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CHANGES IN Δ-DESATURATION AND FATTY ACID COMPOSITION IN RATS CHRONICALLY TREATED WITH SUCROSE IN THE DRINKING WATER

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Summary

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We studied the influence of long-term treatment with sucrose in drinking water on the lipogenesis. Male Wistar rats were supplemented with 30% sucrose (w/v) in water (Sucrose group) or with plain water (Control group). Fatty acid profile was characterised by increase in saturated and monounsaturated fatty acids and decrease in n6 polyunsaturated fatty acids. The most significant changes were observed for 16:1n7 (increase) and 18:2n6 and 18:3n3 (decrease) fatty acids and for the hepatic tissue in general. The expression of SREBP1c was significantly increased in all organs indicating increased lipogenesis. The expression of the Δ9D was strongly increased in the hepatic tissue without difference in other tissues. The expression of the Δ5D was decreased in the liver and kidney and increased in the brain tissue. In conclusion, results shows that chronic sucrose intake significantly changes fatty acid profile with increase in saturated and monounsaturated fatty acids and decrease in n6 fatty acids, but these changes are partially organ-specific.

Key words: desaturation, fatty acids, lipogenesis, sucrose

INTRODUCTION

The increase of simple sugar consumption via sweetened beverages is nowadays connected to metabolic syndrome and diabetes type 2 (Malik *et al.*, 2010). In these diseases, as well as in many other metabolic diseases, lipogenesis and consequent fatty acid concentrations are changed in different organs. The fatty acids present in tissues originates from food or they are synthesised *de novo* are further metabolised into fatty acids with more carbon atoms and/or more unsaturated fatty acids. These processes are highly regulated by different transcriptional factors, metabolites, hormones, sex and dietary factors (Jump *et al.*, 2013)

The purpose of this study was to investigate lipid metabolism in the model of metabolic syndrome based on the chronic intake of sucrose via the drinking water (SDW).

MATERIAL AND METHODS

Two months old male Wistar rats were divided into two experimental groups: control rats (plain water, Control, n=6) and rats given 30% sucrose in their drinking water for 20 weeks (Sucrose, n=6). At the end of the experiment (20th week), the organs were harvested and samples analysed. The isolation of total RNA, quantitative real-time PCR and the calculation of gene expression was performed as described previously (Mašek *et al.*, 2017).

Total lipids (TL) were extracted using chloroform/methanol (2:1, v/v) in the presence of the antioxidant butylated hydroxytoluene (Folch *et al.*, 1957). Total phospholipids (PL) were isolated by solid-phase extraction on a 500 mg aminopropyl bonded silica cartridge. Fatty acids from TL and PL were transmethylated using 2M KOH in methanol. The analysis of fatty acid composition was performed as described previously (Starcevic *et al.*, 2015).

Data were analysed using the GraphPad Prism program and MetaboAnalyst 3.0 (http://www.metaboanalyst.ca/MetaboAnalyst/). Data were tested by the t-test. Volcano plots were constructed using GraphPad Prism and sPLS-DA using MetaboAnalyst 3.0.

RESULTS

The proportions of fatty acids in the TL of the liver, brain, testis and kidney tissue are indicated on Fig. 1A-F. Sucrose treatment increased the proportion of 16:0 in the liver and kidney and summed 16:1n7 and 18:1n7 in all tissues. The content of oleic acid was increased in the liver, testis and kidney. The content of 18:2n6 and 20:3n6 decreased in all tissues while arachidonic acid decreased in the liver, brain and kidney. The expression of SREBP1c increased in all organs (it was not measured in testis). The expression of Δ9D extremelly increased in the hepatic tissue while the Δ5D expression decreased in the liver and kidney and increased in the brain.

DISCUSSION

Nowadays, the relation between the consumption of sugar and particularly sugar-sweetened beverages and the development of obesity gained significant interest (Ludwig *et al.*, 2001; Bray *et al.*, 2004). Therefore, the animal models that include treatment with different sugars via the drinking water could be very useful models in the investigation of the metabolic syndrome.

Our trial showed increase in the expression of SREBP1c in all tested organs after the chronic treatment with the sucrose in the drinking water which points to disturbance in kidney lipogenesis. SREBP1c is a transcription factor which responds to insulin and is essential for the lipogenesis and fatty acid homeostasis (Ferré & Foufelle, 2007). Fatty acid profile of rat tissues in our trial was characterised by increased palmitic acid content indicating increased lipogenesis. As expected, the expression of Δ9-desaturase significantly increased in the liver tissue and consequently the content of monounsaturated fatty acids also increased in the sucrose treated rats. In contrast, the content of C18 fatty acids and n6 fatty acids significantly decreased. Linoleic and linolenic acids must be supplied by the food and therefore, their decrease in metabolic syndrome is explained by partitioning into oxidation (El Hafidi *et al.*, 2001). In different models of metabolic syndrome the content of arachidonic acid (20:4n6) is usually decreased in hepatic tissue and

