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The effect of physical activity and dietary modification on adiponectin expression in autism spectrum disorder

Abstract

Adiponectins are considered as important health related indicator. The expression of adiponectin gene, can be affected by lifestyle including physical activity status and dietary pattern. Low physical activity level and poor dietary pattern are important health challenges among individuals with autism spectrum disorder (ASD) which may decrease their quality of life and increase the prevalence of chronic complications including obesity, metabolic impairment and cardiovascular disease. Increase the level of physical activity along with dietary pattern modification, an increase the expression of adiponectin which may have beneficial outcomes in individuals with ASD. It has been suggested that the combination of physical activity and nutritional modification, may improve adiponectin gene expression by cellular cascade activation, which may improve metabolism, insulin sensitivity especially in target tissues and glucose homeostasis. The most beneficial and recommended type of physical activity and nutritional intervention for improving adiponectin level and its circulation, is not clear yet and it seems that interventions should be recommended according to ASD individuals health status and underlying complications.

Keywords: autism, diet, physical activity, adiponectin, metabolism

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Kimia Moiniafshari,[1] Golbarg Shabani Jafarabadi,[2] Ghazal Salimian,[3] Hafez Behzadi Nezhad[4]

[1]Department of Physical Education and Sport Sciences, Faculty of Literature, Humanities and Social Sciences, Science and Research Branch, Islamic Azad University, Iran
[2]Department of Physical Education and Sport Sciences, Faculty of Literature, Humanities and Social Sciences, Central Tehran Branch, Islamic Azad University, Iran
[3]Faculty of Food Science, Science and Research Branch, Islamic Azad University, Iran
[4]Department of physical education and sport sciences, University of Tehran, Iran

Correspondence: Kimia Moiniafshari, Department of physical education and sport sciences, Faculty of Literature, Humanities and Social Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran, Email kimia.moinafsha@gmail.com

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Introduction

Adiponectin, a member of adipokine family

Adiponectins are bioactive molecules with physiologic function including energy balance, lipoprotein metabolism, insulin sensitivity, appetite, inflammatory responses and vascular homeostasis.[1] These may include pre-inflammatory cytokines such as fatty acid binding proteins which attach to the adipocyte and unti-inflammatory adipokines including adiponectin. In obesity and diabetes type 2, insulin resistance may impair endocrine function in adipose tissue which may lead to increase in reactive oxygen species (ROS). Studies have suggested that the maintenance of adiponectins level or their receptors gene expression can improve insulin sensitivity and cardiovascular function. This may become more important as according to world health organization (WHO), the incidence of obesity has gained a growing trend which can be considered as global health challenge.[2]

Adiponectin, as Acrp30, AidpoQ, GBP-28 and apM1 have also been recognized which are adipocyte like cell riched with protein. Adipocytes may produce secrete several adiponectin including:

- Trimers with high molecular weight
- Trimers with medium molecular weight
- Trimers with low molecular weight

Adiponectins increase the secretion of anti-inflammatory cytokine called IL-10 from macrophage and in macrophage M1, the gene expression of TNF-α, IL-6 and IL-2. In macrophage M2, adiponectin may increase the gene expression of IL-10 without affecting the receptor levels.[3–5]

Some facts about adiponectins

- They have adverse relation with body mass index and insulin resistance,
- May decrease the production of glucose from the liver
- Increase glucose uptake and fatty acid oxidation in skeletal muscle
- Decrease inflammation and vascular obstruction.[6]

Adiponectin receptors: AdipoR1, adipoR2, T-cadherin

AdipoR1 and AdipoR2, seem to regulate metabolism and insulin sensitivity in the target tissue and is important in pathophysiology of insulin resistance in diabetes. Each of these receptors have domains which pass the cell membrane 7 times and belong to PAQR family. The morphology of these receptors seems to be opposite of G-coupled proteins and the amine domains are located in the cytoplasm, while the carboxylic domains are located in extracellular area. Further than AdipoR1 and AdipoR2, T-cadherin is also considered as adiponectin receptor with high molecular weight, not trimer or globular. The lower cell structural domain, has made T-cadherin to be a connective protein for adiponectins which plays an important role in adiponectins signaling. It has been suggested that the circulation of adiponectin, especially high molecular weight, may increase in the absence of T-cadherin.

