

## Spark Motor Program reduced oxidative stress in boys with Down syndrome

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### Abstract

*Introduction:* Oxidative stress (OS) level is higher in individuals with Down syndrome (DS). Malondialdehyde (MDA) is a marker for lipid peroxidation and the effect of exercise training on MDA in DS patients is not well known. The aim of this study was to examine the effects of selected Spark Motor Program on MDA in boys with DS.

*Material & Methods:* Twenty Down syndrome boys aged between 10~14 participated in this study as the subjects. The subjects were randomly divided into experimental group (n=10) or control group (n=10). The experimental group was performed selected Spark Motor Program 3 days a week

for 8 weeks. MDA concentration was measured before and 48h after the intervention.

*Results:* The results showed that MDA decreased after 8 weeks selected experimental in compare to the control group.

*Conclusions:* In summary, Spark Motor Program that selected in this study decreases MDA of boys with DS.

**Keywords:** Oxidative stress, Down syndrome, Malondialdehyde, Spark training.

## 1. Introduction

Down syndrome (DS) is a genetic disorder associated with trisomy 21. Although pathological mechanisms leading to DS phenotypes are not known yet, it is obvious that the presence of the third chromosome 21 is responsible for altered development during embryogenesis and organogenesis (1). The incidence of DS is approximately 1/1.000 to 1/1.200 of live births (2). DS begins during childhood and involves deficits in mental abilities, social skills, and core activities of daily living when compared to same-aged peers (3). DS is a disability characterized by significant limitations in both intellectual functioning and in adaptive behavior, which covers many everyday social and practical skills. This disability originates before the age of 18 (4,5).

In addition, the brain abnormalities observed in DS have been linked to an inherent oxidative stress (OS), for example, characteristics of accelerated aging and high incidence of hyperactivity, with accompanying attention deficits (6,7). The concept of OS has been introduced for research in redox biology and medicine in 1985, now 30 years ago, in an introductory chapter 1 in a book entitled 'Oxidative Stress' (8). Briefly, OS is a term used to describe the effect of oxidation in which an abnormal level of reactive oxygen species, such as free radicals (e.g. hydroxyl, superoxide radicals) or non-radical (e.g. lipid peroxide), lead to damage of specific molecules with consequential injury to cells or tissues (9). OS is a phenomenon that is often discussed in connection with many diseases, such as atherosclerosis and cardiovascular diseases, neurodegenerative diseases, rheumatoid arthritis,

diabetes mellitus, cancer and mental disorders (10-15). OS is also considered as one of the main causes of aging (16).

OS level is higher in individuals with DS (17,18) due to the excess of Cu/Zn superoxide dismutase (Cu/ZnSOD) coded in the 21 chromosome (19). The excess of free radicals saturates antioxidant mechanisms of an organism, and the lipid peroxidation caused by the action of the free radicals on membrane phospholipids creates high quantities of aldehydes as MDA, which indicates a high level of OS (19).

Previous studies indicate that exercise programs have physiologic and psychological benefits on the overall health of adults with DS, thereby increasing the quality of life and lifespan of these individuals (20). Exercise training attenuates OS in humans (21) and animals population (22), but effect of exercise training on OS in DS children is not well known and further scientific endeavor is requested regarding exercise and OS in a population with DS (23,24). Thus the present study was conducted to examine the effect of 8 weeks selected Spark Motor Program on MDA in boys with DS.

## **Material & Methods**

### *Subjects*

The subjects of this experimental study are 20 DS patients, aged between 10~14 with second to third degree of mental disability ratings which included autistic patients. The parents or guardian of the subjects were given both verbal and written instructions outlining the experimental procedure, and written informed consent was obtained. The study was approved by the Islamic Azad University, Marvdasht branch Ethics Committee. The subjects were divided into experimental group (n=10) or control group (n=10) randomly.

