Skeletal muscle structural and energetic characteristics in subjects with sickle cell trait, α-thalassemia, or dual hemoglobinopathy

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Vincent L, Féasson L, Oyono-Enguéllé S, Banimbek V, Monchanin G, Dohhoba M, Wouassi D, Martin C, Gozal D, Geyssant A, Thiriet P, Denis C, Messonnier L. Skeletal muscle structural and energetic characteristics in subjects with sickle cell trait (SCT), α-thalassemia, or dual hemoglobinopathy. J Appl Physiol 109: 728–734, 2010. First published June 24, 2010; doi:10.1152/japplphysiol.00349.2010.—Previous studies have shown that subjects with sickle cell trait (SCT), α-thalassemia (α-t), and the dual hemoglobinopathy (SCT/α-t) manifest subtle, albeit significant, differences during exercise. To better understand such differences, we assessed skeletal muscle histomorphological and energetic characteristics in 10 control HbAA subjects (C), 5 subjects with α-t (α-t), 6 SCT carriers (SCT) and 9 SCT carriers with α-t (SCT/α-t). Subjects underwent a muscle biopsy and also performed an incremental maximal exercise and a time to exhaustion test. There were no observable differences in daily energy expenditure, maximal power output (Pmax), or time to exhaustion at 110% Pmax (TEX) among the groups. Blood lactate concentrations measured at the end of the TEX, muscle fiber type distribution, and mean phosphorylfructokinase (PFK), lactate dehydrogenase (LDH), β-hydroxyacyl-CoA-dehydrogenase (HAD), and citrate synthase (CS) activities were all similar among the four groups. However, SCT was associated with a lower cytochrome-c oxidase (COx) activity in type IIa fibers (P < 0.05), and similar trends were observed in fiber types I and IIx. Trends toward lower creatine kinase (CK) activity (P = 0.0702) and higher surface area of type Ix fibers were observed in SCT (P = 0.0925). In summary, these findings support most of the previous observations in SCT, such as I) similar maximal power output and associated maximal oxygen consumption (V̇O2max) values and 2) lower exercise performances during prolonged submaximal exercise. Furthermore, performances during short supramaximal exercise were not different in SCT. Finally, the dual hemoglobinopathy condition does not seem to affect muscle characteristics.

Skeletal muscle structural and energetic characteristics in subjects with sickle cell trait (SCT) are related to a genetic abnormality of red blood cells (RBCs) due to a single amino acid substitution in the hemoglobin β-chain. This mutation leads to the expression of an abnormal protein, called hemoglobin S (HbS), that polymerizes under its deoxygenated form, inducing sickling of the RBC. This genetic disease affects mainly African populations and their descendants. The sickle cell trait (SCT) is the heterozygous form of the inherited disease and is characterized by the presence of both HbS (<50%) and A.

Because of lower RBC deformability, higher blood apparent viscosity, and higher endothelial adhesion (11, 38), SCT carriers are susceptible to local blood flow disturbances that may explain the lower index of oxygen supply to the tissues (11) and a lower ability to sustain prolonged submaximal exercise in various settings (29, 30, 31, 31). Indeed, Le Gallais et al. (31) found no SCT carriers among 22 international-level athletes having taking part in the Abidjan half-marathon, even though 8.7% of the runners were SCT carriers. The same group of investigators (29) also reported higher ventilation and heart rate (HR) in SCT carriers than control subjects (HbAA) during an endurance exercise test, which would attest to a poor cardioventilatory adaptation in those subjects (10). Thiriet et al. (51) reported that during the Mount Cameroon Ascent Race, performance times of SCT runners were lower during the portion at high altitude. Connes et al. (9) reported a significantly higher oxygen consumption (V̇O2) slow component during constant heavy exercise among SCT athletes that led the authors to conclude (based on Ref. 53) on lower aerobic capacity and greater exercise intolerance during prolonged submaximal endurance exercise in those subjects.

