Correlation between long-lasting psychosocial stress and adipose tissues in the rat: alteration of adipogenesis, cannabinoid systems andoxidative stress

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Both typical neuroleptic agents and second generation antipsychotics are associated with many side effects, most notably weight gain (Medici et al 2016), adipose tissue dysfunctions, body mass index alterations (Konarzewska et al 2014) and metabolic dysfunctions. However, some studies have evidenced that both drug-free and drug-naive schizophrenic patients showed increased visceral fat, suggesting that antipsychotic medication might not be the main responsible of metabolic alterations (Thakore et al 2002). One of the non-pharmacologic rodent models of psychosocial stress-induced psychosis is the rat social isolation, which is able to determine long-term alterations reminiscent of several symptoms seen in psychotic patients (Weiss et al 2001).

To evaluate the possible relationship between metabolic abnormalities and chronic psychosocial stress-induced psychosis, we quantified total and visceral fat amount by using dual-energy X-ray (DEXA) absorptiometry. The expression of specific ROS producers genes (Nox1, Nox4, Hmox1, Pparg), degrading enzymes (Prdx1, Ucp1,) and oxidative stress-related damage (Cidea, Slc2a4 and Acacb) was also investigated on white adipose tissue (WAT) of seven week isolated rats by qPCR. The impact of oxidative stress on Adrb3 was also assessed. We found that social isolation induced an increase in total and visceral fat amount, as well as an overexpression of Pparg (Lefterova et al 2008). Social isolation induces a decrease of Ucp1 mRNA and an increase of Adrb3 gene expression. In the WAT of social isolated rats an increase of Nox1 and Hmox1 mRNA was observed with respect to non-isolated animals, while Nox4 gene expression does not change. Moreover, an increase of Cidea, Slc2a4 and Acacb expression was also observed. In addition, social isolation induces a decrease of gene coding for cannabinoid receptor 1.

The observed increase in visceral fat in isolated animals supports the hypothesis of a direct correlation between psychosocial stress and visceral fat elevation. A crucial finding of this study is represented by the redox imbalance, evidenced by the alteration of the genes correlated with oxidative stress, observed in the visceral fat of the rats following seven weeks of social isolation.

These results might provide a novel understanding of the link existing among psychosocial stress-induced psychosis, adipose tissue dysfunctions and redox imbalance, paving the way for new therapeutic perspectives for the treatment of alterations in peripheral tissues associated with this mental disorder.

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