### *Measurements*

#### *Anthropometric measurements*

Height and weight were measured, and body mass index (BMI) was calculated by dividing weight (kg) by height (m<sup>2</sup>).

### *Biochemical analyses*

5 ml of fasted blood were taken in the morning before and after 8 weeks of study at the same time. All the subjects fasted at least for 12 hours and a fasting blood sample was obtained by venipuncture. Serum obtained was frozen at  $-22^{\circ}\text{C}$  for subsequent analysis. The serum MDA level was measured in duplicate using an enzyme-linked immunosorbent assay (ELISA) kits (Eastbiopharm Co. LTD.; China). The sensitivity of kit was 0.22 nmol/ml.

### *Spark Motor Program*

Selected exercise program was originated from Spark Motor Program that involves exercising and playing. Two kind of Spark Physical Education plan are exist: Elementary PE (1.K-2 PE 2. 3-6 PE) and Secondary PE (1. Middle School PE 2. High School PE). Gross motor skills like crawling, balancing and running are expanded during early childhood and are considered as a necessary item of motor development. The major muscle groups are mostly responsible for gross motor movements. Fine motor skills are those attributed to the coordination of minor groups of muscles for example involved in playing piano. Test of Gross Motor Development-edition 2 called TGMD-2 is a norm-reference measurement of gross motor development (25).

The exercise program includes 45 minutes for each session that is divided into 4 parts. The first 15 minutes is allocated to warm up and then playing for 10 minutes that involves motor skill movements, next 10 minutes for manipulation movement skills and finally 10 minutes for cool down. The experimental group did the selected spark motor program 3 times in the week and for 8 weeks (26). During this period the control group did their routine activities. At the end of the 8 weeks, the posttest was conducted.

### *Statistical analysis*

Results were expressed as the mean  $\pm$  SD and distributions of all variables were assessed by Shapiro-wilk test for normality. Data were analyzed using paired and independent sample t-tests. The level of significance in all statistical analyses was set at  $P < 0.05$ . Data analysis

was performed using SPSS software for windows (version 17, SPSS, Inc., Chicago, IL).

### Res3. ults

Anthropometric parameters of the subjects are presented in Table 1. No significant differences were observed on the anthropometric parameters of the subjects at baseline.

Table 1. Anthropometric parameters (mean  $\pm$  SD) of the subjects

	Experimental group (mean $\pm$ SD)	Control group (mean $\pm$ SD)
Height (cm)	143.0 $\pm$ 10.3	141.5 $\pm$ 8.8
Body weight (Kg)	38.3 $\pm$ 9.4	37.7 $\pm$ 8.3
BMI (Kg/m <sup>2</sup> )	18.3 $\pm$ 2.7	18.5 $\pm$ 2.1

The data on MDA concentration of the training and control group is presented on figure 1. The results indicated that MDA concentration of the experimental group was significantly reduced compared to the control group ( $t = 2.4$ ,  $P = 0.02$ ).