However, the lack of differences in physical performance between SCT and control (HbAA) subjects in response to incremental exercises (5, 21, 29, 38, 42, 43) led some investigators to hypothesize that the putative lower aerobic ability in SCT carriers was compensated for by increased anaerobic metabolism (29, 31). In agreement with this conceptual framework, Freund et al. (18) observed that while volitional exhaustion during an incremental exercise was reached by the SCT carriers at the same absolute work rate as HbAA, the former displayed lower maximal V̇O2 (V̇O2max) values and higher blood lactate concentrations, suggesting a greater anaerobic energy supply component in SCT carriers. This assumption is also compatible with the significantly higher amplitude of the V̇O2 slow component mentioned above (9). Indeed, Barstow et al. (2) have delineated the presence of a significant relationship between the amplitude of the slow component and the net end-exercise blood lactate concentrations during exercise. However, numerous studies have reported unchanged or even lower blood lactate levels in SCT carriers in response to...
various types of exercise (5, 21, 42, 43), thereby challenging the initial hypothesis of a higher anaerobic contribution in the energy supply of SCT carriers.

In contradiction of these findings, several lines of evidence have shown that SCT subjects are more likely to perform better during brief and intense exercise (4, 25, 35). Hue et al. (25) reported higher performances in a jump-and-reach test by SCT carriers than control subjects with normal hemoglobin. This finding is further reinforced by epidemiologic studies that showed that in Ivory Coast a higher percentage of SCT carriers was reported among the track and field throw and jump record holders and title winners than the prevalence of SCT in the general population (4). Similarly, Marlin et al. (35) showed that in the French National sprint team the proportion of SCT carrier record holders was higher than that of athletes with normal hemoglobin.

α-Thalassemia is another hemoglobinopathy characterized by a decreased production of α-globin chains due to a deletion of one or more of the four α-globin genes. It is noteworthy that this blood disorder is frequently associated with SCT (16). Because α-thalassemia is associated with microcytosis and decreases intraerythrocytic HbS concentration in mature RBCs, it has been suggested that coexistence of SCT and α-thalassemia could be considered as potentially protective (17). In addition to a lower mean corpuscular volume (MCV), the lower hemorheological disorders observed in SCT/α-thalassemic (SCT/α-t) than in purely SCT subjects (38) could dampen the degree of microvascular blood flow alterations associated with the isolated SCT carrier state (46). Thus the coexistence of these two hemoglobinopathies could allow for better endurance exercise tolerance and improved performance over SCT carriers (31).

Indeed, the single SCT runner ranked among the 22 international level runners participating in the first Abidjan half-marathon was also a carrier for α-thalassemia (31). Although highly controversial, the hypothetical differences in muscle metabolism and performance related to the SCT carrier state could be mediated by differences in their muscle structural and metabolic characteristics. For instance, performance on the jump-and-reach test has been shown to be closely related to the strength of the lower limb extensor muscles, which is highly dependent on their type II fiber content (6). Along the same lines, it has been previously observed that the relative amplitude of the VO2 slow component was negatively related to the proportion of the type I fibers in the exercising muscle and positively related to the recruitment of type II and especially IIX fibers (2, 40, 54). However, the structural and metabolic characteristics of the skeletal muscle have never been investigated in subjects carrying SCT with or without α-thalassemia, and such analysis could provide important insights on the potential effects of HbS and α-thalassemia on skeletal muscle metabolism and performance. Thus in the present study we examined the muscle fiber type distribution (MFTD), surface area, and key energetic enzymes activity in SCT, α-thalassemia, and dual hemoglobinopathy carriers.

