACT

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1.0 INTRODUCTION

Modern military operations frequently require rapid deployment of personnel into extreme environments (altitude, cold, heat) with little or no time for physiological acclimation. However, rapid deployment of unacclimatized Soldiers to high (>1,500 m) mountainous environments may cause debilitating effects on operational capabilities (i.e., physical work performance) and force health (i.e., altitude sickness).

All unacclimatized Soldiers experience marked decreases in maximal and submaximal aerobic performance at elevations above 1,500 m (7). With increasing altitude VO_{2max} decreases, thus the submaximal oxygen uptake for a given workload at altitude represents a greater percentage of the reduced VO_{2max}. The practical implication is that tasks that require a fixed amount of exercise or work to be performed as quickly as possible (e.g., traveling from point A to B or unpacking a supply truck) must necessarily be conducted at a higher relative exercise intensity at altitude than at sea level.

The natural countermeasure to the aforementioned altitude-induced physical performance decrements is altitude acclimatization. Lowlanders who continuously reside at high altitude develop a variety of physiological adaptations during altitude acclimatization, most notably increased ventilation and hemoglobin concentration. With continuous altitude residence the physiological strain of exercise is lessened, and exercise tolerance at altitude is improved compared to that initially on arrival (9).

For low-altitude residents, acclimatization to a target altitude can be induced by staging (i.e., continuous sojourn) at intermediate altitudes (4; 8; 11; 13). Typically, staging protocols use 4 or more days of continuous residence at altitudes between 1,500- 2,500 m. The expectation is that the modest beneficial adaptations induced during staging will transfer to the higher altitude and thereby help avoid the large reductions in endurance exercise performance that would otherwise occur with rapid, non-staged ascent (5).

Staging to induce altitude acclimatization is dependent on continuous residence at intermediate altitudes and may not be available or logistically practical for low altitude-based military units. In particular, the “altitude residency” requirement reduces their utilization in rapid response military missions that exploit the air mobility capability of modern military forces to quickly deploy to an area of operations on short notice. A more recent approach to altitude acclimatization is the use of daily intermittent hypoxic exposures (IHE) in lieu of continuous residence at high altitudes (10).

IHE treatments can be administered using either hypobaric hypoxia or normobaric hypoxia. In the former, hypoxia is induced by decreased barometric pressure either by ascending to higher elevations (such as in the “live high-train low” paradigm) or by simulated altitude exposure in a hypobaric chamber. Normobaric hypoxia is produced by nitrogen dilution of the inspired air in a small space (tent or room) or mask to lower the PIO_2 to a desired level (for purposes of comparison, throughout this review the level of hypoxia is presented as the equivalent altitude in meters no matter which method of inducing hypoxia is employed). Compared to hypobaric chambers, normobaric hypoxic rooms/tents are relatively inexpensive, and most importantly due to their light weight and small footprint can be shipped and set up to operate anywhere electrical power is available.

IHE treatments consist of three elements: the severity of the hypoxia (simulated altitude), the IHE session duration, and the number of IHE sessions (usually no more than 1 per day) over the trial period (10). In a hypothetical IHE procedure, personnel residing at a low altitude base would participate in daily exposures to simulated altitude prior to deploying on a mission at high terrestrial elevations. However, the effectiveness of normobaric IHE to improve aerobic endurance improvement at high altitude has not been established.

The purpose of this study was to compare the effects of six-seven days of *normobaric* IHE to six days of staging at 2,200 m on endurance performance at 4,300 m altitude. We hypothesized that both approaches to inducing altitude acclimatization would produce similar improvement in a cycle time-trial task conducted within the first 5 hrs (hrs) of exposure to 4,300 m. To test this hypothesis, the results from two independent studies designed and conducted by the authors were compared. Both studies were conducted in our laboratory using identical procedures, equipment and similar facilities. The results of each of these studies have been published elsewhere (1; 6).

2.0 METHODS

All volunteers were active duty male military personnel assigned to the U.S. Army Natick Soldier Center, Natick, MA, USA. All had been living at low altitudes (<1000 m) for at least 3 months prior to the start of the studies. The age, height, weight and sea level VO_2peak (Mean±SE) of the volunteers for each study are presented in Table 1. All volunteers participated in regular Army physical training for 3-4 d•week^{-1} (e.g., running, calisthenics, backpacking). All provided verbal and written consents after being fully informed of the nature of the study they volunteered for, and the possible risks and benefits. The studies was approved by the institutional review boards of the US Army Research Institute of Environmental Medicine (USARIEM), US Army Medical Research and Materiel Command, Human Research Protection Office, and the staging study was also approved by the US Air Force Academy (USAFA).