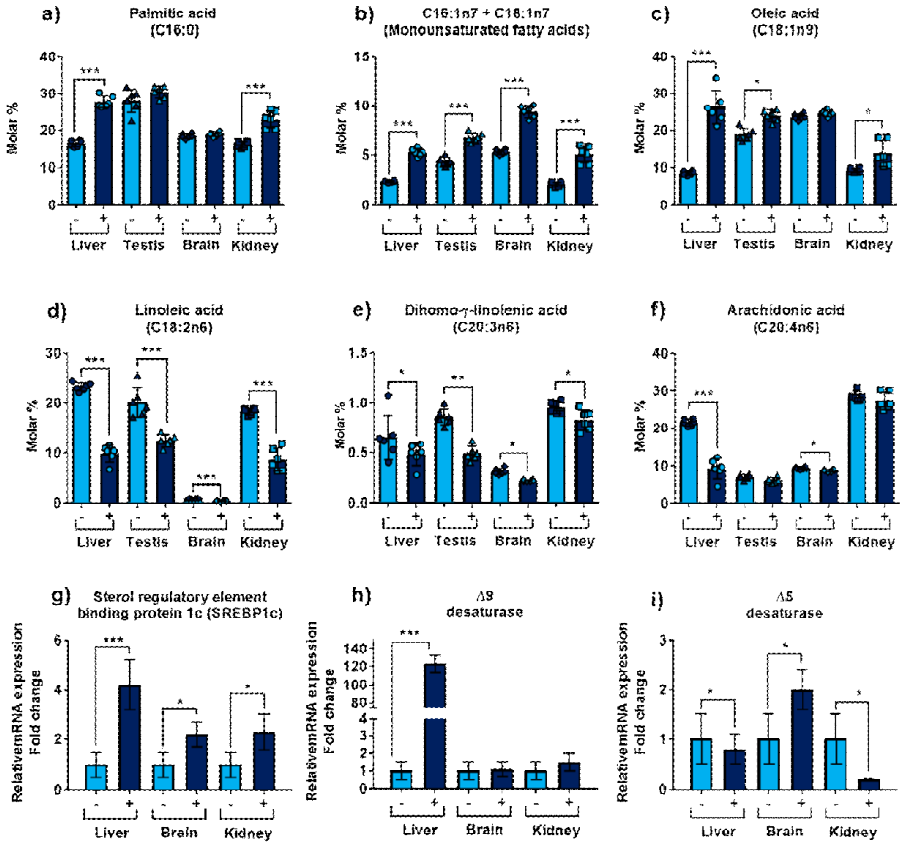

Fig. 1. The influence of sucrose treatment on the fatty acid profile of liver, brain, testis and kidney. Gene expression of SREBP1c (1g), Δ9D (1h) and Δ9D (1i) determined by RTqPCR.

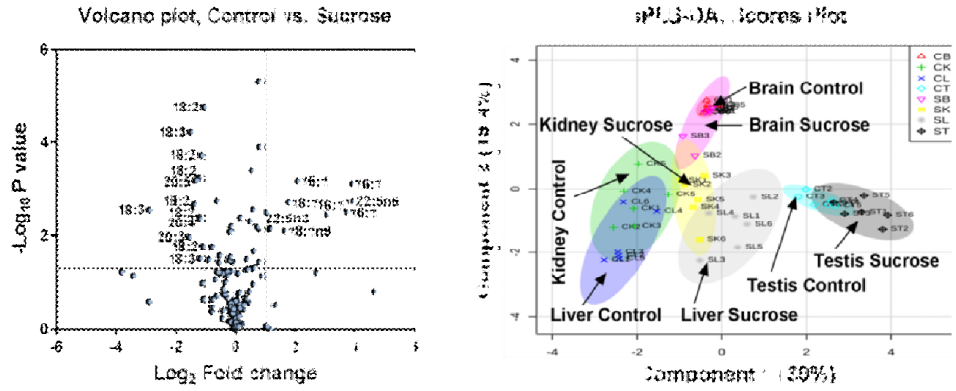

Fig. 2. The fatty acid profile of TL and PL of different organs obtained by GC-MS was used to construct Volcano plot (**A**) and sPLS-DA (**B**).

serum (Wang *et al.*, 2006). Indeed, decreased content of arachidonic acid was visible in our trial in the liver and brain tissue. These changes could be attributed to the decreased Δ5-desaturation in the liver. An interesting finding was the increased Δ5-desaturation in the brain which probably is a compensatory mechanism; nevertheless the desaturation rate was very low in the brain.

In general, it could be observed that the changes with the highest significance were the increase in the content of 16:1n7 and decrease in 18:3n3 and 18:2n6. Based on sPLS-DA score plot we could also observe that the most significant differences after the sucrose treatment were visible in the hepatic tissue.

CONCLUSIONS

In summary, our findings show that chronic treatment with sucrose in the drinking water extensively changes the fatty acid profile of liver, kidney, brain and testis and that these changes are organ-specific. In addition, sucrose treatment also changes lipogenic gene expression with the most significant influence on the hepatic Δ9-desaturation.

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