Gait instability and estimated core temperature predict exertional heat stroke

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ABSTRACT
Objective Exertional heat stroke (EHS), characterised by a high core body temperature (Tcr) and central nervous system (CNS) dysfunction, is a concern for athletes, workers and military personnel who must train and perform in hot environments. The objective of this study was to determine whether algorithms that estimate Tcr from heart rate and gait instability from a trunk-worn sensor system can forward predict EHS onset.

Methods Heart rate and three-axis accelerometry data were collected from chest-worn sensors from 1806 US military personnel participating in timed 4/5-mile runs, and loaded marches of 7 and 12 miles; in total, 3422 high EHS-risk training datasets were available for analysis. Six soldiers were diagnosed with heat stroke and all had rectal temperatures of >41°C when first measured and were exhibiting CNS dysfunction. Estimated core temperature (ECTemp) was computed from sequential measures of heart rate. Gait instability was computed from three-axis accelerometry using features of pattern dispersion and autocorrelation.

Results The six soldiers who experienced heat stroke were among the hottest compared with the other soldiers in the respective training events with ECTemp ranging from 39.2°C to 40.8°C. Combining ECTemp and gait instability measures successfully identified all six EHS casualties at least 3.5 min in advance of collapse while falsely identifying 6.1% (209 total false positives) as the combination of two algorithms that estimate Tcr and ataxic gate appears promising for real-time alerting of impending EHS.

INTRODUCTION
Exertional heat stroke (EHS) is a life-threatening illness in which exercise, environment, clothing and other factors combine to produce a rapid and abnormal increase in core body temperature (Tcr) (often higher than 40.5°C) and central nervous system (CNS) dysfunction.6 7 8 EHS often presents as a state of confusion coupled with extreme fatigue and can rapidly progress to unconsciousness, organ damage and, in ~5% cases, death.4 Gold standard treatment is rapid cooling by whole-body immersion in ice water.15 16 Reducing the time Tcr is at very high temperatures is critical to minimising organ damage and overall prognosis.7 Survival of EHS without medical complications is dependent on the rapid recognition, rapid cooling and rapid advanced treatment.7

While advances have been made in environmental monitoring and managing environmental risk (high temperatures and high humidity) by moving exercise to cooler periods of the day, EHS remains a perennial problem for many high-intensity activities,12 13 14 with many cases occurring in temperate or cool conditions.12-14 A major contributing factor in these cases was individual motivation to complete a task. This is a common theme in team settings, where an individual may be feeling unwell but is motivated to perform/does not want to let down his/her team members or may face other pressure to continue.13 16

Individual attributes may contribute to susceptibility to EHS. Factors such as being unacclimatized to the heat, overweight, lacking in physical fitness, having prior illnesses, underlying medical conditions, dehydration, and drug and alcohol use all have been as associated with EHS.4 5 12 14 17 18 However, no single factor can explain EHS incidence, and only a small percentage of the overall group of study participants who have developed EHS had these literature-identified risk factors.14 19 Likewise, many individuals with these risk factors never develop EHS.18

An approach to reduce the incidence and severity of EHS is to use body-worn sensors to identify individuals with prodromal signs of emerging illness and to refer them for medical care before pathology can evolve.20 21 Practical real-time methods exist to estimate Tcr,22 and actigraphy can be used to assess gait. While Tcr alone is a poor predictor of who will succumb to EHS,3 a high Tcr in combination with CNS dysfunction is quite specific to diagnosing EHS. In a number of studies, ataxic gait/wobbly gait has been identified as one of the precursors to EHS.14 23 24 This change from a regular gait to one of ataxia may offer some insight into CNS dysfunction.

Coordination of human movement (defined as the motion of one body segment relative to another) is regulated by the cerebellum.24 Injury to the cerebellum, such as a cerebrovascular accident or EHS, can cause gait abnormalities, such as ataxia.25 Triaxial torso-worn accelerometers can identify ground contact time during running27 and differentiate between walking with and without an external load,24 and appear suitable for field use.28 Because torso accelerometry can detect small perturbations in different activities, it is plausible
that changes in torso accelerometry profiles could be indicative of ataxic gait due to CNS dysfunction versus exercise-induced balance loss.30,31

The purpose of this study was to examine whether gait markers and estimated core temperature (ECTemp) from high-intensity exercise could be used in combination to predict EHS in advance of occurrence.

