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An Antioxidant Supplementation Hinders the Role of Exercise Training as a Natural Activator of SIRT1 †

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1. Background

Exercise training (ET) is recommended by the International Health Authorities as it provides benefits in healthy individuals and patients belonging to several clinical settings [1–3]. ET contrasts oxidative stress, by decreasing radical oxygen species (ROS) and other oxidant molecules and/or increasing antioxidant ones [4]. On the other hand, because of increased oxygen consumption, during exercise the production of ROS may overcome the capacity of the endogenous antioxidant system to detoxify them, producing oxidative stress [5–7]. ET is a natural activator of Sirtuin 1 (SIRT1), which is a NAD+-dependent deacetylase acknowledged as a life span- and health span-prolonging agent [8–10]. SIRT1 activated during ET can contrast aging and age-associated diseases by increasing the cellular antioxidant capacity [10–12].However, the ET-related effects, including SIRT1 activation, strongly depend on the type, intensity, and duration of the training [13–16]. Other natural activators of SIRT1 include polyphenols, such as resveratrol, and several phenolic plants extracts whose antioxidant properties are widely acknowledged [17,18]. Supplementation of antioxidants can contribute to preventing or contrasting oxidative stress and its associated cellular damage. Indeed, supplements, especially those containing vitamins and other micronutrients, are commonly used to improve athletes' wellness and performance [19–21]. Despite this, the effects of antioxidant supplementation have not yet been elucidated, especially in athletes performing endurance training [20]. Therefore, in this study, we compared the effects on SIRT1 and antioxidant capacity in endurance athletes using or not antioxidant supplements to investigate whether an exogenous source of antioxidants could interfere with ET-related effects.

2. Methods

Thirty-two endurance athletes, that are middle-distance runners (MDR), and 14 age-matched sedentary volunteers (CTR) were enrolled. All participants signed informed consent and the study got approval from the local Ethics Committee (Observational Study n. 86/2020). MDR belonged to an amateur sports association called "Atletica Salerno". They were divided into two groups. One of them (MDR-S) assumed every day an antioxidant supplementation (S) consisting of 240 mg vitamin C and 15 mg vitamin E, together with

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861 mg sodium, 555 mg chlorine, 381 mg potassium, 66 mg magnesium. The other group did not use any antioxidant supplementation (MDR-noS). We recorded athletes' data, including those regarding training regimen as well as information concerning alcohol consumption and tobacco use, and dietary habit. Blood samples were collected in fasting conditions from each participant. Peripheral Blood Mononuclear Cells (PBMCs) were isolated by Ficoll-Paque density gradient. Serum samples were obtained by centrifugation at 1500× *g* for 10 min. Aliquots of serum and PBMCs were frozen at −80 °C until analysis.SIRT1 mRNA and activity were measured in PBMCs by Real-Time PCR and fluorimetric assay, respectively. Total oxidative status (TOS) and total antioxidant capacity (TEAC) were measured in plasma by colorimetric assay and oxidative stress index (OSI) was determined by TOS/TEAC ratio.

3. .Results

The study population consisted of 14 CTR, 14 MDR-noS, and 18 MDR-S. There were no differences in age, tobacco and alcohol use as well as in dietary habits between the two groups of athletes, and between athletes and sedentary controls. CTR had a BMI higher than MDR-S and MDR-noS (both, $p = 0.0001$), while no differences between MDR-S and MDR-noS were found. In addition, neither training time/week nor training frequency/week differed between MDR-S and MDR-noS. MDR demonstrated higher levels of SIRT1 mRNA compared with CTR ($p = 0.0387$). Notably, MDR-noS showed higher levels than CTR ($p = 0.0136$) while MDR-S did not differ from CTR. No differences between MDR-S and MDR-noS were found (Figure 1, panel A). MDR showed higher levels of SIRT1 activity compared with CTR ($p = 0.0055$). MDR-noS had the highest value, significantly higher compared both with CTR ($p = 0.0003$) and MDR-S ($p = 0.0012$) (Figure 1, panel B).

