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**SÍNDROME METABÓLICA INDUZIDA PELA FRUTOSE EM ADOLESCENTES:
UMA REVISÃO**

**SÍNDROME METABÓLICA INDUCIDO POR FRUCTOSA EN ADOLESCENTES:
UNA REVISIÓN**

**METABOLIC SYNDROME INDUCED BY FRUCTOSE IN ADOLESCENCE: A
REVIEW**

Apresentação: Comunicação Oral

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Resumo

A síndrome metabólica (MS) é caracterizada como um conjunto de distúrbios metabólicos, como obesidade abdominal, intolerância à glicose, hiperinsulinemia, dislipidemia e hipertensão. Os fatores que contribuem para o desenvolvimento da MS são o sedentarismo, o alto consumo de dietas ricas em gorduras e carboidratos, como a frutose. A literatura mostra que o consumo de frutose por adolescentes está aumentando. O presente estudo consiste em uma revisão de literatura que tem como objetivo mostrar a MS precoce encontrada em adolescentes que consumiram dieta rica em frutose; explorando mau funcionamento em diferentes tecidos. Os resultados encontrados nesse artigo mostraram que a principal causa de MS em adolescentes é o consumo de sacarose e xarope de milho com alto teor de frutose (HFCS), que produz glicose e frutose em altas doses (55% de frutose e 42% de glicose). O fígado é o principal órgão do metabolismo da frutose. Nesse órgão, a frutose induz a produção de precursores lipogênicos, como acetil-coA, levando a altos triglicerídeos e síntese de gordura. Esse processo causa deposição de gordura no fígado, desenvolvendo esteatose

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hepática e também resistência central e periférica à insulina em adultos e adolescentes. No intestino, a frutose interage com a microbiota intestinal, alterando-a. No pâncreas, a dieta rica em frutose mostrou um aumento nos marcadores de estresse no retículo endoplasmático, no nível de mRNAs e enzimas. A revisão atual destacou que mais cuidados com o adolescente, incluindo a diminuição profunda do conteúdo de frutose em alimentos e bebidas podem ter impacto positivo na saúde do adolescente e adulto.

Palavras-Chave: Frutose, adolescência, síndrome, obesidade.

Resumen

El síndrome metabólico (EM) se caracteriza por un conjunto de trastornos metabólicos como la obesidad abdominal, intolerancia a la glucosa, hiperinsulinemia, dislipidemia e hipertensión. Los factores que contribuyen al desarrollo de la EM son el estilo de vida sedentario, el alto consumo de dietas altas en grasas y carbohidratos como la fructosa. La literatura muestra que el consumo de fructosa en adolescentes está aumentando. El presente estudio consiste en una revisión de la literatura que tiene como objetivo mostrar la EM temprana encontrada en adolescentes que consumieron una dieta alta en fructosa; Explotación de mal funcionamiento en diferentes tejidos. Los resultados encontrados en este documento mostraron que la causa principal de DM en adolescentes es el consumo de sacarosa y jarabe de maíz con alto contenido de fructosa (JMAF), que produce altas dosis de glucosa y fructosa (55% de fructosa y 42% de glucosa).) El hígado es el órgano principal del metabolismo de la fructosa. En este órgano, la fructosa induce la producción de precursores lipogénicos, como el acetil-coA, lo que conduce a altos niveles de triglicéridos y síntesis de grasas. Este proceso provoca un depósito de grasa en el hígado, desarrollo de esteatosis hepática y también resistencia a la insulina central y periférica en adultos y adolescentes. En el intestino, la fructosa interactúa con la microbiota intestinal, alterándola. En el páncreas, la dieta alta en fructosa mostró un aumento en los marcadores de estrés en el retículo endoplásmico, en el nivel de ARNm y enzimas. La revisión actual destacó que una mayor atención a los adolescentes, incluida una disminución profunda en el contenido de fructosa en alimentos y bebidas, puede tener un impacto positivo en la salud de los adolescentes y adultos.