MATERIALS AND METHODS

Subjects

Thirty healthy active male Cameroonians volunteered to participate in the study. Subjects were allocated into four groups, namely, normal Hb control subjects (C, n = 10), α-thalassemic subjects (α-t, n = 5), SCT carriers without α-thalassemia (SCT, n = 6), and SCT carriers with α-thalassemia (SCT/α-t, n = 9). Age, height, and weight were 24 ± 1 yr, 173 ± 1 cm, and 67 ± 1 kg (means ± SE), respectively. The study took place at the General Hospital of Yaoundé. These experiments were approved by the ethics committee of the Faculty of Medicine of the University of Yaoundé 1 (no. 10-12-2005) and were in accordance with the guidelines set by the Declaration of Helsinki for human studies. Before giving their written consent, all subjects were fully informed of the objectives, possible discomforts, and potential benefits of the experiments.

Experimental Design

The experimental protocol included four visits.

Visit 1: inclusion protocol. The subjects were submitted to a thorough physical examination, anthropometric measurements, and blood samplings. Blood samples were drawn from the antecubital vein of the nondominant arm at rest for blood exam, i.e., HbA1, HbA2, HbS, and α-thalassemia phenotype screening, as well as determination of hematocrit (Hct) and MCV. Five microliters of blood were collected in EDTA tubes to determine the various types of Hb, which were isolated and quantified twice by HPLC. Positive test results for SCT were determined by the presence of HbS at a level <50% of total hemoglobin. The presence of α-thalassemia was detected with a single-tube multiplex-PCR assay, capable of detecting any combination of the six common single and double gene deletions in α-thalassemia. Only one form of α-thalassemia was found in the present study, the heterozygous form marked by the deletion of 3.7 kb of DNA containing one of the two linked α-globin genes (αα/−α-t). Volunteers who 1) presented any hemoglobinopathy other than SCT and α-thalassemia, 2) suffered from a malaria bout within the past 2 mo, 3) were human immunodeficiency virus (HIV) carriers, or 4) took part in another research program were excluded from the study.

Visit 2: incremental exercise to exhaustion. The subjects arrived at the hospital at either 8:00 AM or 12:00 PM. After a standardized breakfast or lunch followed by at least 90 or 150 min of rest, respectively, on site, subjects performed a graded exercise up to volitional exhaustion with a leg-cycle ergometer (Kettler, Ense-Parsit, Germany). The exercise started at 70 W. After 3 min of exercise at this load, the work rate increased by 35 W every 3 min thereafter. The exercise stopped when the subjects were no longer able to sustain the work rate and the required pedaling frequency set at 70 rpm. HR (beats/min) was measured continuously with a chest belt (Polar Electro, Kempele, Finland). Initially, it was planned to measure oxygen uptake continuously. Unfortunately, the oxygen sensor broke down. Because it was not possible to measure oxygen uptake for all subjects and because we are not confident in the obtained measurements, oxygen uptake data are not presented. This exercise session was used for determination of maximal HR (HRmax, beats/min) and the work rate associated with HRmax [maximal power output (Pmax), W and W/kg], which was determined by linear interpolation from the HR vs. work rate curve.

Visit 3: muscle biopsy and physical activity questionnaire. Subjects arrived at the hospital at either 8:00 AM or 12:00 PM. Subjects were placed on a bed in the dorsal decubitus position. A small incision was made in the skin and fascia under local anesthesia. A biopsy of the vastus lateralis muscle was taken with Kiel-Blakesley forceps at rest. Part of the biopsy sample containing well-identified fascicles was oriented under a stereomicroscope, mounted in Cryomount, and then frozen and stored in liquid nitrogen until histochemical and immunohistochemical analyses. This part was used for determination of different muscle fiber type analysis. The remainder was also frozen and stored in liquid nitrogen until analysis of enzyme activity. Finally, we conducted a structured interview consisting of a physical activity questionnaire (19) aiming to estimate the daily energy expenditure (DEE).
Photographs were taken at the Netherlands) connected to a digital camera (Coolpix 990, Nikon). Under a light microscope (Eclipse E400, Nikon, Badhoevedorp, The Netherlands) monoclonal antibodies. The fiber types were identified on serial preparations with anti-fast IIa myosin heavy chain N2.261 (Sigma Biochemicals) and anti-slow myosin heavy chain A4.951 (Alexis Biochemicals) monoclonal antibodies. The fiber types were designated as I, Ila, and IIX (previously referred to as IIb by Brooke and Kaiser) and coexpressions IIa-IIx and Ia-Ix.