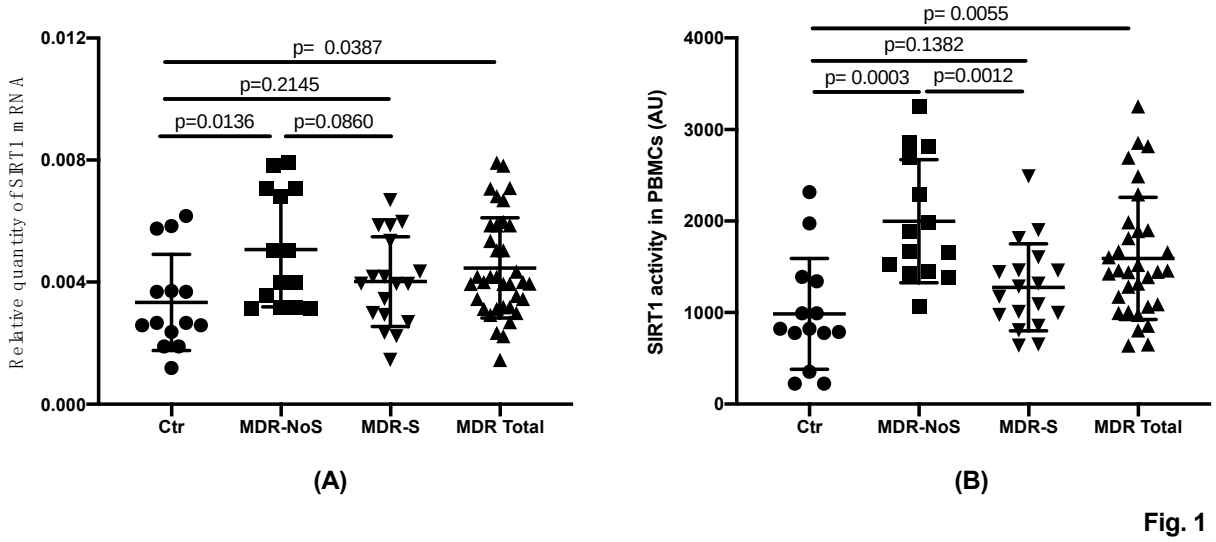


Figure 1. Caption.

As shown in Figure 2 (panel A), no differences in TOS levels were found among the groups.MDR showed higher levels of TEAC compared with CTR ($p = 0.0001$). Notably, both the MDR-S and MDR-noS showed higher levels than CTR (MDR-noS vs CTR, $p = 0.0003$ and MDR-S vs CTR, $p = 0.0007$). No differences were found between MDR-S and MDR-noS (Figure 2, panel B). CTR demonstrated the highest levels of OSI (TOS/TEAC) than the other groups (CTR vs MDR, $p = 0.0002$; CTR vs MDR-noS, $p = 0.0015$ and CTR vs MDR-S, $p = 0.0086$). No differences were found between MDR-S and MDR-noS (Figure 2, panel C).