Palabras Clave: Fructosa, adolescencia, síndrome, obesidad.

Abstract

Metabolic syndrome (MS) is characterized as a set of metabolic disorders such as abdominal obesity, glucose intolerance, hyperinsulinemia, dyslipidemia and hypertension. Factors that contribute to the development of MS are sedentary lifestyle, high consumption of diets high in fat and carbohydrates such as fructose. The literature shows that fructose consumption by adolescents is increasing. The present study consists of a literature review that aims to show the early MS found in adolescents who consumed a high fructose diet; exploiting malfunction in different tissues. The results found in this paper showed that the main cause of DM in adolescents is the consumption of high fructose corn syrup (HFCS), which produces high-dose glucose and fructose (55% fructose and 42% glucose).). The liver is the main organ of fructose metabolism. In this organ, fructose induces the production of lipogenic precursors, such as acetyl-coA, leading to high triglycerides and fat synthesis. This process causes fat deposition in the liver, developing hepatic steatosis and also central and peripheral insulin resistance in adults and adolescents. In the gut, fructose interacts with the gut microbiota,

altering it. In the pancreas, the high fructose diet showed an increase in stress markers in the endoplasmic reticulum, in the level of mRNAs and enzymes. The current review highlighted that more adolescent care, including a profound decrease in fructose content in food and beverages, can have a positive impact on adolescent and adult health.

Keywords: Fructose, adolescence, syndrome, obesity.

Introduction

Metabolic Syndrome (MetS) is characterized as a set of metabolic disorders such as abdominal obesity, glucose intolerance, hyperinsulinemia, dyslipidemia and hypertension (NACAGAWA *et al.*, 2006). It is estimated 20 to 25% of the adult population is diagnosed with this syndrome. The clinical characteristics of MetS depend on lifestyle, environmental factor, gender, ethnicity, and others (GRUNDY *et al.*, 2005; KWON *et al.*, 2017). Many studies have suggested a combination of abdominal adipose tissue and MetS (OKOSUN *et al.*, 2000). The factors that contribute to development of metabolic syndrome are sedentary lifestyle, high consumption of diets rich in fats and carbohydrates, such as fructose (JEAN-LUC GRADIDGE *et al.*, 2016; KWON *et al.*, 2017).

Fructose is a simple monosaccharide widely used as a sweetener in foods and beverages. Its form of consumption is as a free monosaccharide or as part of the disaccharide sucrose (JANSSENS *et al.*, 2017). Fructose metabolism occurs mainly in liver, which increased production of lipid precursors, inducing a large production of triglycerides, total cholesterol and fractions, leading to a central and peripheral insulin resistance and hepatic steatosis. This evidence was found in adult rodents (CASTRO *et al.*, 2015; BEZERRA *et al.*, 2000), however, same metabolic pathway was observed in adolescent rats (LEGEZA *et al.*, 2017). In humans, fructose intake was associated with high fasting glucose, total triglycerides and high levels of apolipoproteins in adolescents (EGLI *et al.*, 2013) and increased triglycerides in adult men (BANTLE *et al.*, 2000) (Table2).

High ingestion of fructose, especially in the form of sweetened beverages, has been identified as a serious risk factor for the development of metabolic diseases in humans. Studies using experimental adolescent rats have shown that chronic consumption of fructose-rich diet induces systemic metabolic disorders that mimic aspects of the metabolic syndrome in humans, including hypertension, hypertriglyceridemia and hyperinsulinemia (SADOWSKA *et al.*, 2017; WHITE *et al.*, 2008).

Diets high in fructose are directly related to excess calorie consumption. The high

palatability favors the high consumption of sweetened foods and beverages mainly with HFCS (High Fructose Corn Syrup). It is a bad economic reasons, HFCS is a constituent of a industrial food and beverage why HFCS is really cheap and to have high economical profits. The capitalists don't care about health population (FERNÁNDEZ-NOVELL *et al.*, 2014; HARRELL *et al.*, 2015).