Muscle fiber morphology analysis. Muscle sections were viewed under a light microscope (Eclipse E400, Nikon, Badhoevedorp, The Netherlands) connected to a digital camera (Coolpix 990, Nikon). Photographs were taken at ×400 magnification for MFTD, morphometric analysis, and cytochrome-c oxidase (COX) activity (vide infra). Photographs were analyzed with SigmaScan Pro 5.0 software (SPSS Science, Chicago, IL) by an investigator blinded to the nature of the samples.

Enzyme Activity Analysis

Muscle samples (30 mg) were freeze dried (Lyovac GT2, Leybold-Heraeus, Köln, Germany), dissected free from connective tissue and blood, and powdered in a chamber of controlled humidity (<40% relative humidity). Part of the muscle powder was weighed to a microtome at −20°C (HM 560, Microm, Walldorf, Germany). Immunochemical and histochemical assays. Fiber type distribution was studied on serial sections stained for myofibrillar adenosine triphosphate (ATPase) after preincubation at different pH (pH 4.35 and 4.55) according to the methodology of Brooke and Kaiser (7). Fiber type distribution was also studied on immunohistochemical preparations with anti-fast IIa myosin heavy chain N2.261 (Alexis Biochemicals) and anti-slow myosin heavy chain A4.951 (Alexis Biochemicals) monoclonal antibodies. The fiber types were designated as I, Ila, and IIX (previously referred to as IIb by Brooke and Kaiser) and coexpressions IIIa-IIx and IIa-IIX.

Statistical Analysis

Descriptive statistics are expressed as means ± SE. Two-way ANOVA procedures were used to determine the effects of SCT, α-thalassemia, and the interaction of these two factors on the various parameters of interest. Differences between values were considered to be significant at P ≤ 0.05 and to represent a tendency at 0.05 < P ≤ 0.10.

RESULTS

Physiological Characteristics and Physical Activity

HRmax and Pmax were 181 ± 3 beats/min and 3.02 ± 0.7 W/kg, respectively. Table 1 shows that there were no differences among the different subjects for HRmax and Pmax, and also no differences emerged among groups for DEE.

Hematologic Data

The percentages of HbA1 and HbA2 were higher and lower, respectively, in the control group compared with the two SCT groups (Table 1). The percentage of HbsS was significantly higher in the SCT group compared with the SCT/α-t group (P < 0.05).

Time to exhaustion at 110% Pmax

Table 2 shows that there were no differences among the different groups for either Tex or Hrex. Moreover, blood lactate concentrations reached at the end of the test were not statistically different among the four groups. Unfortunately, some
subjects did not reach their HR\text{max} at the end of the TE\text{ex} and some blood lactate samples could not be obtained on time at the end of the TE\text{ex}, such that some values of HR\text{ex} and TE\text{ex} are missing for some of the subjects (see Table 2).

Muscle Fiber Type Distribution

The distributions of muscle fiber types were 32.5 ± 2.2%, 2.2 ± 0.7%, 52.8 ± 2.6%, 8.3 ± 1.0%, and 10.4 ± 1.8% for types I, I-IIa, IIa, IIa-IIx, and IIx, respectively. No fiber type distribution intergroup differences were detected (Fig. 1). However, it should be noted that type IIa fibers account for half of the overall fiber population, and that SCT carrier muscle almost did not exhibit type I-IIa coexpression fibers. Therefore, for convenience of presentation and statistical analysis, data on type I and I-IIa fibers were merged.

