Maintained cerebral oxygenation during maximal self-paced exercise in elite Kenyan runners

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THE DOMINANCE of Kenyan athletes at international distance-running events over the last four decades is among the most remarkable examples of variation in human physiology and performance (41, 45). Various studies have proposed a combination of favorable somatotypical characteristics leading to exceptional running economy (31, 42), environmental factors including chronic exposure to high altitude (15), targeted moderate-volume, high-intensity training (3), strong motivation (24), higher efficacy in the use of recoil of elastic energy from the tendinous structures (32), favorable oxidative enzyme profile (31), and genetic factors (35, 41) to explain this dominance. The majority of the successful Kenyan runners come from a single tribe, the Kalenjin in the highlands of the Rift Valley (24, 40). The Kalenjin tribe, which consists of 5 million people (~0.07% of the world population), have won 34% of all global medals in the middle- and long-distance running events in the Olympic Games and World Championships since 1964 (40). A shared characteristic of the elite Kalenjin distance runners is that they are born and raised at an elevation of ~2,000 to 2,500 m. This early-life factor has been proposed to influence fetal growth, particularly in individuals of multigenerational high-altitude ancestry, which is the case for Kalenjin runners. This may in turn have implications for later-life endurance performance, including a reduction in the degree to which arterial desaturation occurs during heavy exercise in elite performers (5). Other early-life factors shared by Kalenjin runners, such as high levels of physical activity during their childhood, may provide further explanation for the Kenyan athletic success (5, 9, 23). The effects of these considerable levels of physical activity during childhood have been confirmed and include increased left ventricular mass, neuronal growth, and augmented cerebral circulation through increased vascularization of the brain (19, 28).

Importantly, augmented vascularization of the brain can be critical during aerobic exercise. A drop in cerebral oxygenation (Cox) has been associated with exhaustion during whole body exercise at high intensities on several occasions (2, 34), likely affecting cerebral cortex activity and, therefore, muscle recruitment (27, 30). Such deoxygenation occurs in prefrontal, premotor, and motor cortices during maximal aerobic exercise, suggesting that multiple regions of the brain may contribute to fatigue and/or conscious decisions to stop exercising (37). Although the consequences of an impairment in brain uptake of O2 for exercise performance are not fully understood, there is evidence that fatigue resulting from severe, self-paced exercise in healthy humans is associated with a decline in Cox (4), and that athletes who can maintain Cox are likely to perform better (21).

No research has investigated the hemodynamic response to maximal exercise in elite Kenyan runners. Since changes in brain vascularization may be one of the adaptations resulting from the particular early-life factors shared by elite Kenyan runners, we hypothesized that these athletes have the capacity to maintain cerebral oxygenation at maximal speeds, which may contribute to their extraordinary performance.

MATERIALS AND METHODS

Participants. Fifteen elite Kenyan runners from the Kalenjin tribe with a mean 21-km race time of 62.2 ± 1.0 min were recruited for the study through their personal agent in Kenya. The Research Ethics Committee of the University of Cape Town approved this study.
Anthropometry. For descriptive purposes, height (cm) and body mass (kg) were recorded using a high-precision balance (Seca 899, Seca, Germany) and a stadiometer (Charder HM200P, Charder Electronic, Taiwan), and the body mass index (BMI) was calculated. Eight skinfold sites (triceps, biceps, subscapular, suprailiac, supraspinale, abdominal, front thigh, and median calf) were measured in duplicate with skinfold calipers (Holtain Tanner-Whitehouse, Crymych, UK) by the same researcher to the nearest millimeter, and body fat was calculated (46). All measurements were taken following the guidelines outlined by the International Society for the Advancement of Kinanthropometry (ISAK).

Exercise tests. All participants completed three tests on two consecutive days: 1) a 5-km time trial, 2) a maximal incremental test for maximal oxygen consumption ($V\dot{O}_{2\text{max}}$), and 3) constant-speed running bouts for running economy determination. All testing sessions were performed under similar environmental conditions (20–24°C, 45–55% relative humidity at 130 m of altitude). 5-km time trial. All participants completed a 5-km time trial (TT) on a treadmill (H/P/Cosmos Saturn, Nussdorf-Traunstein, Germany) at a gradient of 1% after a self-selected warm-up of at least 10 min. Athletes were required to complete 5 km in the shortest time possible and were encouraged through financial incentives to run as fast as possible. A ranking list, which included the best final times, ensured interindividual competition. Athletes were free to select their own pace and were able to adjust it throughout the time trial by verbal instruction or nonverbal signals to the researcher. Split times were provided to the athlete every 0.5 km during the time trial.