The literature has shown the fructose consumption by adolescents is increasing. The main cause is the consumption of sucrose and HFCS wich provide high doses of glucose and fructose (55% fructose and 42% glucose) (WHITTON *et al.*, 2011; WHITE *et al.* 2008, CAMPOS *et al.*, 2016). It was suggested that fructose leads to long-term dysregulation in HPA (Hypothalamic-Pituitary- Adrenal Axis), compromising adult life health (HARREL *et al.*, 2015).

Adolescence is a transition phase between childhood and adulthood, marked by brain changes responsible specifically for behavior, mainly sexual ones. These alterations are modulated by hormones characteristic of this phase, such as testosterone to male individuals (WIERENGA *et al.*, 2018). According to the literature, hyperinsulinemia and obesity are related to a decline in testicular function and consequently changes in testosterone levels (HART *et al.*, 2018). In a study, high fructose diet caused testicular degeneration and low testicular concentration of testosterone in adolescent rats (YILDIRIM *et al.*, 2018). Meydanli *et al.*, 2017 found destruction of the germinal epithelium, a decrease in seminiferous tubules diameters and an increase in apoptotic index in adult rats. Lower testicular weight was also found in periadolescet rats (SHIBATA & FUKUWATARI, 2013).

High ingestion of fructose, especially in the form of sweetened beverages, has been identified as a serious risk factor for the development of metabolic diseases in adults, as well as in adolescents. Sadowska *et al.*, 2017, in their study showed that the effects of beverages sweetened with HFCS were important in significantly reducing plasma HDL (High Density Lipoproteins) levels. The currently study consists in a literature review that aims to show that early metabolic syndrome found in adolescent who consumed high rich fructose diet; exploring malfunctions in different tissues.

Theoretical foundation

The consumption of fructose is currently a global problem and is strongly associated with the metabolic syndrome. Adolescents are the largest consumers of this sugar, consuming

the equivalent of 78.2 g / day of fructose in the USA. In this country, a daily caloric intake of 15% is estimated, only from fructose (VOS *et al.*, 2008). The high consumption of this sugar is related to the high rates of diabetes mellitus among the youngest (HARREL *et al.*, 2015, de OLIVEIRA *et al.*, 2013). Fructose-sweetened foods are known to provide high palatability and are cheaper for the food industry. Its wide consumption is associated with the high consumption of fast foods as fast and tasty food alternative. Hypercaloric food intake is also associated with a reduction in healthy foods consumption. Since adolescence is a sensitive period of development of HPA axis, high fructose consumption can lead to development of metabolic alterations, which constitute the metabolic syndrome, such as diabetes mellitus, dyslipidemia, obesity, impaired glucose tolerance, among others (BASCIANO *et al.* al.,2005). The lifestyle of many people in the world today favors the high consumption of unhealthy foods, such as those high in fructose. Added to this nutrient-poor diet is a sedentary lifestyle where children stay in front of the TV, computer or video game for most of the day (HARREL *et al.*, 2015).

Several studies have shown that fructose has a broad spectrum of action in the human body, from the moment it is ingested, interfering in the metabolism of many organs such as liver (main metabolizer), pancreas, adipose tissue, intestine, brain, among others, causing its undesirable effects on the body, which characterize MetS (BASCIANO *et al.*, 2005; FELICE *et al.*, 2017). The table 2 shows a selection of published articles where the authors treated adolescent rats with varying concentrations of fructose in water and observed a range of effects on various organs and tissues.

Methodology

This work is a bibliographic review research carried out on the following research platforms: Pubmed, Medline and Lilacs. The articles selected were those published between 2000 and 2018 and that worked with animals in late childhood, adolescence and early adulthood. The keywords used were 'fructose' and 'adolescence'.

In total, 129 articles were found using the keywords. However, after analyzing each of these articles, it was noticed that most did not meet the criteria of this study, with only 42 articles being used (Table 1).