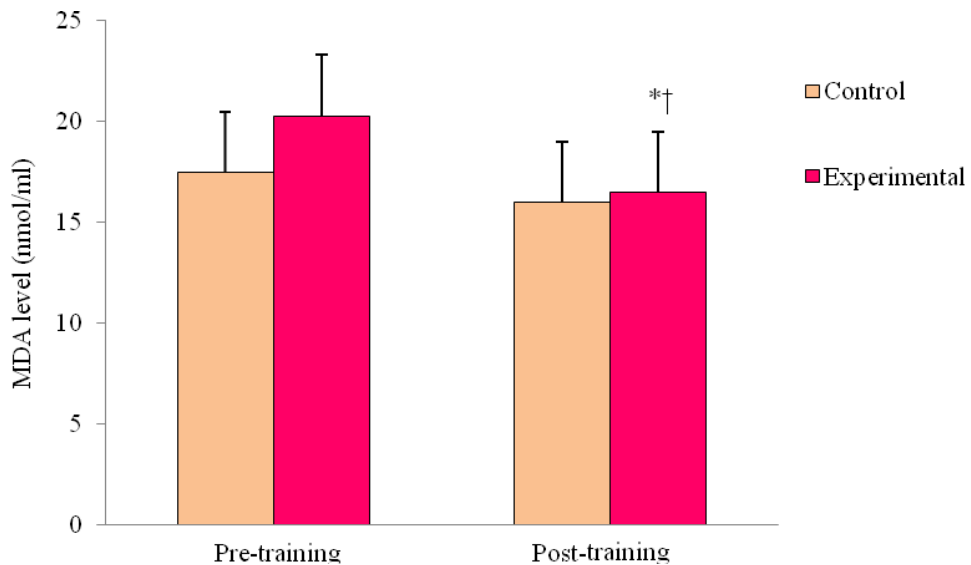


Figure 1. MDA concentration of the subjects

#### 4. Discussion

The excess of genetic information in patients with DS produces an increase superoxide dismutase (SOD1) activity, an antioxidant enzyme coded on chromosome 21 (27). This overactivity of SOD1 is not balanced, as the ratio of SOD1 to catalase plus glutathione peroxidase is also increased (28). The  $H_2O_2$  thus generated is more than the catalase and glutathione peroxidase can catabolize. The excess of the resulting  $H_2O_2$  might react with  $O_2^{\bullet}$  producing  $OH^{\bullet}$ , which is one of the most reactive oxygen species. This excess of OS has recently been supported by a multiple prooxidant state, which seems to play a major role in the DS phenotype and in the pathologies frequently seen in this syndrome (29), such as neurological disorders, atherosclerosis, diabetes, accelerated cell ageing and cellular mutagenicity (30). Previous studies demonstrated that exercise training attenuates OS in humans (21) and animal's population (22), but effect of exercise training on OS in DS children is not well known. Therefore, in this study, we tested the effects of selected Spark Motor Program on MDA in boys with DS.

OS generally causes damage to the cell membrane's polyunsaturated fatty acids, leading to the generation of MDA, a thiobarbituric acid reacting substance. It is considered a major end-product of oxidation of polyunsaturated fatty acids and has been frequently measured as an indicator of lipid peroxidation and OS in vivo. Increased lipid peroxidation products in individuals with DS have been reported (31). Recent studies have demonstrated higher levels of MDA and thiobarbituric acid reactive substances in Alzheimer disease (32).

Our data in line with previous studies (33,34) showed that regular exercise for 8 weeks significantly reduced serum MDA levels in the DS group compared with levels at the beginning of the exercise programme. Similar results have been reported by Meguid et al. (2014) who showed that MDA level reduces after a selected treadmill training programme in adolescents with DS (33). Javier Ordonez and Rosety-Rodriguez (2007) also observed that a 12-week exercise programme significantly reduced lipid peroxidation in terms of plasmatic MDA content in male adolescents with DS (34). Meguid et al. (2014) noted that this finding may be due to improved serum lipid profiles in adolescents with Down

syndrome, as high-density lipoprotein (HDL) cholesterol increased whereas low-density lipoprotein (LDL) cholesterol decreased (33). This may contribute, at least in part, to improving lipoperoxidation in exercised individuals, since LDL oxidation can be inhibited by HDL through its oxidizable components or associated enzymes such as paraoxonase and platelet-activating factor acetylhydrolase (35). Zambrano et al. (2009) also reported a decrease in salivary lipid hydroperoxides in persons with DS after aerobic exercise and suggested that aerobic exercise could be considered as a way to reduce OS in these persons (19).

## 5. Conclusion

In conclusion, Spark Motor Program that selected in this study reduces MDA in boys with DS. Previous studies addressing the role of physical exercise in OS and antioxidant status in people with DS have shown conflicting results. The extensive literature indicates that moderate exercise similar to that used in the present study exerts low stress without oxidative damage consequences in non-DS (36). Further studies are recommended to detect the effect of Spark Motor Program on OS in different age groups of DS individuals.