**METHODS**

**Subjects**

Data were collected on 1806 (1701 men and 105 women) US military personnel (mean±SD: age=23±4 years, height=1.77±0.08 m, body weight=78.1±10.4 kg) who were recruited from various military units and monitored while engaged in high-intensity military training activities (n=42) that, in most cases, included a pass/fail motivational component. Personnel participated in one (n=95), two (n=1043), three (n=460) or one of two multiday (n=208) activities (<72 hours), and except for the multiday participants, activities were separated by 24–48 hours.

**High-intensity military training activities**

The military training activities where data were collected were chosen based on their history of heat stroke incidents to increase the likelihood of recording data from an individual who succumbed to an EHS. Activities monitored included runs of 4 and 5 miles to be completed in 40 min or less while wearing shorts and t-shirts; 7-mile (2-hour completion requirement) and 12-mile (3-hour completion requirement) ruck marches, where participants wore long pants and long-sleeved shirts as part of their regular military uniform and carried a 14 kg load which included a military rifle. Two multiday training activities (~3 days’ duration) that included periods of ruck marching, runs and other periods of movement were also monitored.

Adequate fluid intake was encouraged prior to the events by training and medical staff, and for the 5-mile runs and ruck marches, water stations were located every 2.5/3.0 miles along the event route.

**Measures**

Prior to the training event, questionnaires were administered to collect self-reported demographic and wellness information from individuals regarding age, height, weight, Army Physical Fitness Training (APFT) 2-mile run times (that can be related to aerobic fitness32), whether feeling unwell, currently taking medications, currently using dietary supplements, received any immunisations within the last 30 days, whether they had visited a doctor or had an illness in the last 60 days, and to estimate their fluid intake within the last 12 hours. Heart rate (from ECG, recorded every 5 s) and triaxial accelerometer (128 Hz, ADXL362 chip, ±8 g; Analogic Devices, Norwood, Massachusetts, USA) were logged using a custom torso-worn physiological monitoring system (Heat Illness Prevention System; Odic, Littleton, Massachusetts, USA: weight=16 g, dimensions=7.0×4.3×0.9 cm), which was donned the day before the activity.

For participants who suffered an EHS, rectal temperatures were taken by trained medical officers (analogue thermometer) as they were cooled via the ice sheet method33 prior to evacuation to the military base’s medical facility. Final diagnoses for each of the patients who had EHS were obtained from the training unit as provided by the medical facility.

To examine whether an EHS case differed from their cohort for age, height, weight or APFT times, we identified when any of these parameters deviated from the cohort mean by more than 2 SDs. In these cases and after testing for normality (Shapiro-Wilk test, IBM SPSS Statistics V26), we used the generalised extreme Studentised deviate test (computed according to the NIST/SEMATECH e-Handbook of Statistical Methods34) to examine if this parameter could be considered a significant (α=0.05) outlier compared with the cohort. The intent of this analysis was to document any unique factors among EHS cases compared with their cohort. Results are presented as mean±SD.

**Estimated core temperature**

ECTemp was computed according to Buller et al.,22 where initial core temperatures were estimated at 37.1°C and the initial variance was set to 0.02°C. Overall, the ECTemp algorithm has been validated in over 14 studies with more than 300 subjects and generally performs reliably from study to study, with similar root mean square error values (<0.30°C), bias, and limits of agreement (generally less than ±0.63°C).35

**Gait instability assessment**

A gait instability score was developed from two separate features derived from the three-axis accelerometry data: autocorrelation peak heights and a dispersion score. Both of these features were baseline to each individual. The autocorrelation peak height features represent gait regularity by the consistency of acceleration time series at the periodicities of steps (vertical and longitudinal axes) and strides (lateral axis). Similarly, the dispersion features represent gait regularity by the level of clustering (and hence consistency) of repeated gait patterns across multiple steps, within each acceleration axis (figure 1 illustrates this concept).

As our dataset contained bouts of either running alone (5 and 4 mile runs) or walking and running combined (ruck marches of 7 and 12 miles), it was necessary to segment the data into periods of walk and run so that periods of activity were compared with like previous periods. The full accelerometry processing pipeline and computation of the gait instability risk score are described in the online supplemental data 1.