Table 1. Results of articles found and used in bibliographic research.

BASE DE DADOS	FOUNDED	ARTIGOS USED
PUBMED	105	27
MEDLINE	20	13
LILACS	1	1
TOTAL	129	42

Results and discussion

According to literature, the high fructose consumption causes changes in many organs and tissues. Table 2 lists the articles selected for this review, with lineage of used animals, as well as the age, the concentration of fructose, treatment period and its effects on the organism.

In selected studies, the animals treatment age corresponds to adolescence and early adulthood. These results can be extrapolated to humans since the metabolism of rats reliably mimics human metabolism.

Due its wide spectrum of action in animal and human organism, it is necessary to study separately the performance of fructose in each organ and tissue.

Table 2. Experimental studies showing different consequences of fructose treatment from periadolescence to early adulthood, varying the concentrations of fructose, treatment period and animal strains.

AUTHOR	LINEAGE	AGE (or body weight)	FRUCTO SE CONCE NTRATI ON	TREATMEN T TIME	TREATMENT CONSEQUENCES
Orlandi et al., (2015)	Wistar	7 weeks	10%	5 weeks	Plasma: Hyperglycemia, increased triglycerides, total cholesterol and fractions. Adipose Tissue: Increased retroperitoneal and periepididimal fats.
Vasiljevic et al., (2014)	Wistar	21 days	60%	9 weeks	Liver: Increased levels of 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD1), increased pro-inflammatory status, through activation of NF κ B and increased TNF. Plasma: Hypertriglyceridemia Adipose tissue: Increased visceral fat.
Svendsen et al., (2017)	Sprague-Dawley	120-140 g	70%	12 weeks	Liver: Rapid progression to steatosis, followed by inflammation, hepatic ballooning (hepatocyte death), and fibrosis.

Román et al., (2014)	Wistar	180-200g	10%	3 weeks	<p>Plasma: Increased levels of triacylglycerol, insulin and lipid peroxidation, associated with a state of insulin resistance and impaired glucose tolerance.</p> <p>Pancreas: Lower number of islets/area and lower density of beta cell.</p>
Maiztegui et al., (2009)	Wistar	180-200g	10%	3 weeks	<p>Plasma: Impaired glucose tolerance, hypertriglyceridemia, hyperinsulinemia with increased HOMAindex.</p> <p>Pancreas: A 33% decrease in beta cell mass and a 44% increase in apoptotic cells percentage.</p>
Koo et al., (2008)	Sprague-Dawley	5 weeks	63%	2 weeks	<p>Liver: Increased hepatic glycogen, indicating a rapid fructose conversion to hepatic glycogen, through gluconeogenesis, induction of genes that favor new lipogenesis and increased triglycerides levels.</p>
Jiménez-Maldonado et al., (2017)	Sprague-Dawley	8 weeks	8 e 15%	7 days	<p>Brain: Decreased levels of neural proteins (NeuN, Myelin Basic Protein and Axonal Growth Associated Protein 43), Decreased levels of Cytochrome C oxidase (indicative of mitochondrial dysfunction) and increased levels of GLUT 5 fructose transporter in hippocampus.</p>
Felice et al., (2017)	Wistar	8 weeks	10%	2 weeks	<p>Plasma: Hyperglycemia, hyperinsulinemia with increase in HOMA index, hypertriglyceridemia.</p> <p>Bone tissue: Decreased expression</p>

Fructose Effects On Liver

Liver is the main organ of fructose metabolism. Unlike glucose is captured by GLUT2 transporter, fructose absorption is carried out by GLUT5 transporter, whose expression is positively regulated in response to fructose availability. Glucose metabolism is regulated by phosphofructokinase I (PFK I), an important glycolysis regulator. However, fructose enters the glycolytic pathway at the trioses level, bypassing the regulation by PFK I. This difference alters the metabolism of carbohydrates, as gluconeogenesis, increasing glycogen stores. Fructose also induces lipogenic precursors production, such as acetyl-coA, leading to a high triglycerides and fats production. This process causes fat deposition in liver, developing hepatic steatosis and also central and peripheral insulin resistance. These changes induce alterations in expressed hepatic genes involved in expression of enzymes involved in

lipogenic, glycogenic and gluconeogenic activities (Basciano et al., 2005).

