Epigenetic regulation of adenosine A_{2A} and dopamine D2 receptor gene transcription on compulsive food consumption

M.V. Micioni Di Bonaventura[1], M. Pucci[2], M.E. Giusepponi[1], C. Lambertucci[3], R. Volpini[3], M. Maccarrone[4], C. D'Addario[2], C. Cifani[1]

[1]University of Camerino, School of Pharmacy Pharmacology Unit, Camerino (MC), Italy
[2]University of Teramo, Faculty of Bioscience and Technology for Food Agriculture and Environment, Teramo, Italy
[3]University of Camerino, School of Pharmacy Medicinal Chemistry Unit, Camerino (MC), Italy
[4]University of Rome, Campus Bio-Medico, Rome, Italy

Satisfactory treatments for eating disorders, such as binge eating disorder and bulimia nervosa, are not available at present. Using a well-characterized animal model of binge eating, we investigated the epigenetic regulation of the adenosine A_{2A} Receptor (A_{2A}AR) and dopamine D2 (D2R) gene.

The animal model included four groups (rats fed normally, and then stressed or not, rats exposed to cycles of restriction/refeeding, and then stressed or not).

Gene expression analysis carried out on the amygdala complex of restricted and stressed rats revealed a significant increase of A_{2A}AR and D2R mRNA when compared to non-stressed and non-restricted rats. Administration of the A_{2A}AR agonist (VT 7) induced in restricted and stressed rats a significant increase of A_{2A}AR and D2R mRNA levels when compared to vehicle group, whereas a significant decrease in rats pre-treated with the A_{2A}AR antagonist (ANR 94) was observed.

Pyrosequencing analysis revealed a significant reduction of the % of DNA methylation at A_{2A}AR promoter region in restricted and stressed compared to the non-stressed and non-restricted animals. We did not find any difference in D2R DNA methylation among different groups. Significant changes in the DNA methylation status of A_{2A}AR promoter were found in restricted and stressed rats after administration of VT 7 or ANR 94. We observed a decrease of DNA methylation in VT 7 treated rats and a hypermethylation in ANR 94 rats with respect to the vehicle group.

The increase in A_{2A}AR mRNA observed in restricted and stressed rats could be due to a compensatory mechanism to counteract the effect of binge eating, suggesting that the A_{2A}AR activation, inducing receptor gene up-regulation, could be relevant to reduce food consumption. We here demonstrated for the first time the epigenetic regulation of A_{2A}AR in an animal model of binge eating.