Table 1: Volunteer Demographics

Study	Number	Age (yrs)	Height (cm)	Weight (kg)	VO_2peak (ml/kg/min)
IHE Study (IHE Group)	11	22±1	179±2	79±3	47± 5
Staging Study (STG Group)	10	21±1	177±3	78±4	51±7

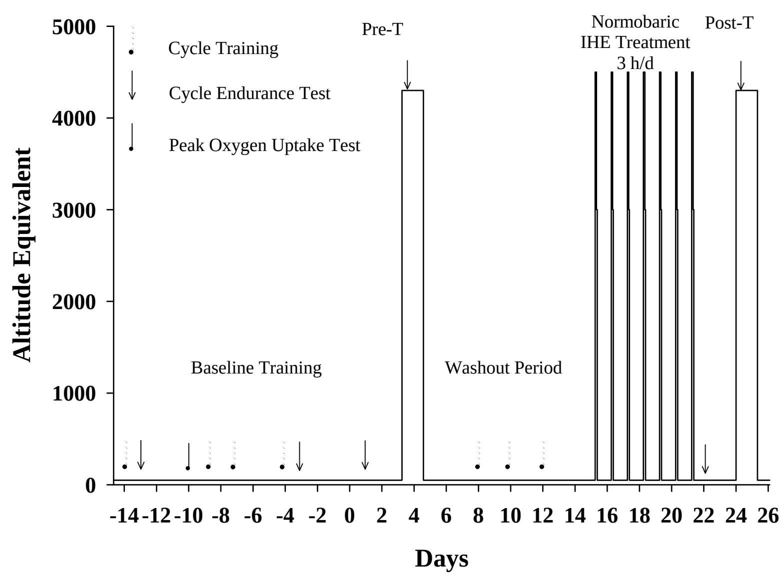
2.1 IHE Study Protocol

The study was designed as a single-blind, sham-controlled trial with one independent factor (IHE vs. SHAM) and two repeated measures factors (environment and test condition). In this paper, only the IHE group data were used in the comparison to the staging study. An outline of the study design and testing schedule is shown in Figure 1. The environments were defined as sea level (SL) and high altitude (HA). The test conditions were defined as pre-treatment (Pre-T) and post-treatment (Post-T).

During the 2-wk SL baseline training, all volunteers performed two cycle endurance tests and four cycle exercise training sessions (consisting of two 25-min exercise bouts on a cycle ergometer at 80±5% of HR_{peak}). Each volunteer also completed a peak oxygen uptake ($\dot{V}O_{2peak}$) test to set appropriate training workloads during treatment and during the cycle endurance test. After baseline training, each volunteer completed Pre-T cycle endurance testing at SL and within the first 5 h at HA (4300 m hypobaric chamber). Given that even one altitude exposure may partially acclimatize an individual upon subsequent exposure to altitude (12), there was a 12-d washout period between the cycle endurance testing at Pre-T and the start of the IHE treatment. During this washout period, the volunteers participated in 3 d of cycle exercise training sessions, defined above, to maintain their fitness level.

The IHE treatment consisted of 2 h rest at a PO_2 of 90 mmHg (4500 m equivalent) followed by two 25-min bouts of cycle exercise at 80±5% of peak heart rate (HR_{peak}) at a PO_2 of 110 mmHg (3000 m equivalent) in a hypoxia room (Colorado Altitude Training System, Boulder, CO). Power output was increased, if necessary, as exercise training progressed to ensure achievement of appropriate training HR. Six of the volunteers in the IHE group completed 7 d of treatment and five volunteers completed 6 d of treatment. Volunteers were not allowed to exercise at SL during the week of IHE treatment. Approximately 60 hrs after completing the final IHE, volunteers ascended to HA to complete the Post-T cycle endurance test.