Vasiljevic et al., 2014 in your study with adolescent rats suggests the lipids increase in liver, caused by the high fructose intake, occurs by increased production and, consequently, increased glucocorticoid levels. Although MetS isn't characterized by increases in circulating glucocorticoid levels, there are specific tissue changes in glucocorticoid pre-receptor in cellular membrane. In this same work high levels of 11-hydroxysteroid dehydrogenase type 1 protein (11bHSD1) were found in liver microsomes, although gene expression wasn't affected.

Energy production via fructose increases citrate concentration in mitochondria. Citrate is a potent phosphofructokinase blocker. Phosphofructokinase is a glycolysis allosteric regulator. Therefore, less glucose will be directed to energy production and fructose will be metabolized into fats. This process contributes to hepatic resistance to insulin action. Resistance to insulin action impairs glucose uptake by skeletal muscle and adipose tissue and induces neoglycogenesis in the liver (Botezelli et al., 2012).

Fructose Effects On Intestine

Fructose enters the intestinal cell in its apical portion, preferably by the GLUT-5 transporter, which is not regulated in this process and much of the fructose absorbed by enterocytes is directed into the circulation through enterocytes basolateral membrane via GLUT-2 transporter. Fructose, which is not immediately absorbed, interacts with the intestinal microbiota. Noble et al. (2016) argue that diet quality interferes with adolescent gut microbiota. Different fructose concentrations concomitant with glucose were tested in rat drink and he found altered amounts of Prevotella, Lachnospiraceae incertae sedis, Bacteroides, Alistipes, Lactobacillus, Clostridium sensu, Bifidobacteriaceae and Parasutterella. A study using adult rats (DiLucia 2015) showed an increase in genera Sutterella, Coprococcus and Ruminococcus and decrease in the bacteria of the genus Firmicutes. Changes in the intestinal microbiota caused by fructose affect the adolescent metabolism, with metabolic disorders development.

Literature has shown that intestinal cells contain the highest amount of enzymes necessary for the metabolism of fructose, such as lipogenic and gluconeogenic enzymes (Campos 2016). There are few studies that confirm if fructose is mainly delivered to liver, thus leaving the supposition that enterocyte perhaps has a very significant contribution in

fructose metabolism.

Fructose is a potent precursor to new lipogenesis, since this monosaccharide only requires a phosphorylation step via fructose kinase to form fructose-1-phosphate prior to conversion to the 3- carbon precursors (glyceraldehyde and dihydroxyacetone phosphate). Glucose, in addition to being controlled by insulin, is also regulated by ATP and citrate, which inhibit phosphofructokinase (Ibrahim et al., 2017).

Increased trioses phosphate production may lead to production of methylglyoxal (MG), which is a precursor to formation of advanced glycation products (AGEs). Methylglyoxal is known in literature as causing damage to proteins through glycation (Gugliuti et al., 2017). Studies using adolescent rats that ingested only fructose found greater production of AGEs in fructose-treated rats, compared with glucose (Mastrocola et al., 2013).

ATP depletion promotes uric acid formation. An accelerated fructose metabolism into fructose-1-phosphate, through fructose kinase, consumes ATP forming ADP. This ADP, if not converted again to ATP through Adenylate-Cyclase, will be transformed into AMP, which will be converted to uric acid (Jhonson et al., 2013). Elevated levels of uric acid have been associated with a number of pathological conditions in adolescent rats such as insulin resistance, obesity, type II diabetes and chronic kidney disease and have been proposed as a risk for myocardial infarction and neurological disorders such as stroke (Legeza et al. al.,2017).

