Genetic and epigenetic regulation of adenosine A_{2A}receptor gene transcription on compulsive food consumption

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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 A2A receptor (A2AAR) and dopamine D2 receptor (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 A2AAR and D2R mRNA when compared to non-stressed and non-restricted rats. Administration of the A2AAR agonist (VT 7) induced in restricted and stressed rats a significant increase of A2AAR and D2R mRNA levels when compared to vehicle group, whereas a significant decrease in rats pre-treated with the A2AAR antagonist (ANR 94) was observed.

Pyrosequencing analysis revealed a significant reduction of the % of DNA methylation at A2AAR promoter region in restricted and stressed rats 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 A2AAR 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 A2AAR mRNA observed in restricted and stressed rats could be due to a compensatory mechanism to counteract the effect of binge eating, suggesting that the A2AAR activation, inducing receptor gene up-regulation, could be relevant to reduce food consumption.

We here demonstrated for the first time the epigenetic regulation of A2AAR in an animal model of binge eating.