Peak treadmill speed test. All athletes also completed a maximal incremental running test on a treadmill at a gradient of 1%. The test started at 11 km/h without previous warm up, and the speed was increased by 0.5 km/h every 1 min until volitional exhaustion. During the PTS test, gas exchange data were collected using an automated breath-by-breath system (COSMED Quark CPET, Rome, Italy), which was calibrated before each session according to the instructions of the manufacturers. Volume calibration was performed with different flow rates with a 3-liter calibration syringe (Cosmed, Rome, Italy) allowing an error <2%. Calibration of the gas analyzer was performed automatically by the system using both ambient and precision reference gases (16% O$_2$, 5% CO$_2$). Heart rate (HR) was recorded by a heart rate monitor (Suunto T6, Vantaa, Finland).

Athletes were considered to have achieved a maximal performance, and therefore reached their $V\dot{O}_{2\text{max}}$ when at least two of the following criteria were fulfilled (11): 1) a plateau in $V\dot{O}_2$, defined as an increase of less than 1.5 ml·kg$^{-1}$·min$^{-1}$ in two consecutive workloads; 2) respiratory exchange ratio (RER) > 1.15; and 3) maximal HR value (HR$_{\text{max}}$) > 95% of the age-predicted maximum (220 – age). The prevalence of the $V\dot{O}_{2\text{max}}$ plateau phenomenon in this group of elite Kenyan runners was 93.3%.

Peak treadmill speed (PTS; in km/h) was calculated as follows, taking every second into account (17):

$$PTS = \text{completed full intensity (km/h)} + \left[\text{seconds at final velocity} \cdot 60 \text{s}^{-1}\right] \cdot \text{0.5 km/h}$$

Running economy sets. All athletes completed three constant-speed running sets of 6 min each, separated by 5-min recovery periods, at a gradient of 1% on the treadmill. A slow increase in $V\dot{O}_2$ during a constant-work rate exercise performed above the lactate threshold has been described, also known as the slow component of the $V\dot{O}_2$ (13). Thus, to ensure steady-state measurements, all the speeds selected (15, 17, and 19 km/h) were slower than the individual lactate threshold of each athlete (further confirmed during the test by RER being below 1.0 during the whole running bout for all athletes at every speed). $V\dot{O}_2$ (ml·kg$^{-1}$·min$^{-1}$) values collected during the last 60 s of each stage were averaged and designated as steady-state running economy (ml·kg$^{-1}$·km$^{-1}$).

Brain oxygenation measurements. A continuous-wave, functional, near-infrared spectrometer (NIRO-200X, Hamamatsu, Japan) was used to monitor changes in cerebral hemoglobin concentrations during the 5-km TT and the PTS test. The theory of functional near-infrared spectroscopy (fNIRS) and its application in brain research have been reviewed elsewhere (26).

During the 5-km TT and the PTS, all runners were instrumented with an fNIRS optical probe to monitor absorption of infrared light in cerebral tissue. The probe consisted of one emitter and one detector separated by 3.0 cm and housed in a black, rubber holder attached to the skin with clear double-sided adhesives to ensure no change in their relative positions. The probe holder was also covered and maintained with a headband and tape to reduce the intrusion of extraneous light and the loss of transmitted near-infrared light from the field of investigation. The probe was positioned over the left prefrontal lobe between Fp1 and F3, according to the modified international EEG 10–20 system. While we acknowledge that this area of the brain is not directly involved in the neural control of movement, the deoxygenation of the prefrontal cortex has been reported to contribute to the cessation of exercise during controlled and self-paced exercises on many occasions (1, 4, 34, 36).