Fructose metabolism is known in literature for destroying many ATP molecules. This intense destruction causes oxidative stress and inflammatory response by disrupting organs and tissues functioning, resulting in an abnormal insulin production, inflammatory cytokines, adiponectin, leptin and and toxins, further aggravating the metabolic syndrome (Zhang et al., 2017).

Fructose Effects on Non-Insulin-Dependent Tissues

In high levels of glucose conditions (hyperglycemia), non-insulin-dependent tissues such as nerve tissue, lenses and erythrocytes can activate the polyol pathway and induce endogenous fructose production. This new fructose produced can cross the membrane passively or be transported, wich cause increase of fructose blood circulation adding to exogenous fructose intake. It was found that increased polyol pathway causes diabetic and vascular complications in adolescent rats (Gugliuti et al.,2017).

Fructose Effects On Adipose Tissue

According to Legeza et al., (2017) there is an interrelation between fructose concentration in adolescent body and glucocorticoids production in adipose tissue. Glucocorticoid production plays a key role in adipocytes differentiation and proliferation. The literature shows the metabolism of fructose in adipocyte results in generation of precursors of fatty acid synthesis, expression of GLUT-5 transporters in adipocyte plasma membrane and greater expression of glucocorticoids production enzyme responsible, 11-hydroxysteroid dehydrogenase type 1 (11-HSD1) (Vasiljevic' et al.,(2014).

Orlandi et al., 2015 found retroperitoneal, periepididimal, hypertriglyceridemia and HDL increased after a treatment with 10% fructose for 5 weeks (Table 2). It can be explained by the fructose mechanism that form forming fructose-1-phosphate and is rapidly cleaved into tri- phosphate, rising triglyceride levels.

Studies that tested adult human consumption of fructose and glucose separately in water showed the fructose consumption increased new lipogenesis, promoting a large lipid deposition in visceral adipose tissue, dyslipidemia, altered lipoprotein remodeling, decreased insulin sensitivity in overweight or obese individuals (Stanhope et al., 2009). Another theory proposes that fructose contributes to development of obesity by stimulating the insulin-independent Steroid Receptor 1-c Binding Protein Receptor (SREBP-1c), which activates genes involved in new lipogenesis, generating fatty acids for production of triglycerides in liver. However, this increase in lipids on liver is associated with an increase in synthesis and secretion of very low density lipoprotein VLDL. This systemic elevation of fatty acids and VLDL leads to an increase in lipid uptake by the peripheral organs, such as adipose tissue and skeletal muscle, contributing to a systemic insulin resistance. In addition, fructose is also linked to leptin resistance, worsening obesity and insulin resistance (Shapiro et al.,2008).

Studies in adolescents have shown that excessive fructose consumption exceeds the liver capacity to metabolize it and a small fraction remains in circulation, being captured by peripheral tissues. Although adipocytes have GLUT-5 receptor and are perfectly capable to capturing fructose, the mechanism of GLUT-5 hasn't been fully elucidated, although GLUT-5 is indicated in some studies as a regulator of adipocyte differentiation (Du et al., 2012; Legeza et al., 2017). In adipocyte, fructose is converted to fructose-6-phosphate by hexokinase enzyme, and converted to glucose-6-phosphate, which can promote

glucocorticoids production by stimulating 11-HSD1. Varma et al., Found that increasing fructose concentration enhances the conversion of pyruvate to acetyl-CoA via pyruvate dehydrogenase reaction, leading to glutamate. The pyruvate dehydrogenase flux enters in TCA cycle and result in an expanded acetyl-coA/citrate cycle in the synthesis of fatty acids and release of free palmitate. Therefore, the presence of fructose in adipocytes drives this alternative pathway, resulting in increased energy and CO₂ production, which can be used in induced fructose lipogenesis and fat storage in adipocytes.