Muscle Fiber Surface Area

The mean surface area of type IIx fibers tended to be greater in the SCT groups compared with the control group (P = 0.0925) (Fig. 2).

Enzyme Activities

Some of the skeletal muscle key enzyme activities are shown in Table 3. No significant differences among the groups emerged except for a trend toward elevated CK (P = 0.0702). As shown in Fig. 3, SCT carriers had significantly lower COx enzyme activity within type IIa fibers (P < 0.05) compared with control subjects and \(\alpha\)-thalassemic subjects. Moreover, COx activity tended to be also lower in type I, IIa-IIx, and IIx fibers.

DISCUSSION

This study assesses for the first time skeletal muscle histomorphological and metabolic characteristics in subjects with SCT, \(\alpha\)-thalassemia, and the dual hemoglobinopathy. We found that neither SCT nor \(\alpha\)-thalassemia, nor their coexpression, is associated with any significant changes in MFTD or activity in key enzymes of the glycolytic or tricarboxylic acid (TCA) cycle pathways. However, SCT subjects displayed some unique changes in mitochondrial enzyme activity, namely, significantly lower COx activity in type IIa fiber, with similar trends in type I and IIx fibers. Furthermore, trends toward lower CK activity and higher type IIx fiber surface area were also found in SCT carriers.

General Considerations

Type IIa fibers predominated in our overall population of Cameroonian. This fiber type represents more than half of the total myocytes (52.0%) present in the vastus lateralis muscle, whereas type I fibers accounted for ~33.6% (Fig. 1). These results are in agreement with those of Ama et al. (1), who reported a distribution of type I and IIa fibers in healthy black Africans diametrically opposed to that observed in a Caucasian population matched for the level of physical fitness (37, 47). Together, the present results and those of Ama et al. (1) clearly indicate that ethnic origins are major determinants of muscular fiber typology.

Sickle Cell Trait

Type I fiber distribution and CS activity have been shown to be closely associated with VO\text{2max} (28). The similar MFTD and TCA cycle enzyme activities found in the present study in SCT carriers and HbAA subjects may therefore account for the similar VO\text{2max} values measured in SCT carriers and HbAA control subjects (5, 21, 29, 38, 42, 43) and also explain the similar peak power outputs achieved at exhaustion during the graded exercise among the different groups of subjects in the present study (Table 3).

Previous studies have emphasized specific aspects of physical ability and/or physiological responses to exercise in SCT carriers. Among these, higher lactate production (18), better performances for throws, jumps, and sprints (4, 25, 35), and greater VO\text{2} slow component (9) have all been reported in SCT. We hypothesized that different MFTD, blood lactate concentration, and PFK and LDH activities would be present in SCT.