A modified form of the Beer-Lambert law was used to calculate changes (in μmol/cm) in tissue oxyhemoglobin (ΔO$_2$(Hb)) and deoxyhemoglobin (ΔHHb) across time using received optical densities from three continuous wavelengths of near-infrared light (735, 810, and 850 nm). Further, the tissue oxygenation index [TOI = $k$·O$_2$(Hb)/(O$_2$(Hb) + HHb)] and the normalized total hemoglobin index (nTHI = [ΔO$_2$(Hb) + ΔHHb]) were measured as absolute values using spatially resolved spectroscopy, where $k$ is an unknown but constant tissue parameter (38). TOI represents the tissue saturation and nTHI an absolute figure of the total hemoglobin.

Data were collected over the last 30 s of each 0.5-km segment during the 5-km TT and every minute during the PTS test at a frequency of 5 Hz and were expressed relative to a baseline period (4). The baseline period took place immediately before the warm-up, where athletes sat down and were asked to close their eyes and eliminate extraneous thoughts to establish a 120-s baseline of fNIRS data (4).

Arterial oxygen saturation. Arterial oxygen saturation (SpO$_2$) was estimated via pulse oximetry (Nellcor N-200; Nellcor, Hayward, CA), with an adhesive optode placed on the right side of the forehead. This technique has been shown to be in good agreement (intraclass correlation coefficient = 0.88) with hemoglobin O$_2$ saturation based on arterial blood analysis (27), and has been used elsewhere (4, 33). SpO$_2$ was recorded at baseline and every 0.5 km during the trial and every minute during the PTS test.

Statistics. All values are expressed as means ± SD, and the statistical analyses of data were performed using the Statistical Package for the Social Sciences 21.0 software package (SPSS, Chicago, IL). Data were screened for normality of distribution and homogeneity of variances using a Shapiro-Wilk normality test and a Levene test, respectively. One-way ANOVA with repeated measures for time was used to compare the fNIRS measurements (Δ[O$_2$(Hb), ΔHHb], TOI, and nTHI) and SpO$_2$ values. If a main effect was detected, post hoc comparisons were made with Tukey’s honestly significant difference.
test for pairwise comparisons. The magnitude of differences or effect sizes (ES) were calculated for significant differences according to Cohen’s d (6) and interpreted as small (>0.2 and <0.6), moderate (≥0.6 and <1.2), and large (≥1.2 and <2). Significance for all analyses was set at \( P < 0.05 \).

RESULTS

Descriptive characteristics and maximal treadmill test results of Kenyan runners participating in this study are listed in Table 1. Subjects can be considered elite competitive runners, as indicated by the average 10-km race time of 28.7 ± 0.3 min corresponding to a pace of 5.8 ± 0.06 m/s (CV = 1.0%). The mean \( \text{VO}_{2\text{max}} \) and running economy were 71.9 ± 5.1 ml·kg\(^{-1}\)·min\(^{-1}\) and 185.2 ± 9.4 ml·kg\(^{-1}\)·km\(^{-1}\), respectively (CV = 7.1% and 5.1%). The homogeneity of the group is indicated by a coefficient of variation (CV) < 4% for all performance-related variables: 10-km race time (CV = 1.0%), half-marathon time (CV = 1.6%), and PTS (CV = 3.7%). With respect to anthropometry, the group was also homogenous: height 170.5 ± 6.3 cm (CV = 3.7%); body mass 54.8 ± 6.3 kg (CV = 11.5%); BMI 18.8 ± 1.3 (CV = 6.9%), and body fat content 8.7 ± 0.5% (CV = 5.7%).

The average treadmill speed recorded every 0.5 km during the 5-km TT in this elite Kenyan group is displayed in Fig. 1. The average time taken to complete the 5-km TT was 15.2 ± 0.2 min (CV = 1.3%).

Table 1. Physical characteristics and maximal test results of the Kalenjin runners