Fructose Effects On Pancreas

Little is known about the specific action of fructose on insulin resistance and pancreatic beta cell function. Some articles have already linked a high consumption of fructose-rich diet to impaired glucose tolerance and insulin resistance, regardless of changes in body weight. Among several mechanisms studied to understand insulin resistance and beta cell functioning, oriented studies of the endoplasmic reticulum stress are an important molecular mechanism behind such pathologies.

Young adult rats undergoing a high fructose diet showed an increase in markers of stress in endoplasmic reticulum both in pancreas and in liver at the level of mRNAs and enzymes. The study showed a decrease in the mRNAs of the INSIG1 (regulates cholesterol metabolism, lipogenesis and glucose homeostasis) and PDX1 (transcription factor necessary for pancreatic development, including beta cell maturation) proteins, and increased mRNA levels of the regulatory proteins binding to sterol (SREBP1c), a regulator of cholesterol synthesis to fatty acids. The convergence of chronic ER stress for apoptosis in the pancreas/liver was also indicated by increased CHOP mRNA levels and increased JNK and Caspase-3 activity (Balakumar et al., 2016). Other work has shown that fructose-induced beta cell dysfunctions cause deregulation of leptin signaling and activation of protein kinase B in adolescent rat islets (Li et al., 2013). The Akt/FoxO1 pathway binds leptin signaling to Pdx1 uptake, related to the function and growth of pancreatic β cells. Akt/FoxO1 and

INS-1 β -cells activation contributes to increased beta cell mass and insulin secretion. Under physiological conditions, leptin suppresses insulin secretion. Leptin resistance in the beta cell is related to hyperinsulinemia, beta cell failure, and glucose intolerance in obese rats (Morioka et al., 2007). The absence of leptin increases the phosphorylation of Akt and FoxO1, resulting in an increase in size and mass of the beta cell.

Pancreatic beta-cell failure in response to increased insulin demand will result in impaired glucose tolerance and type 2 diabetes development. According to Maiztegui et al., adolescent rats treated with fructose presented reduced number of islets, endocrine total area, beta cell area, individual islet area and number of beta-cells/islet with a concomitant increase of 44% of apoptotic cells. This apoptosis is related to stress mechanism of endoplasmic reticulum and glycolipotoxicity. Román et al. showed that adolescent rats fructose treated had a decrease in number of islets (50.3%) and beta-cell (36.8%), with an increase in plasma oxidative stress levels (elevated plasma Thiobarbituric Acid Reactive Substances-TBARS levels). These islets showed high levels of O_2 , and high NADPH oxidase activity, demonstrating the presence of local oxidative stress, which depends in part on the high enzymes activity in this complex.

Fructose Effects On Brain

Jimenez-Maldonado et al. (2011) showed one week of fructose supplementation in adolescent rats was able to alter some brain functions related to hippocampal plasticity, such as reduction of NeuN (Neuronal Nuclear Protein), Myelin Basic Protein, and Protein 43 associated with axonal growth concomitant with a reduction in hippocampal weight (table 2). There was also a reduction in the coactivator of gamma-receptor peroxisome-1 proliferator and cytochrome c oxidase II subunit as indicative of mitochondrial dysfunction and elevation of GLUT5 levels, indicating that fructose treatment is able to modulate positively the expression of its transporter. Agrawal et al. (2016) found that fructose consumption by young adult rats disrupts energy balance of hippocampus, decreasing the mitochondria functional bioenergetics (oxygen consumption rate and cytochrome C oxidase) and a worsening in effects of traumatic brain injury in molecular systems involved in cellular energy (sirtuin 1, gamma-1 peroxisome proliferator-activated receptor co-activator) and synaptic plasticity.

Concluding remarks

The high fructose consumption among adolescents is related to development of metabolic syndrome. This spectrum of changes is widespread and affects homeostasis of various organs and tissues, such as liver, adipose tissue, intestine, pancreas, brain, among others. The current review highlighted that food and beverages enriched by high fructose put in high risk the teenage health and open possibilities to also compromise their health

adulthood. However, more care with adolescent, including deep decrease of fructose content in food and beverage to have impact in adolescent and adult health.

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