Abstract

Human metabolism is a network of interrelated biochemical pathways, many of which still need to be clarified. One such unknown, is the question of the relationship between body weight determination, lipid metabolism and one-carbon metabolism (OCM).

Recent studies have shown that the diet of obese people is low in vitamins. Moreover, obese people are more predisposed to having deficiencies of these in the body. Several studies suggest that nutrient deficiencies, particularly of vitamin B9 (folate), betaine, and choline, compounds that are key to OCM, may affect lipid metabolism and glucose metabolism, resulting in other diseases, including insulin resistance, metabolic syndrome, and fatty liver disease. OCM may be regulated, for example, by nutrient availability, genotype, and the activity of enzymes key to this metabolism (e.g., dihydrofolate reductase (DHFR), methylenetetrahydrofolate reductase (MTHFR), betaine-homocysteine methyltransferase (BHMT), and phosphatidylethanolamine N-methyltransferase (PEMT)), and body weight may also play a role.

In order to clarify the link between OCM and obesity and related disorders of lipid and glucose metabolism, we formulated a research hypothesis that disturbances of OCM caused by genetic polymorphisms in key genes encoding enzymes of OCM or by inadequate intake of compounds such as folate, choline, betaine, B vitamins is associated with increased body weight and excessive accumulation of body fat and the lipid metabolism disorders.

The research tasks included in this dissertation were: analysis of anthropometric parameters (fat mass and lean body mass were determined using whole-body air-displacement plethysmography), analysis of folate and choline metabolism markers (were estimated using an ELISA method, ultra-high-performance liquid chromatography electrospray ionization mass spectrometry, and HPLC) analysis of lipid metabolism markers (standard enzymatic methods with a fully automated analyzer Konelab 20i), analysis of hepatic steatosis indices, analysis of the rs180113 polymorphism of *MTHFR*, the rs7946 and rs12325817 polymorphisms of *PEMT*, the rs2236225 polymorphism of *MTHFD1*, and the rs70991108 polymorphism of *DHFR (*TaqMan probes*)*, overall food intake (a three-day food diary). The participants were recruited in 2016-2018 at the University of Life Sciences in Poznań.

The first stage of the study was to analyze the differences of markers of OCM in normal weight and overweight subjects. The next stage of the study was to analyze the associations between OCM markers and anthropometric parameters. The final stage of the study was to analyze the

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associations between OCM markers and markers of lipid metabolism and markers of fatty liver separately for people with normal and excessive body weight.

The results indicated that overweight subjects had 8.5% lower serum folate levels ($p < 0.01$), 5.81% higher choline levels ($p < 0.05$), 10.1% higher plasma l-carnitine levels ($p < 0.001$) and 12% lower dietary folate intake compared to normal weight subjects. Analyses using multivariate linear regression showed that higher serum folate concentrations and intake were associated with lower body fat ($p < 0.05$) and lower waist circumference ($p < 0.001$ and $p < 0.05$, respectively).

It was also shown that plasma choline concentration was associated with a higher body mass index (BMI) ($\beta = 0.19$; $p < 0.01$), higher body weight ($\beta = 0.13$; $p < 0.05$), fat mass ($\beta = 0.11$; $p < 0.05$), waist circumference ($\beta = 0.15$; $p < 0.01$) and hip circumference ($\beta = 0.12$; $p < 0.05$). Choline concentration in turn, was associated with lower fat mass ($\beta = -0.13$; $p < 0.05$) and a lower waist circumference ($\beta = -0.12$; $p < 0.05$). Further, the CC genotype of *MTHFR* (rs1801133) was associated with a higher WHR value ($\beta = 0.15$, $p < 0.05$) in women only. The negative association of plasma betaine and BMI ($\beta = -0.20$, $p < 0.05$) and lower body weight ($\beta = -0.16$, $p < 0.05$) were observed in men.

Significant associations were also found between OCM markers and markers of lipid metabolism and fatty liver. Among other things, it was shown that higher serum folate and betaine concentrations were associated with lower total cholesterol ($p < 0.001$ and $p < 0.05$, respectively) and LDL cholesterol ($p < 0.001$ and $p < 0.05$, respectively). Furthermore, we found that the CC genotype in the *PEMT* gene (rs12325817) was associated with higher HDL cholesterol concentrations ($p < 0.01$) only in overweight and obese subjects, while the AA genotype in the *PEMT* gene (rs7946) was associated with lower triglycerides (TG) concentrations ($p < 0.05$) in normal weight subjects.

The present study demonstrated that OCM is associated with anthropometrics and lipid metabolism. Furthermore, the associations between OCM markers and lipid metabolism, fatty liver markers, and anthropometrics were shown to vary with body weight.