**EHS detection**

EHS detection algorithms were developed that used ECTemp, Gait Instability Score and the two measures combined. For EHS detection based on ECTemp, a Gaussian log-likelihood model was used, as shown in equation (1)

\[
\log\text{ECTemp}_{\text{risk}}(n) = -0.5 \left( \frac{\text{ECTemp}(n) - \text{ECTemp}_{\text{max}}}{\text{ECTemp}_{\text{σ}}} \right)^2, \tag{1}
\]

where ECTemp_{\text{max}}=41.0°C and ECTemp_{\text{σ}} was set to 1.0; if ECTemp(n) ≥ 41.0, then log\text{ECTemp}_{\text{risk}}(n) was set to 0 (the maximum log-likelihood value). The final combined EHS_{\text{risk}} score is computed by summing the ECTemp_{\text{risk}} likelihood with the individualised gait instability score for both walking and running movement types, and picking the highest combined score for either walking or running (equations 2, 3, and 4).

\[
\text{Fused}_{\text{risk}}(n)_{\text{walk}} = \text{Gait}_{\text{risk}}(n)_{\text{walk}} + \text{ECT}_{\text{risk}}(n) \tag{2}
\]

\[
\text{Fused}_{\text{risk}}(n)_{\text{run}} = \text{Gait}_{\text{risk}}(n)_{\text{run}} + \text{ECT}_{\text{risk}}(n) \tag{3}
\]

\[
\text{EHS}_{\text{risk}}(n) = \max \left( \text{Fused}_{\text{risk}}(n)_{\text{walk}}, \text{Fused}_{\text{risk}}(n)_{\text{run}} \right). \tag{4}
\]

EHS_{\text{risk}} is a unitless score that can increase due to either ECT_{\text{risk}} or Gait_{\text{risk}} or both. For EHS classification we varied the thresholds of the EHS_{\text{risk}}, Gait_{\text{risk}} and ECT_{\text{risk}} so that we could identify all EHS cases (100% true positive rate) and minimise the number of false positives when all EHS cases were identified.
Performance of the classifiers was examined by determining the false-positive rates (per event) when all EHS cases were identified. Further, we examined how the false-positive rates changed when the classifier thresholds were adjusted to increase the time of EHS prediction. We examined whether the predict-ahead time and the false-positive rate could be improved by increasing the number of allowed false negatives to be one and two.

The acceptability of false-positive rates will be governed by an organisation’s tolerance of risk along with their resources to respond to real-time predictions of EHS. For the military units, we have worked with, conducting a visual check-in and exertional heat illness assessment on 10 soldiers out of 150 during the course of a 3-hour exercise is well within their capacity.

Finally, the total number of examples of high-risk movement activities that could be used in the gait and ECTemp analysis was 3422 generated from participants whose data contained acceptable HR and accelerometry.

**RESULTS**

**EHS cases**

Six individuals suffered from an EHS while completing one of the observed training events. Table 1 provides the event and individual characteristics and whether the individuals who had EHS differed from their cohort. All individuals who suffered from an EHS were male.

Prior to the event, all individuals who had EHS reported feeling well and had no recent illness. None reported taking medications or dietary supplements; only one had a recent immunisation, and all reported consuming a similar amount of

<table>
<thead>
<tr>
<th>Event (date)</th>
<th>WBGT (°C)</th>
<th>Air temperature (°C)</th>
<th>Relative humidity (%)</th>
<th>Age (year)</th>
<th>Height (m)</th>
<th>Weight (kg)*</th>
<th>APFT 2-mile run time (min:s)</th>
<th>ECTemp at point of collapse (°C)</th>
<th>Casualty rectal Tcr (°C)†</th>
<th>Pre-event risk factors</th>
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<tbody>
<tr>
<td>5-mile run</td>
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<tr>
<td>17 July 2018</td>
<td>21.5±1.2</td>
<td>23.2±0.3</td>
<td>84.9±8.2</td>
<td>30</td>
<td>1.75</td>
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<tr>
<td>7 August 2018</td>
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<td>21.8±0.7</td>
<td>75.0±5.4</td>
<td>22</td>
<td>1.91</td>
<td>102.1¶</td>
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<tr>
<td>11 March 2019</td>
<td>14.2±0.2</td>
<td>14.5‡</td>
<td>90.5±4.9</td>
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<td>1.70</td>
<td>72.6</td>
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<td>40.1</td>
<td>41.9§</td>
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<td>14.7±0.8</td>
<td>88.3±4.3</td>
<td>33</td>
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<td>77.1</td>
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<tr>
<td>17 July 2019</td>
<td>22.5±0.4</td>
<td>22.6±0.4</td>
<td>94.1±2.5</td>
<td>27</td>
<td>1.78</td>
<td>88.5</td>
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<td>20 August 2019</td>
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<td>95</td>
<td>30</td>
<td>1.83</td>
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<td>15:05</td>
<td>39.2</td>
<td>42.3</td>
<td>0</td>
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</table>