Figure 1: IHE Protocol Study Design and Timeline



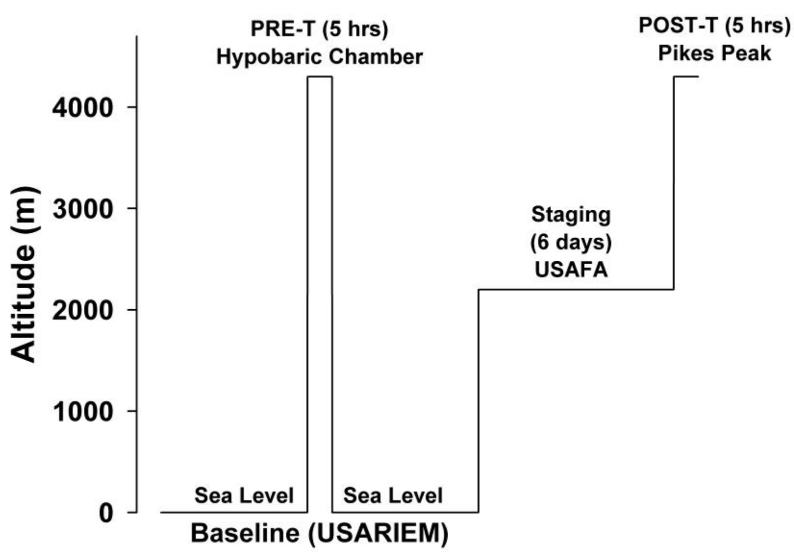
2.2 Staging Study Protocol

This study was organized into three distinct phases at three different test facilities over a period of 12 weeks in the following order (Figure 2): [1] a baseline sea-level and pre-staging (Pre-T) high-altitude assessment phase at USARIEM, Natick, MA, [2] a moderate altitude acclimatization phase at the USAFA (Colorado Springs, CO; 2200 m), and [3] a post-staging (Post-T) high-altitude phase at the summit of Pikes Peak (Colorado Springs, CO; 4300 m). The same equipment that was used at USARIEM also was used at the USAFA and on the summit.

Exercise training and assessments occurred on multiple occasions at USARIEM during the baseline phase and Pre-T testing at sea level (SL, P_B =~760 mm Hg), and within the first 5 h of an 8 h HA exposure (hypobaric chamber, P_B 459 mmHg, similar to the summit of Pikes Peak).

After all testing was completed at USARIEM the volunteers were flown non-stop via airline to Colorado (~ 6 hrs) in groups of two on consecutive days to participate in the staging phase that was conducted over a 6-day period in the Human Performance Laboratory (HPL) at the USAFA (~601 mm Hg). Sending only two volunteers at a time to Colorado allowed the subsequent high-altitude timing and sequence of procedures on Post-T to be maintained identically to those used on Pre-T in the USARIEM hypobaric chamber. The number of days between Pre-T and Post-T testing ranged from 34 to 52 days (median: 46 days) among volunteers. In addition to laboratory-based testing procedures, all volunteers participated in two to four supervised hikes (<3 hr) on trails located on the USAFA base to simulate military scouting patrols, and several cycle exercise training sessions to maintain their fitness level. At 0600 h of the 7th day at the USAFA, the volunteers were driven (~1.5 hrs) to the summit of Pikes Peak. Within two hrs of arriving at the Pikes Peak laboratory, volunteers commenced the Post-T cycle endurance test.

Figure 2: Staging Protocol Design and Timeline



2.3 Test Procedures

Incremental, progressive exercise bouts to volitional exhaustion on an electromagnetically braked cycle ergometer (model: Excalibur, Lode BV, Groningen, The Netherlands) were used to assess peak oxygen uptake (VO_2peak) at USARIEM twice while at SL (1st practice/ familiarization, 2nd definitive). Continuous measurements of O_2 uptake were obtained throughout the tests using a calibrated metabolic cart (True Max 2400, Parvo Medics, Sandy, UT). Data from the VO_2peak tests were used to determine the steady-state power outputs during cycle maintenance training and the cycle endurance tests.

Cycle exercise training was conducted using electromagnetically braked cycle ergometers (model: Corival, Lode BV, Groningen, The Netherlands).

The cycle endurance test was conducted using an electromagnetically braked cycle ergometer (model: Excalibur, Lode BV, Groningen, The Netherlands). The volunteers were instructed not to perform any non-study related leg exercise for 24 hr before each test session. On the morning of their cycle endurance test, for breakfast volunteers were provided with two commercially available energy bars and fruit juice (food composition = 510 kcal, 14 gm fat, 65 gm carbohydrate, 32 gm protein) at 1 to 2 hrs prior to the beginning of each of the cycle endurance test.