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CV, %</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>17.7</td>
<td>23.7 ± 4.2</td>
</tr>
<tr>
<td>PTS, km/h</td>
<td>3.7</td>
<td>21.6 ± 0.8</td>
</tr>
<tr>
<td>( \text{VO}_{2\text{max}} ), ml·kg(^{-1})·min(^{-1})</td>
<td>7.1</td>
<td>71.9 ± 5.1</td>
</tr>
<tr>
<td>10-km race time, min</td>
<td>1.4</td>
<td>28.7 ± 0.4</td>
</tr>
<tr>
<td>Half-marathon time, min</td>
<td>1.6</td>
<td>62.2 ± 1.0</td>
</tr>
<tr>
<td>Mean RE, ml·kg(^{-1})·km(^{-1})</td>
<td>5.1</td>
<td>185.2 ± 9.4</td>
</tr>
<tr>
<td>Training, km/wk</td>
<td>14.6</td>
<td>128.9 ± 18.8</td>
</tr>
<tr>
<td>Height, cm</td>
<td>3.7</td>
<td>170.5 ± 6.3</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>11.5</td>
<td>54.8 ± 6.3</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>6.9</td>
<td>18.8 ± 1.3</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>5.7</td>
<td>8.7 ± 0.5</td>
</tr>
<tr>
<td>( \Sigma ) Skinfold, mm</td>
<td>19.5</td>
<td>34.2 ± 6.7</td>
</tr>
</tbody>
</table>

Values are means ± SD; \( n = 15 \) participants; CV, coefficient of variation; PTS, peak treadmill speed; \( \text{VO}_{2\text{max}} \), maximum oxygen uptake; RE, running economy; BMI, body mass index, \( \Sigma \) skinfolds, biceps, triceps, subscapular, supraspinale, abdominal, suprailiac, mid-thigh, and medial calf.

DISCUSSION

The novel aspect of the present study is that we examined the cerebral oxygenation response to maximal performance in elite Kalenjin runners, who are considered the best long-distance runners in the world (18, 40). We have found that changes in cerebral oxyhemoglobin and deoxyhemoglobin in these elite runners are similar to what has been reported for well-trained runners during maximal incremental exercise to volitional exhaustion. However, their cerebral oxygenation response differs from that previously observed during self-paced 5-km time trials and offers another possible physiological mechanism for their unparalleled, multifactorial sporting...
success. That is, the Kalenjin runners were able to maintain the oxygenation of their prefrontal lobe through the 5-km time trial. This may contribute to the attenuation of the development of central fatigue and a subsequent decline in performance, as has been observed on several occasions during maximal exercise in well-trained athletes (4, 26, 27).

The Cox profile measured during the PTS test is in agreement with the literature (2, 27, 37). We found a typical increase in Cox in the first part of the test (Fig. 3) (12, 30), which has classically been attributed to a local increase in cerebral blood flow in response to increased O2 demand (30) from progressive neuronal activation (7). This typical increase was followed by a reduction in Cox at running speeds greater than the second ventilatory threshold, and continued until exhaustion. This too agrees with previous studies (27, 30) and can be explained by a reduction in arterial carbon dioxide tension (PaCO2) as a result of increasing hyperventilation at higher workloads, a phenomenon that has been confirmed in previous research on Kenyan runners (8). This has been shown to cause cerebral vasoconstriction and diminished cerebral blood flow (2, 20, 30).

In contrast, the Cox profile observed during the 5-km TT differed from the PTS test and previous studies (4). As in the PTS, Cox increased from rest to 2.5 km during the 5-km TT, driven by a local increase in cerebral blood flow subsequent to enhanced O2 demand from neuronal activation (4, 7). Following this first increase, Cox remained constant until the completion of the time trial, which contrasts with previous research showing a significant decline in Cox during a 5-km TT in well-trained runners (4). In that study, it was proposed that a reduction in Cox was related to the pacing strategy employed during the trial, and only occurred once the known endpoint of exercise was approaching as part of the regulation to prevent premature fatigue caused by excessive disruptions to homeostasis.

Our results do not necessarily contradict these previous findings by Billaut et al. (4), as the pacing strategy was different between the two studies. The prefrontal cortex plays a fundamental role in movement planning and decision-making, as well as the control of pacing (14). The treadmill speed curve observed in the present study does not represent the typical pace in a running time trial (22), because the Kenyan runners did not exhibit a final end spurt at the end of the 5-km TT (Fig. 1). Pacing strategy involves the conscious and/or subconscious variation of workload over the exercise in order to optimize performance by avoiding premature fatigue (39). Usually, the presence of an end spurt is associated with a reserve, and Billaut et al. (4) proposed that this reserve was utilized to produce the final end spurt, which then caused the deoxygenation they observed in the final part of the time trial. This implies that the stable Cox during the second half of the 5-km TT in the present study may simply be a consequence of a more aggressive pacing strategy (due to the financial incentives) in the whole group (CV < 6% in the speed curve during the whole 5-km TT, Fig. 1), which subsequently negated the end spurt at the end of the trial (39).