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**Conflict of interests:** There was no conflict of interest among authors.

## References

1. Muchová J, Žitňanová I, Ďuračková Z. Oxidative stress and Down syndrome. Do antioxidants play a role in therapy? *Physiol Res* 2014; 63: 535-542.
2. World Health Organization. Down syndrome. Genes and human diseases. World Health Organization; 2007. Available at:

<http://www.who.int/genomics/public/geneticdiseases/en/print.html>.

3. Kaneshiro NK. Intellectual disability. MedlinePlus, U.S. National Library of Medicine, 2016. Available at: <https://medlineplus.gov/ency/article/001523.htm>.
4. Faal Moghanlo H, Hosseini F, Mikaili Manee F. Effect of Spark Motor Program on the development of gross motor skills in Down syndrome boys. *J Birjand Univers Med Sci* 2013; 20: 262-270.
5. Daily DK, Ardinger HH, Holmes GE. Identification and evaluation of mental retardation. *Am Fam Physician* 2000; 61: 1059-1067.
6. Ribeiro LMA, Jacob CMA, Pastorino AC, KimCA, Fomin AB, Castro AP. Avaliação dos fatores associados a infecções recorrentes e/ou graves em pacientes com Síndrome de Down. *J Pediatr (Rio J)* 2003; 79: 141-148.
7. ShichiriM, Yoshida Y, IshidaN, Hagihara Y, Iwahashi H, TamaiH, et al.  $\alpha$ -Tocopherol suppresses lipid peroxidation and behavioral and cognitive impairments in the Ts65Dn mouse model of Down syndrome. *Free Radic Biol Med* 2011; 15: 1801-1811.
8. Sies H. Oxidative stress, Academic Press, London; 1985, pp: 1-507.
9. Mazza M, Pomponi M, Janiri L, Bria P, Mazza S. Omega-3 fatty acids and antioxidants in neurological and psychiatric diseases: an overview. *Prog Neuropsychopharmacol Biol Psychiatry* 2007; 31: 12-26.
10. Siti HN, Kamisah Y, Kamsiah J. The role of oxidative stress, antioxidants and vascular inflammation in cardiovascular disease (a review). *Vascul Pharmacol* 2015; 71: 40-56.
11. Radi E, Formichi P, Battisti C, Federico A. Apoptosis and oxidative stress in neurodegenerative diseases. *J Alzheimers Dis* 2014; 42: S125-S152.
12. Wruck CJ, Fragoulis A, Gurzynski A, Brandenburg LO, Kan YW, Chan K, et al. Role of oxidative stress in rheumatoid arthritis:



- insights from the Nrf2-knockout mice. *Ann Rheum Dis* 2011; 70: 844-850.
13. Maiese K. New insights for oxidative stress and diabetes mellitus. *Oxid Med Cell Longev* 2015; 2015: 875961.
  14. Sosa V, Moliné T, Somoza R, Paciucci R, Kondoh H, LLeonart ME. Oxidative stress and cancer: an overview. *Ageing Res Rev* 2013; 12: 376-390.
  15. Chen Z, Zhong C. Oxidative stress in Alzheimer's disease. *Neurosci Bull* 2014; 30: 271-281.
  16. Shaw PX, Werstuck G, Chen Y. Oxidative stress and aging diseases. *Oxid Med Cell Longev* 2014; 2014: 569146.
  17. Carratelli M, Porcaro L, Ruscica M, De Simone E, Bertelli AA, Corsi MM. Reactive oxygen metabolites and prooxidant status in children with Down's syndrome. *Int J Clin Pharmacol Res* 2001; 21: 79-84.
  18. Flore P, Bricout VA, van Biesen D, Guinot M, Laporte F, Pépin JL, et al. Oxidative stress and metabolism at rest and during exercise in persons with Down syndrome. *Eur J Cardiovasc Prev Rehabil* 2008; 15: 35-42.
  19. Zambrano JC, Marquina R, Sulbarán N, Rodríguez-Malaver AJ, Reyes RA. Aerobic exercise reduced oxidative stress in saliva of persons with Down syndrome. *Res Sports Med* 2009; 17: 195-203.
  20. Barnhart RC, Connolly B. Aging and Down syndrome: implications for physical therapy. *Phys Ther* 2007; 87: 1399-1406.
  21. Takahashi M, Miyashita M, Kawanishi N, Park JH, Hayashida H, Kim HS, et al. Low-volume exercise training attenuates oxidative stress and neutrophils activation in older adults. *Eur J Appl Physiol* 2013; 113: 1117-1126.
  22. Li G, Liu JY, Zhang HX, Li Q, Zhang SW. Exercise training attenuates sympathetic activation and oxidative stress in diet-induced obesity. *Physiol Res* 2015; 64: 355-367.