Table 2. Time to exhaustion test findings

<table>
<thead>
<tr>
<th></th>
<th>C (n = 9)</th>
<th>(\alpha)-t (n = 5)</th>
<th>SCT (n = 5)</th>
<th>SCT/(\alpha)-t (n = 8)</th>
<th>HbS</th>
<th>(\alpha)-thal</th>
<th>Crossed</th>
</tr>
</thead>
<tbody>
<tr>
<td>T\text{ex}, s</td>
<td>160 ± 10</td>
<td>168 ± 25</td>
<td>170 ± 12</td>
<td>161 ± 13</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HR\text{ex}, beats/min</td>
<td>184 ± 3</td>
<td>178 ± 4</td>
<td>188 ± 10</td>
<td>185 ± 4</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>[La\text{b-ex}, mmol/l]</td>
<td>9.1 ± 0.3</td>
<td>10.6 ± 1.0</td>
<td>8.1 ± 0.4</td>
<td>8.8 ± 0.8</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>110% P\text{max}, W</td>
<td>214 ± 8</td>
<td>228 ± 11</td>
<td>209 ± 25</td>
<td>232 ± 11</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values presented are means ± SE for n subjects. T\text{ex} is time to exhaustion; HR\text{ex} is heart rate at exhaustion; [La\text{b-ex}, blood lactate concentration -3 min into recovery after exhaustion. See Table 1 for definitions of other symbols.
carriers, based on the following considerations: 1) height of jumps has been related to MFTD (6, 2) the VO2 slow component has been linked to MFTD and lactate accumulation (2), 3) performance during sprint exercise correlates with lactate accumulation and PFK and LDH activities (32, 33, 34), and 4) lactate accumulation was found to be associated with MFTD and LDH activity (26, 50). However, neither MFTD nor the activities of key enzymes within the glycolytic pathway in SCT carriers differed from those found in HbAA subjects (see Tables 1 and 3). Thus, the lactate accumulation during high-intensity exercise, which is correlated to blood lactate accumulation during exercise (36), was also not different among groups. Moreover, no differences in the blood lactate concentrations reached at the end of the Tex test emerged between SCT carriers and control subjects with normal Hb (Table 2). The similarity between groups for Tex blood lactate concentrations, and LDH and PFK activities supports previous reports on normal blood lactate concentrations in SCT carriers (3, 42). However, such findings were not consistent, as evidenced by other studies showing elevated lactate (18) or reduced lactate (5, 21, 43) levels in SCT carriers in response to various types of exercise. Further experiments using tracer methodologies should be performed in the future to improve our understanding of energetic and especially lactate metabolism in exercising SCT carriers.

In the present study, a trend toward a higher type IIX fiber surface area was observed in SCT carriers (+17%, P < 0.0925) (Fig. 2). At the present time, it would be too speculative to interpret those findings, and further studies are necessary to confirm this trend. However, if the higher surface area of type IIX fibers is subsequently confirmed, this might constitute a possible explanation for the better performances during jump-and-reach tests in SCT carriers (25). Indeed, Hautier et al. (23) indicated that squat jump performance is related to the cross-sectional surface area of the IIX fibers.

Of note, CK activity showed a tendency toward lower values in SCT carriers (10%, P = 0.0702). At first sight, this result might indicate reduced alactic anaerobic metabolism, which may appear somewhat contradictory with previous studies reporting better performances achieved by SCT carriers than control counterparts during brief and intense exercise (4, 25, 35). However, we also found a lower COx activity in SCT carriers (especially in the type IIA fibers that account for the majority of the myocytes) (Fig. 3). The reduced COx activity in the presence of HbS indicates that oxidative energy metabolism may be limited in SCT. Because CK has a key role in oxidative phosphorylation regulation (20, 41), COx and CK work concurrently to provide ATP for energy metabolism of contracting muscle cells. Taken together, the lower CK and COx activities could provide a possible explanation for the decreased repeated sprint ability (RSA) reported by Connes et al. (12) in SCT carriers compared with control subjects. Indeed, RSA and muscle oxidative capacity have been shown to be highly correlated (8, 14). Furthermore, in addition to the local blood flow perturbations that can develop in SCT carriers (12, 38), lower CK and COx activities could also underlie the reduced ability to engage in prolonged submaximal exercises that has been repeatedly reported among SCT carriers (29, 30, 31, 51).

The mechanisms underlying putatively lower CK and COx activities are unclear, and our study was not designed to provide any potential insights into this issue. However, it has been shown that 1) erythrocytes of SCT carriers produce and accumulate higher reactive oxygen species (ROS) at rest or in response to physical exercise (13, 44) and that 2) ROS lead to inhibition of both CK (20, 27, 28) and COx (15, 22, 45) activities. We therefore speculate that the trend for and actual lower muscle CK and COx activities, respectively, could be derived from alterations in skeletal muscle ROS metabolism in SCT carriers. Studies on ROS metabolism in skeletal muscle in SCT during rest and exercise will be needed in the future.