Alternatively, the absence of progressive and potentially limiting cerebral deoxygenation during the 5-km TT may be viewed as a result of the exercise intensity not being high enough to tax the brain, since a drop in Cox only occurs at intensities beyond the ventilatory threshold (Fig. 2A). How-

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Fig. 2. Changes in cerebral oxyhemoglobin (\( \Delta [O_2\text{Hb}] \)) (A), deoxyhemoglobin (\( \Delta [HHb] \)) (B), tissue oxygenation index (TOI) (C), and normalized total hemoglobin index (nTHI) during the 5-km time trial. *Different from values at 2.5 km (\( P < 0.05 \)).
ever, we discarded this possible explanation as the heart rates measured were near peak levels (compared with the incremental test to maximal effort) and TOI values were even lower than those measured at exhaustion during the PTS test (Figs. 2C and 3C).

Rather, we propose the influence of early-life factors, such as prenatal exposure to high altitude and high physical activity levels during childhood (5) to explain the ability to maintain Cox in elite Kenyan runners. Prenatal exposure to high altitude triggers cerebral vasodilator responses at muscle and endothelium level by stimulating extensive cerebrovascular remodeling that increases wall thickness but decreases overall contractility (25). Many of these adaptations to chronic hypoxia appear to be homeostatic and mediated by vascular endothelial growth factors (VEGF). The main member of the VEGF family, VEGF-A165, is upregulated in response to hypoxia and directly influences the expression and function of different contractile proteins of the cerebrovascular smooth muscle, such as α-actin and SM1 myosin (25). Therefore, this particular early-life factor may allow an increased Cox response during later-life maximal exercise through gene expression adjustments during fetal growth. With regards to the high physical activity levels during childhood, they may cause, among other adaptations, the stimulation of trophic factors and neuronal growth as well as augmented cerebral circulation through increased vascularization of the brain (28).

In addition, we also propose that the elite Kenyan runners may have an attenuated reduction in P_{aCO2} during the 5-km TT, which would delay the cerebral vasoconstriction that has been demonstrated at high intensities. In fact, African runners display an increased oxidative enzyme activity and a subsequent lower lactate production (16, 31, 33, 44). The consequences of this more-efficient aerobic metabolism would be that Kenyan runners are able to exercise at higher intensities, relying more on aerobic sources of energy and producing less CO₂ through the bicarbonate breakdown to compensate for acidosis. This would ultimately attenuate hyperventilation, hypocapnia, and, finally, vasoconstriction (30).

However, some technical limitations have to be acknowledged. First, we acknowledge that prefrontal lobe oxygenation is a regional measurement that may not be reflective of global Cox. However, this area of the brain has been associated with global changes in cerebral blood flow, oxygenation of premotor and motor cortices, and locomotor muscle performance (1, 30, 34, 36, 37). Another limitation of the present study was that NIRS-determined cerebral oxyhemoglobin measurements may be affected by changes in extracranial blood flow (10) and that skin pigmentation may interfere with the reflected NIRS signal (43). Although we used a probe where emitter and detector were separated by 3.0 cm to avoid decreases in signal quality, this also implies that our Cox measurements were more superficial than those from studies using a distance of 4.5 cm. Therefore, results reported in this study should be interpreted with caution.

In conclusion, this study shows that elite Kenyan runners maintain their cerebral oxygenation within a stable range during a self-paced maximal 5-km time trial, possibly due to specific early-life factors shared by Kenyan runners including prenatal exposure to high altitude and high physical activity levels during childhood. This maintained cerebral oxygenation
might be a new contributing factor to the current multifactorial explanation of the Kenyan running phenomenon.

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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS
Author contributions: J.S.-C., F.B., T.D.N., and R.T. edited and revised manuscript; J.S.-C., F.B., T.D.N., and R.T. analyzed data; J.S.-C., J.O., and R.T. interpreted results of experiments; J.S.-C. and J.O. prepared figures; J.S.-C. and J.O. designed research; J.S.-C., L.G., J.O., and R.T. performed experiments; J.S.-C., L.G., T.D.N., and R.T. provided final version of manuscript.

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