*In combination, height and weight show all our EHS cases with a BMI close to or exceeding 25, which in the civilian world would be considered overweight. However, for these military candidates, this BMI is much more reflective of muscle mass versus fat mass and thus, BMI may inaccurately label the demographic overweight.
†Rectal temperatures were taken for patients who had EHS prior to casualty evacuation.
‡Estimated using general weather data for Fort Benning, Georgia.
§Volunteer reported a recent immunisation.
¶Individual value >2 SD from cohort mean but not a significant outlier according to the generalised ESD test.
APFT, Army Physical Fitness Training; BMI, body mass index; ECTemp, estimated core temperature; EHS, exertional heat stroke; ESD, extreme Studentised deviate; Tcr, core body temperature; WBGT, wet bulb globe temperature.
As predict-ahead times were increased from 30 s to 300 s, the classification threshold became progressively smaller, resulting in a rise in false-positive rates (figure 5). For the EHS\textsubscript{0.001} (ECTemp+gait instability), as the prediction interval was doubled, there was a doubling in false-positive rate such that at 30, 60, 120 and 240 s, the false-positive rate was 0.9%, 1.9%, 4.5% and 9.4%, respectively. Predicting 300 s in advance resulted in a false-positive rate of 17.9%. However, between 120 s and 210 s, the false-positive rate remains fairly constant, increasing from 4.5 to 6.1. Figure 6, shows the EHS\textsubscript{risk} score computed for all 3422 activities with the six EHS cases plotted in black and with the 210 s prediction threshold of 1.95 highlighted.

As the number of false negatives was increased from one to two, the false-positive rate at 210 s decreases from 5.7% to 3.5%. When two false negatives were accepted, the predict-ahead time could be extended to 300 s with a false-positive rate of 4.4%.

**DISCUSSION**

This study demonstrates the ability to predict EHS cases up to 3.5 min before occurrence with the combined assessment of ECTemp and gait instability metrics. The ability to predict and respond to EHS events and apply rapid cooling techniques that reduce Tcr at >0.15 °C/min within the first 30 min of EHS is key for good outcomes. Similarly, an ability to receive an early indication of impending EHS is suggested as a means of reducing the incidence of EHS in elite sporting events. While small, the 3.5 min early warning provided by the EHS\textsubscript{risk} algorithm is more than 10% of this time window and would provide a cooling advantage of >0.5°C over current approaches of responding to collapse. In many remote settings, time is lost by identifying the location of a collapsed individual and sending medical and cooling resources to that point. Often the patient has to be transported to reach effective cooling mechanisms, such as ice water immersion.

Self-reported data showed no common risk factors among the EHS cases. Only two of the EHS cases indicated potential pre-existing risk factors where one volunteer was on the heavier end of the weight distribution than others in his cohort, and one had recently received an immunisation. These factors often do show up in combination with others for EHS cases, but by themselves would not predict EHS. This is highlighted when these factors are considered in the context of all subjects who had these same initial starting factors but did not experience an exertional heat illness. Additionally, all six EHS cases reported no use of medications and dietary supplements; all reported feeling well the morning of the training event; and all reported consuming adequate fluids within 12 hours of the event. While a deficit in fluid replacement can systematically lead to increased
heat storage and additional rise in $T_{cr}$. The ECTemp algorithm performs similarly in both populations of euhydrated and dehydrated.

All six of the EHS cases occurred at relatively high humidities, but care should be taken in these results. Efficient thermoregulation comes from the combination of three major heat transfer mechanisms of convection, radiation and evaporative heat loss. Early success in reducing military exertional heat illness came by moving events to early in the morning before the rise in daytime temperatures and where individuals would not be subject to solar radiation. While humidity is naturally higher at these early morning times, the reduction in temperature and limited solar radiation far out way the effect of high humidity. The activities for all our EHS cases were predawn and occurred at low WBGT levels that would not call for any modification of work rates. Additionally, two of the six EHS cases occurred in relatively mild environmental conditions (air temperature <15°C). This is consistent with previous findings of significant numbers of EHS cases and fatalities occurring in moderate temperatures.