**α-Thalassemia**

α-Thalassemia does not seem to induce particular structural and metabolic adaptations in skeletal muscle. Indeed, none of the parameters studied in the present study differed in α-thalassemic subjects compared with control subjects. Furthermore, no differences in muscle structural or metabolic profiles were observed in subjects with the dual hemoglobinopathy (SCT/α-t) compared with SCT carriers. A previous study has reported a potential benefit of α-thalassemia on muscle function and exercise capacity in SCT carriers (31). If such a benefit exists, albeit subsequently challenged (see Ref. 9), it does not seem to be explained by any structural or metabolic characteristic of the skeletal muscle. More likely, dampened hemorheological and microcirculatory disturbances and improved oxygen delivery to the muscle tissues might explain the improved

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**Table 3. Muscle enzyme activities**

<table>
<thead>
<tr>
<th></th>
<th>C (n = 10)</th>
<th>α-t (n = 5)</th>
<th>SCT (n = 6)</th>
<th>SCT/α-t (n = 9)</th>
<th>HbS</th>
<th>α-thal</th>
<th>Crossed</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK</td>
<td>1.834 ± 101</td>
<td>1.890 ± 154</td>
<td>1.752 ± 165</td>
<td>1.579 ± 45</td>
<td>0.0702</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>PFK</td>
<td>278.8 ± 31.2</td>
<td>245.2 ± 31.2</td>
<td>278.7 ± 30.9</td>
<td>314.8 ± 24.5</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>LDH</td>
<td>882.2 ± 64.4</td>
<td>846.4 ± 81.4</td>
<td>841.4 ± 81.4</td>
<td>795.4 ± 66.9</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CS</td>
<td>19.4 ± 1.8</td>
<td>18.6 ± 1.4</td>
<td>19.3 ± 1.6</td>
<td>20.6 ± 1.7</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>HAD</td>
<td>15.3 ± 1.4</td>
<td>14.0 ± 2.4</td>
<td>13.3 ± 1.9</td>
<td>13.2 ± 0.9</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values (in μmol·min⁻¹·g dry muscle⁻¹) are means ± SE for n subjects. CK, creatine kinase; PFK, phosphofructokinase; LDH, lactate dehydrogenase; CS, citrate synthase; HAD, β-hydroxacyl-CoA-dehydrogenase. See Table 1 for definitions of other symbols.
exercise capacity of SCT carriers who coexpress α-thalassemia (31). Indeed, RBC deformability was reduced and blood apparent viscosity was increased in SCT carriers, while no such differences were present in SCT/α-t subjects and in HbAA control subjects (38). Furthermore, α-thalassemia induces microcytosis (48) that favors the flow of RBCs through the capillary network. Finally, we recently reported (52) that α-thalassemia was associated with a higher muscle capillary tortuosity, which should improve oxygen supply to the tissues. Together, these particular adaptations associated with α-thalassemia may constitute a possible explanation for the putative, albeit debatable (9), improved ability for prolonged submaximal exercise in subjects who coexpress SCT and α-thalassemia over SCT carriers (31).

Limitations

The major limitation of the present report lies in the low number of subjects studied in each group. Hence, the failure to reach statistical significance in several of the comparisons could be due in part to the small sample size. Further experiments are de facto needed to confirm the trends observed, and to allow a better understanding of the effects of SCT and α-thalassemia on muscle metabolism.

Summary

MFTD and the activities of key enzymes in the glycolytic and TCA cycle pathways are preserved in SCT, α-thalassemia, or both. However, the trends for lower CK and the reduced COX activities observed in SCT carriers could explain their diminished performance achievement during prolonged submaximal exercises (31). The trend toward increased type IIx fibers surface area in SCT are worthy of confirmation by further studies. Finally, the MFTD and energetic characteristics of subjects with the dual hemoglobinopathy are similar to those reported in SCT carriers, supporting the concept of framework that the beneficial effects of α-thalassemia on exercise among SCT carriers are likely to originate from improved hemorheological characteristics rather than being mediated by any particular changes in muscle characteristics.

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DISCLOSURES

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

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