The activation of insulin and adiponectins by the ligands, will activate the cellular cascade and signaling pathways. In most of the circumstances, insulin metabolic effects, will be facilized PI3K/AKT which lead to biological responses and as a result, protein synthesis, lipid synthesis, glucose uptake and glycogenosis will increase. In

adiponectin, APP1 and the attachment to Adipo1 and Adipo2 may activate PPAR-α, AMPK and p38MAPK. As a result, it may lead to increase in fatty acid oxidation, energy expenditure, decrease in inflammation and improve insulin function.[7] When adiponectins are secreted from adipose tissue, their attachment to their receptors in the insulin sensitive tissues such as liver, skeletal muscle and adipose tissue, anti-diabetic outcomes may happen.[8]

Adiponectin and obesity- the relation with ASD

Adipose tissue is considered as an endocrine tissue which produce and secrete several factors including adiponectin which is involved in energy metabolism and can bring anti-inflammatory outcomes. The increase in the level of adiponectins, can reduce the risk of chronic diseases especially in obese individuals. Although adiponectins are secreted from adipose tissue, the level is lower in obese people. Moreover, it has been suggested that the level of adiponectins have inverse correlation with neurodevelopmental disorders including ASD incidence. As the higher level of adiponectin may bring beneficial effect on health, lifestyle modification seems to be considered as beneficial strategy. As the incidence of obesity in individuals with autism, is in contrast, life style modification, including increasing the level of physical activity, dietary pattern modification and weight management, seem to improve the level of adiponectins.[9–11]

Physical activity and adiponectin

Physical activity and active lifestyle can decrease the risk of several chronic disease and decrease the risk of inflammation. It has been suggested that increase in the level of physical activity along with weight management, is related with the level of adiponectin and circulating leptin.[12,13] The suggested mechanism for the effect of physical activity on the regulation of adiponectin and metabolic status, is that physical activity may increase the gene expression of AdipoR1 and AdipoR2 by the in adipose tissue and skeletal muscle which may lead to inflammation management.[14]

Dietary management and adiponectin

Several studies have suggested that dietary pattern modification may bring beneficial effect for health, not only in individuals with chronic health complication, but also in individuals diagnosed with ASD. Nutritional problems including restrictive dietary pattern, food selectivity, food intolerance and food allergies, food refusal and poor dietary pattern, in among common nutritional challenges in autism population which may affect metabolic condition, weight and general health. Studies regarding weight status and whether the prevalence of obesity is higher among individual with autism, or not, indicated in contrast results. Although it has been suggested that calorie restriction or dietary pattern improvement such as recruiting dietary pattern similar to Mediterranean can be an intervention for weight management in obese autistic individuals which may lead to adiponectin level modification.[15–18]

Discussion and conclusion

Level of circulating adiponectins can be considered as health predictor which may affect the incidence of chronic health complications. Lower level of adiponectins, have inverse correlation with the incidence of ASD which can be modified by lifestyle-related interventions including physical activity and dietary pattern improvement. The importance of adiponectins in ASD can be manifested in metabolic regulation, systemic inflammation and oxidative stress, which are considered as important health challenges among individuals with ASD. Overweight and obesity can be also correlated with adiponectins level in an inverse manner. Due to the higher prevalence of health complications, which may increase the risk of chronic disease in ASD and their possible relation with adiponectins, physical activity and dietary pattern modification and improving the level of adiponectins in individuals with ASD, may decrease the risk of metabolic impairment, systemic inflammation and oxidative stress. The lifestyle interventions including physical activity and dietary modifications, should be recruited specifically according to individual's history.

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Conflicts of interest

The author declares that there is no conflicts of interest.

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