Each cycle endurance test consisted of two parts. After a 5-min of warm up at 50 W, volunteers completed steady-state exercise for 20 min at ~40% followed by 20 min at ~60% of their altitude-specific VO_2peak. After a 5 to 10 min rest, the volunteers commenced a 720 kJ maximum effort cycle Time-Trial (TT) task. The volunteers were asked to complete the 720 kJ TT as fast as possible. A shorter completion time from one testing condition to the next was considered an improvement in performance. Volunteers were allowed to alter pedaling speed and adjust power output by any watt increment at any time. Volunteers were continuously informed of the volume of work performed and remaining (via computer screen); but not the time elapsed. To minimize possible interference with volunteer concentration and cycling pace, O_2 uptake measurements and blood samples were not obtained during the TT. Throughout the duration of each test water was provided *ad libitum.* These procedures and the justification for their use have previously been described in detail (5). The TT part of the endurance test provided the primary outcome variable to compare the effects of six-seven days of *normobaric* IHE to six days of staging at 2,200 m on endurance performance at 4,300 m altitude.

Heart rate via HR watch (Polar Electro, Woodbury, NY), SaO_2 via noninvasive finger pulse oximetry (Model 8600, Nonin Medical, Inc, Plymouth, MN), and ratings of perceived exertion (RPE, 6 to 20 Borg scale) (3) were determined every 5 min during the TT. During all testing, the temperature and relative humidity during testing were 21 ± 3^oC and 45 ± 10%, respectively.

For all measurements, a mixed-factorial ANOVA was used to analyze differences between the independent group factor (IHE vs. STG) and the repeated measures factor (Pre-T and Post-T). Significant main effects and interactions were analyzed using Tukey's least significant difference test (Statistica v7.1, Statsoft, Tulsa, OK). Statistical significance was accepted when $P \leq 0.05$. All values are expressed as means ± SE unless otherwise indicated.

3.0 RESULTS

Because nine volunteers could not finish the 720 kJ cycle time trial at HA, the cycle TT analysis was limited to the time to reach 360 kJ (i.e., halfway point) at both SL and HA for all volunteers in both studies.

3.1 IHE Study

During the six days of IHE, in the hypoxia room the volunteers demonstrated a 5% increase ($P<0.05$) in resting SaO_2 (75±1% to 80±1%) measured at 4,500 m equivalent altitude. The exercise SaO_2 during IHE (3,000 m equivalent altitude) was 87±1% and was not different between IHE Days.

At 4,300 m in the hypobaric chamber, from Pre-T to Post-T resting SaO_2 was increased ($p<0.05$) from 81±1% to 82±1%. The IHE group Pre-T SL TT duration was 38.9±1.9 min and following ascent to 4,300 m, increased to 62.0±4.8 min. Post-T at 4,300 m, there was no improvement in TT performance (63.7±5.2 min). Similarly, from Pre-T to Post-T, the IHE group TT mean work rate (103±7 and 104±9 W), SaO_2 (74±1 and 76±1%), HR (146±4 and 144±4 bpm) or RPE (13±1 and 13±1) were not altered.