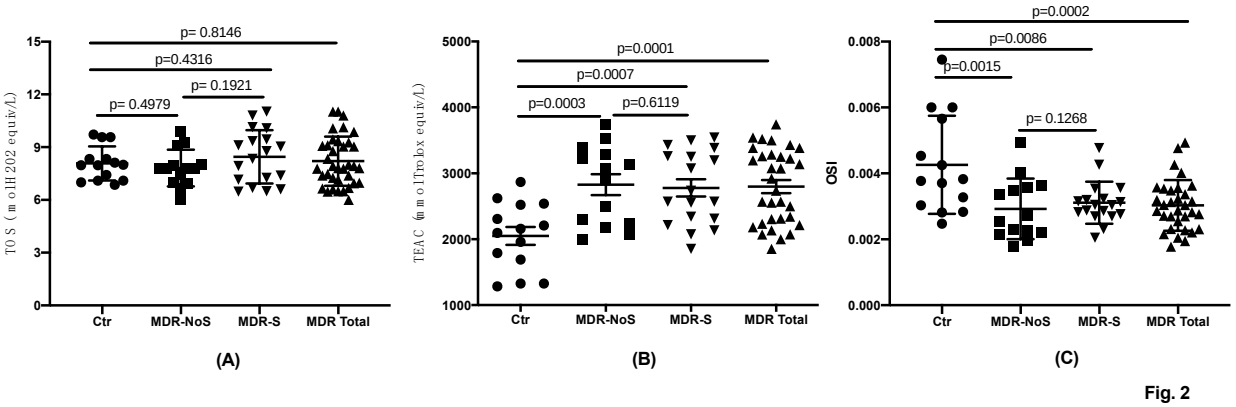
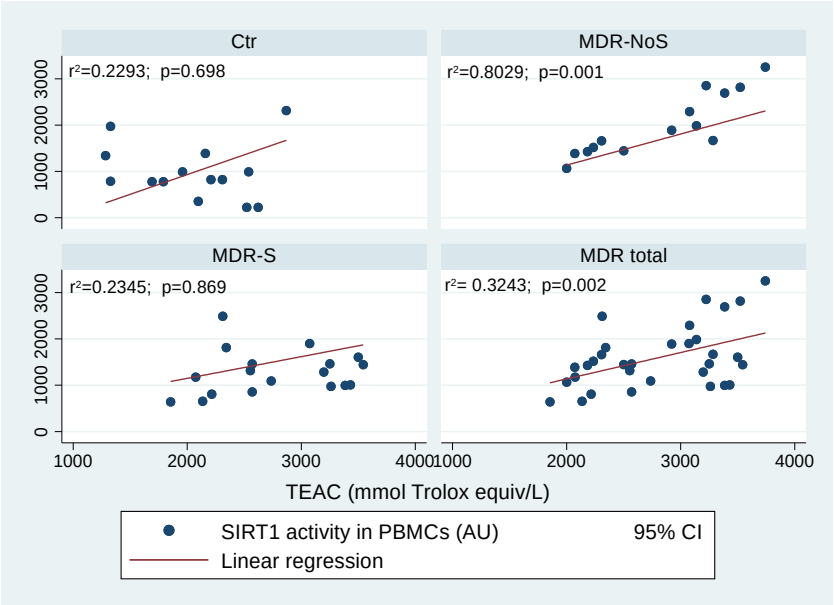
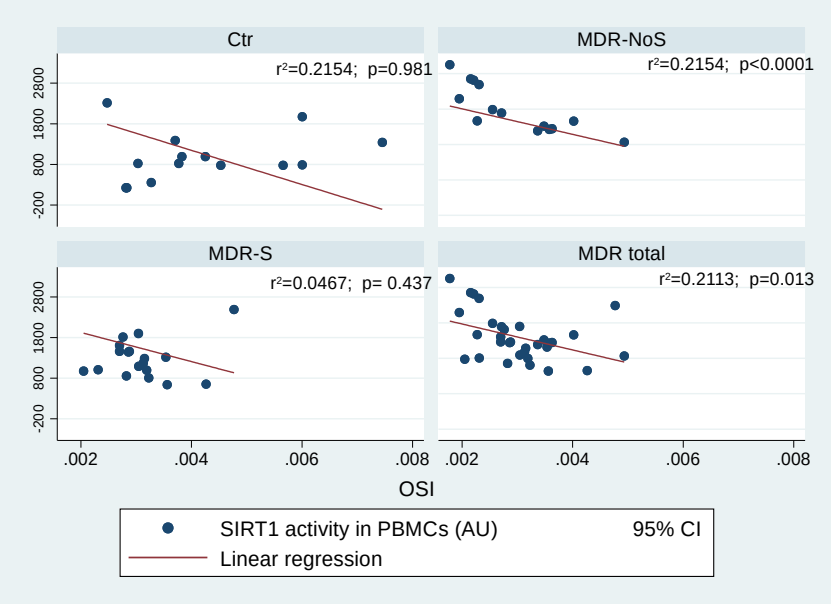


Figure 2. Caption.

A statistically significant correlation by linear regression analysis between SIRT1 activity and TEAC ($p = 0.002$, $r^2 = 0.2345$) was found. This correlation was determined by the results of MDR-noS ($p = 0.001$, $r^2 = 0.8029$) (Figure 3, panel A). Conversely, an inverse correlation between SIRT1 activity and OSI was found in MDR ($p = 0.013$, $r^2 = 0.213$). This finding was determined by the inverse correlation between the two considered parameters in MDR-noS ($p < 0.0001$, $r^2 = 0.2154$) (Figure 3, panel B).



(**A**)



(**B**)

Figure 3. Caption.

4. Conclusions

This study demonstrated that TEAC increased in MDR compared with CTR irrespective of an antioxidant supplementation intake. SIRT1 mRNA and activity increased in MDR-noS but not in MDR-S when compared with CTR. Notably, SIRT1 activity is strongly correlated with TEAC in MDR-noS but not in MDR-S. An exogenous source of antioxidants seems to hinder the role of endurance training as a natural activator of SIRT1.

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