

Physical activity blunts oxidative stress response to exercise in sickle cell trait carriers
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In this study, we demonstrate that regular physical activity decreases oxidative stress and increases nitric oxide metabolism in response to a maximal incremental exercise in sickle cell trait carriers. This improvement is likely explained by the increase in antioxidant enzymes activities observed in trained subjects. These results suggest that physical activity may help to control oxidative stress in carriers of hemoglobin S. Since the relationships between oxidative stress and vascular adhesion markers or nitric oxide bioavailability are well documented, the lower oxidative stress in active sickle cell trait carriers argue in favor of dampened endothelial dysfunction and subsequent vascular disorders in those subjects.

Keywords: sickle cell trait carriers, oxidative stress, physical activity, nitric oxide

BACKGROUND

Sickle cell trait (SCT) is the heterozygous form of sickle cell disease, resulting from a single mutation in the β -globin chain. SCT is characterized by hemorheological and endothelial abnormalities, possibly related to an increase in oxidative stress. Habitual exercise training has been shown to depress oxidative stress through an up-regulation of anti-oxidant defenses thereby halting the overexpression of oxidative stress. We therefore hypothesize that regular physical activity will alter oxidative stress in SCT carriers compared to sedentary counterparts.

DESIGN AND METHODS

Plasma levels of oxidative stress [advanced oxidation protein products (AOPP), protein carbonyl, malondialdehyde (MDA), and nitrotyrosine], anti-oxidant markers [catalase, glutathione peroxidase (GPX) and superoxide dismutase (SOD) in plasma], NO metabolism (NOx), P- and E-selectins were assessed at baseline (Base) and time points immediately following a maximal incremental exercise test (T_{ex}) and into recovery (T_{1h} , T_{2h} , T_{24h}) in 40 trained (T: 8 hours/week minimum) or sedentary (S: no regular physical activity) subjects (age: 23.5 ± 2.16 years), carriers (SCT) or not (CON) of the sickle cell trait (T-SCT: n=8, T-CON: n=10, S-SCT: n=11, S-CON: n=11).

RESULTS

At T_{ex} , T-SCT had a lower level of AOPP (174 ± 121 vs. 224 ± 130 $\mu\text{mol/l}$, $p=.012$, Figure 1), nitrotyrosine (70.6 ± 46.6 vs. 127 ± 29 nmol/l , $p=.003$), and protein carbonyl (86.9 ± 26.8 vs. 114 ± 34.0 nm/ml , $p=.006$) compared to their sedentary counterparts (S-SCT). In addition, the percentage MDA increase from baseline was significantly higher in S-SCT than the 3 other groups at T_{ex} , T_{1h} , T_{2h} , and T_{24h} .

Compared to S-SCT, T-SCT had a higher activity of SOD (8.50 ± 7.20 vs. 4.30 ± 2.50 U/ml, $p=.002$) and NOx (28.8 ± 11.4 vs. 14.6 ± 6.99 $\mu\text{mol/l/min}$, $p=.003$) at T_{ex} and GPX at T_{1h} (112.0 ± 14.7 U/ml vs. 87.7 ± 9.5 , respectively, $p=.04$). At baseline, catalase activity was higher in trained subjects than in their untrained counterparts ($p<.001$).

Finally, we found significant relationships between changes (baseline vs. T_{ex} , T_{1h} or T_{2h}) in oxidative stress and E- and P-selectins or NO metabolism induced by maximal exercise. These correlations are presented in Table 1.

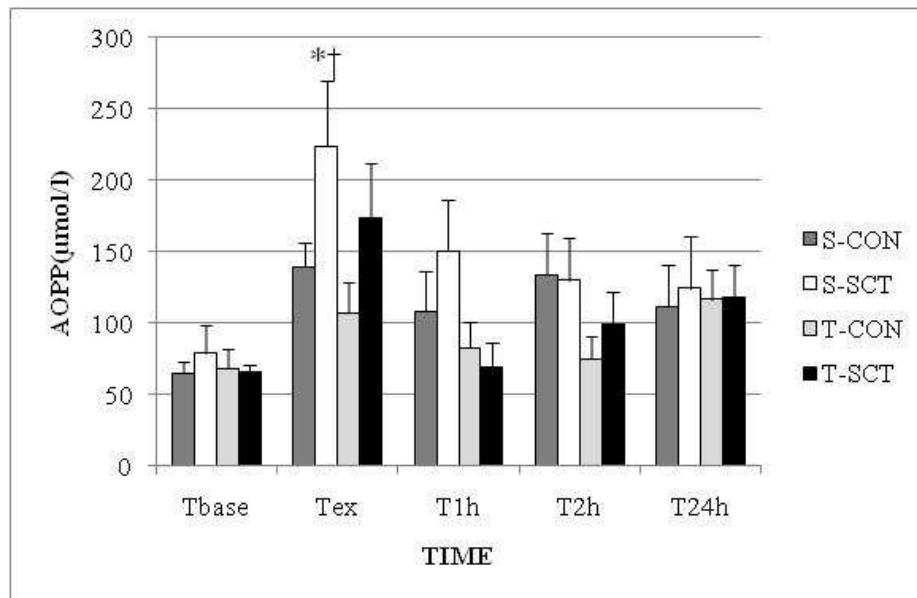


Figure 1. Plasma AOPP at baseline and in response to maximal exercise (Ex, T_{1h}, T_{2h}, T_{24h}) for S-CON, S-SCT, T-CON, T-SCT. * p=.018 vs. Baseline; † p<.05 vs. S-CON, T-CON, T-SCT at Ex.

Table 1. Correlations between oxidative stress and E- and P-selectins, nitric oxide metabolism (NOx) or nitrotyrosine changes at T_{ex}, T_{1h} or T_{2h}.

Variables	Time	Pearson correlation coefficient	P values
AOPP			
vs. <i>E-selectin</i>	T _{ex}	0.39	0.04
vs. <i>NOx</i>	T _{1h}	-0.58	0.01
vs. <i>Nitrotyrosine</i>	T _{2h}	0.57	0.01
Protein carbonyl			
vs. <i>P-selectin</i>	T _{2h}	0.52	0.02
vs. <i>Nitrotyrosine</i>	T _{1h}	0.58	0.01

CONCLUSIONS

This study demonstrates that oxidative stress response to exercise is increased in sickle cell trait carriers compared to healthy subjects.

Our findings also indicate that regular physical training can decrease the overall oxidative stress and improve nitric oxide metabolism in response to exercise in sickle cell trait carriers. This is likely explained by the improvement of antioxidant enzymes activities in trained subjects.

Additionally, the correlations found between oxidative stress, adhesion molecules and NO end-products corroborate the hypothesis that oxidative stress could be involved in adhesion phenomenon and impairment of NO availability in carriers of hemoglobin S.

Finally, these results suggest that physical activity could be a viable method of controlling oxidative stress which is known to be involved in endothelial dysfunction and subsequent vascular impairment in HbS carriers.