Fatty Acid Amide Hydrolase And Monoacylglycerol Lipase Activities In Adipocytes Taken From Obese Surgical Patients

Jemma Cable¹, Garry Tan¹, Stephen Alexander¹,², Saoirse O'Sullivan¹

¹University of Nottingham, Division of Vascular Medicine, DE22 3DT, Derby, United Kingdom,
²University of Nottingham, School of Biomedical Sciences, NG7 2UH, Nottingham, United Kingdom

The role of the endocannabinoid system (ECS) in metabolism is gradually emerging, and there is evidence that the peripheral ECS is dysregulated in obesity. Blood concentrations of the endocannabinoids anandamide and 2-arachidonoyl glycerol (2-AG) are increased in obese humans [1]. Gene expression of the enzymes involved in endocannabinoid catabolism, fatty acid amide hydrolase (FAAH) for anandamide and monoacylglycerol lipase (MGL) for 2-AG, have been investigated in the subcutaneous and omental adipose tissue of lean and obese subjects, but the reported results are highly contradictory. In some studies, expression does not differ between visceral and subcutaneous adipose depots [2], whilst in others, significant differences have been found [1]. These studies are based on mRNA expression. The aim of the present study was to investigate whether FAAH and MGL activities differ between omental and subcutaneous adipocytes in obese subjects. Additionally, the relationship between metabolic health or co-morbidities and enzyme activity was analysed.

Ethical approval for the study was granted by Derbyshire Research Ethics Committee and Research and Development at Derby City General Hospital Trust. Patients undergoing laparoscopic bariatric surgery or cholecystectomy were recruited to the study and anthropometric measurements and fasting venous blood samples were taken prior to surgery. Subcutaneous adipose biopsies were taken during surgery from all patients (n=28) and omental adipose samples were taken from 14 of these. Blood samples were analysed in the hospital pathology department for standard metabolic markers, including lipid profile, glucose and insulin. The adipose tissue samples were stored at -80°C until digestion with collagenase and subsequent homogenisation of the isolated mature adipocytes. The particulate and cytosolic cell fractions were separated using centrifugation and stored at -80°C. FAAH activity in the cell membrane fraction was assayed using 2 μM N-arachidonoyl-[^3H]-ethanolamine as substrate, and 100 μM 2-oleoyl-[^3H]-glycerol was used to measure MGL activity in the cytosolic fraction.

The activities of FAAH and MGL were not found to significantly differ between adipocytes isolated from omental versus subcutaneous adipose depots (paired t-test, n=14). In subcutaneous adipocytes, FAAH and MGL activities were not different between subgroups of metabolically healthy, metabolic syndrome or diabetic patients. FAAH and MGL activity in subcutaneous mature adipocytes showed no correlation with BMI or any of the anthropometric or metabolic parameters measured in this study. The results of this study indicate that the activities of two major ECS enzymes are not altered with increasing adiposity or metabolic disease in the obese population.