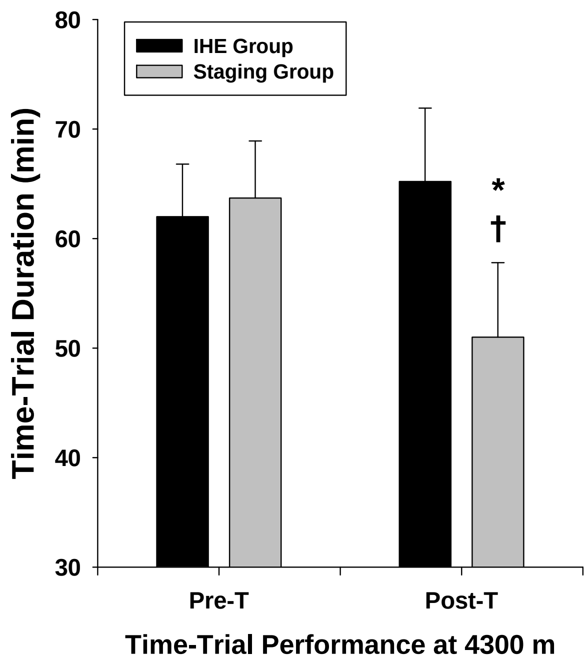
3.2 Staging Study

Over the six days of staging at the AFA, resting SaO_2 was 94±1%. From Pre-T to Post-T, resting SaO_2 increased ($p<0.05$) from 80±1% to 83±1% at 4,300 m (summit of Pikes Peak). The STG group Pre-T sea level TT duration was 40.8±1.3 min, and following ascent to 4,300 m increased ($p<0.05$) to 65.2±6.7 min. Post-T at 4,300 m TT performance improved ($p<0.05$) by 44±8% (51.0±6.8 min). Pre-T to Post-T, the STG group RPE was lower (16±1 vs. 13±1, $p<0.01$), but SaO_2 (74±1 and 76±1%) and HR (148±6 and 148±4 bpm) were unchanged despite a higher ($p<0.01$) work rate (100±10 and 120±7 W). Individual increases in exercise SaO_2 from Pre-T to Post-T were inversely related to decreases in TT duration at HA.

3.3 Comparison of IHE and Staging

Prior to either treatment, TT duration was similar in the IHE and STG groups at SL (38.9±1.9 and 40.8±1.3 min, respectively) and at HA (62.0±4.8 and 65.2±6.7 min). Likewise, Pre-T at HA SaO_2 during rest (81±1 and 80±1%) and TT (74±1 and 74±1%) were not different between the IHE and STG groups, respectively. Post-T (Figure 3), the STG group TT duration was shorter ($p<0.05$) than the IHE group (51.0±6.8 and 63.7±5.2 min, respectively). Post-T, the TT SaO_2 (76±1 and 76±1), HR (144±4 and 148±4 bpm) and RPE (13±1 and 13±1) were not different between the IHE and STG groups, respectively.

Figure 3: Effect of Treatments on Time-Trial Performance at 4300 m



*p<0.05 from Pre-T STG group; † p<0.05 from Post-T IHE group

4.0 DISCUSSION

The results of this study do not support our hypothesis that six-seven days of normobaric intermittent hypoxic exposures and six days of staging at 2200 m produce similar improvement in a cycle time-trial task conducted within the first 5 hrs of exposure to 4,300 m. The results clearly show that staging at 2200 m for six days significantly improved endurance performance following rapid ascent to 4300 m, whereas IHE did not improve endurance performance.

Both IHE and staging strategies induced ventilatory acclimatization as measured by increased resting SaO_2 during the Post-T HA exposure. Although not statistically different, resting SaO_2 was higher in the STG compared to the IHE group at 4300 m. Interestingly, Post-T the SaO_2 during the TT was not different between groups. As reported by Beidleman et al (1), following the last IHE the volunteers remained for ~60 hrs at sea level prior to ascending to 4300 m for the Post-T studies. During this period their ventilatory acclimatization may have been lost, thus negating any improvement in endurance performance Post-T. In contrast, the STG group immediately ascended to 4300 m following 6 days of staging and did not lose any of their ventilatory acclimatization. Although Pre-T to Post-T the STG group's mean TT SaO_2 was not higher, individual increases in exercise SaO_2 from Pre-T to Post-T were inversely related to decreases in TT duration at HA. This relationship between individual increases in SaO_2 and TT performance is consistent with prior results (2) from our lab and illustrates the significant role ventilatory acclimatization has on improving endurance performance at HA. However, this observation does not rule out the possibility that other adaptations may also have contributed to improving TT performance at HA Post-T.

In summary, staging of previously unacclimatized sea level residents at a moderate altitude of 2200 m for six days greatly improved endurance performance during a subsequent exposure to 4300 m. By comparison, six-seven days of a normobaric IHE protocol did not improve endurance performance during a subsequent exposure to 4300 m. The latter finding may have been caused by loss of ventilatory acclimatization during the ensuing 60 hrs of sea level residence after the last IHE. Thus, it remains to be determined if normobaric IHE can improve endurance performance during a subsequent exposure to high altitude as effectively as a similar period of altitude staging. Based on these results, military personnel planning to conduct operations up to at least 4300 m will greatly benefit from a relatively short (6 day) period of moderate altitude residence prior to ascending to higher altitudes.

5.0 DISCLAIMERS

Approved for public release; distribution is unlimited. The views, opinions and/or findings contained in this publication are those of the authors and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation. For the protection of human subjects, the investigators adhered to policies of applicable Federal Law CFR 46. Human subjects participated in these studies after giving their free and informed consent. Investigators adhered to AR 70-25 and USAMRMC Regulation 70-25 on the use of volunteers in research. Any citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement of approval of the products or services of the organizations.

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