23. Dodd KJ, Shields N. A systematic review of the outcomes of cardiovascular exercise programs for people with Down syndrome. *Arch Phys Med Rehabil* 2005; 86: 2051-2058.
24. Lotan M. Quality physical intervention activity for persons with Down syndrome. *ScientificWorldJournal* 2007; 7: 7-19.
25. Ulrich DA. *Test of gross motor development-2*. Austin, T.X.: Pro-Ed Press; 2000.
26. Rezvankhah Golsefidi N, Emami Hashemi SA. Effect of Selected Spark Motor Program on anxiety of children with asperger. *Physic Treat* 2015; 5: 83-88.
27. Gulesserian T, Seidl R, Hardmeier R, Cairns N, Lubec G. Superoxide dismutase SOD1, encoded on chromosome 21, but not SOD2 is overexpressed in brains of patients with Down syndrome. *J Investig Med* 2001; 49: 41-46.
28. Muchova J, Sustrova M, Garaiova I, Liptakova A, Blazicek P, Kvasnicka P, et al. Influence of age on activities of antioxidant enzymes and lipid peroxidation products in erythrocytes and neutrophils of Down syndrome patients. *Free Radic Biol Med* 2001; 31: 499-508.
29. Pallardo FV, Degan P, d'Ischia M, Kelly FJ, Zatterale A, Calzone R, et al. Multiple evidence for an early age pro-oxidant state in Down syndrome patients. *Biogerontology* 2006; 7: 211-220.
30. Sinet PM. Metabolism of oxygen derivatives in Down's syndrome. *Ann N Y Acad Sci* 1982; 396: 83-94.
31. Casado A, López-Fernández ME, Ruíz R. Lipid peroxidation in Down syndrome caused by regular trisomy 21, trisomy 21 by Robertsonian translocation and mosaic trisomy 21. *Clin Chem Lab Med* 2007; 45: 59-62.
32. Gustaw-Rothenberg K, Kowalczyk K, Stryjecka-Zimmer M. Lipids' peroxidation markers in Alzheimer's disease and vascular dementia. *Geriatr Gerontol Int* 2010; 10: 161-166.

33. Meguid NA, Eltohamy AM, Anwar M, Hashish AF, Elnahry A. Efficacy of selected treadmill training programme on oxidative stress in adolescents with Down syndrome. *East Mediterr Health J* 2014; 19: S131-S137.
34. Javier Ordonez F and Rosety-Rodriguez M. Regular exercise attenuated lipid peroxidation in adolescents with Down's syndrome. *Clin Biochem* 2007; 40: 141-2.
35. Brites F, Zago V, Verona J, Muzzio ML, Wikinski R, Schreier L. HDL capacity to inhibit LDL oxidation in well-trained triathletes. *Life Sci* 2006; 78: 3074-3081.
36. Apor P and Rádi A. Physical exercise, oxidative stress and damage. *Orv Hetil* 2006; 147: 1025-1031.