Estimated $T_{cr}$ in five of the six EHS cases was in the upper portion of the cohort prior to EHS onset, but it alone was not a good discriminant of who was going to develop EHS. This finding is in agreement with earlier work suggesting that attainment of an individual core temperature threshold by itself is a poor predictor of heat stroke. In our dataset, two EHS cases have ECTemp values that are relatively low, close to 39.2°C at the point of collapse. Given the algorithm’s 95% CI of ±0.63°C, it could be expected for some individuals to fall at the bottom of this distribution, but it is illustrative that core temperatures alone do not predict EHS with a level of discrimination necessary to be useful for early EHS symptomology detection. The effect of the lower core temperatures on the combined EHS classification can be seen when the false-negative count is relaxed. When two false negatives are tolerated, the EHS classifier predicts the other four heat strokes at least 5 min in advance with a false-positive rate of 4.4%.

Gait instability was acceptably accurate in discriminating the six EHS cases prior to the point of collapse, suggesting that CNS dysfunction, especially cerebellar dysfunction, becomes significant enough to affect a highly trained and basic autonomous function such as gait. This also fits with many anecdotal observations that individuals experiencing heat stroke have an ataxic gait. However, extending the predict-ahead time lead to at least 3.5 min in advance increased the false-positive rate to 14%. Combining gait irregularity and ECTemp reduced this false-positive rate to 6.1%. The low number of false positives would suggest that the EHS score is differentiating well between exercise-induced balance loss from fatigue and ataxic gait induced by EHS. The combination of ECTemp and gait instability as an EHS score corresponds naturally to the clinical definition of high temperature combined with CNS dysfunction.

**Strengths and limitations**

Due to the rare nature of EHS and the ability to collect data prior to an EHS, the gait irregularity score and EHS score were...
CONCLUSION
By combining two independent methods, one assessing body core temperature (ECTemp) and the second assessing gait irregularity, we have demonstrated that a real-time EHS risk algorithm was capable of identifying all six observed EHS cases 3.5 min in advance with only a 6.1% (n=209) false-positive rate out of 3,416 examples. In the current dataset, we have zero examples of false negatives, which are necessary to assess the true efficacy of the algorithm. The EHS\textsubscript{risk} score required only two sensor inputs: minute-by-minute heart rate and triaxis torso accelerometry. These measures are fairly ubiquitous in modern health and fitness wearables. With the use of simple wearables, the EHS\textsubscript{risk} score provides a means to alert medical staff to an individual who is in imminent risk of EHS, thus reducing the time to treatment and hopefully improving prognosis for recovery.

Acknowledgements
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Contributors
Study conception and design: MBul, RF, JS, MG and MBur; significant data acquisition: MBul, MBur, MBG, MB, JM, JM, KD, TM, CK, CR and CM; significant data analysis: MBul, EA, HM, KD, TM, LW, BT and JRW; significant writing: MBul, RF and EA and JRW; critical review and revision input: all listed authors.

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Competing interests
MBul is the listed inventor on a patent for estimating core body temperature from heart rate, also known as estimated core temperature (ECTemp). Ownership of the ECTemp patent is held by the US Department of the Army. MBul, RF, JS, BD and JRW and LW are the listed inventors on a patent application, “System and Method to Predict Exertional Heat Stroke from Torso-Worn Sensor”. This patent is jointly owned by the US Department of the Army and Massachusetts Institute of Technology, Lincoln Laboratory. As part of the Department of Defense employee incentive programmes, MBul, RF and JS are entitled to receive a portion of royalty payments for any licensing of the algorithm.

Patient consent for publication
Not applicable.

Ethics approval
This study involves human participants and was approved by the Medical Research and Development Command Institutional Review Board (Frederick, Maryland) on 15 June 2018 (number M-10720). Participants gave informed consent to participate in the study before taking part. This study was conducted under the oversight of the US Army Medical Research and Development Command Institutional Research Board in accordance with the principles embodied in the Declaration of Helsinki and in accordance with the US statutory requirements.

Provenance and peer review
Not commissioned; externally peer reviewed.

Data availability statement
No data are available. Data are not publicly available.

Supplemental material
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What are the findings?

► Exertional heat stroke (EHS) can be predicted several minutes in advance of collapse from measurements of heart rate and accelerometry that assess body temperature and gait instability.

► Physiological measurements from six volunteers prior to and postcollapse from EHS are used to develop a heat stroke classification algorithm.

► Over 3400 examples of runs and timed road marches show only a 6.1% false-positive rate for a 3.5 min advance warning of EHS.

How might it impact on clinical practice in the future?

► Use of common wearable physiological monitors could provide advance warning of EHS to both individuals and medical personnel, allowing timely interventions.
REFERENCES