Long-lasting psychosocial stress leads to altered adipogenesis and thermogenesis functions in rats

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In humans, psychotic disorders, together with mental impairments, are characterized by several metabolic disturbances, such as hypertension, cardiovascular dysfunctions and obesity. In this regard, it is unclear if the observed adipose tissue increase could really be associated to pharmacological therapy or if it could be due to the pathological condition itself. Unfortunately, only few studies are available from the pre-medication era, and methodological aspects make their interpretation arduous. For these reasons, in the present study, we used the social isolation model, which represents a stressful condition for rats and provides a non-pharmacological tool to investigate long-lasting alterations reminiscent of a psychotic condition. Here we evaluated the potential development and prevalence of metabolic abnormalities in chronic psychosocial stress-induced psychosis in rats. To this end, we compared biometric composition, lipidic and genomic profiles in animals reared either in social isolation (7 weeks) or in social groups. We analyzed the genes related to adipogenesis, thermogenesis and storage/transport of fatty acid in white adipose tissue (WAT). Results showed that social isolation did not induce alterations of total body weight, when rats were maintained at a standard chow diet. However, densitometric analysis revealed that social isolation significantly increased visceral fat, while lipidic composition (serum tryglicerides and cholesterol) was not modified. Furthermore, we found that the expression of peroxisome proliferator-activated receptor gamma *(PPARγ),* which is necessary for normal adipogenesis (Kajimura et al., 2010), was up-regulated in isolated animals with respect to controls. Accordingly, the social isolation induced a down-regulation of *Ucp1*, principally involved in thermogenesis, expression in WAT, highlighting a possible reduction in energy expenditure and thermogenesis. In line with the results obtained for *Ucp1*, isolated rats showed an up-regulation of *Cidea*, in WAT. No alterations were found on the expression of genes related to the synthesis and transport of fatty acids, such as *Acacb*, *Fasn* and *Fabp4* genes. Taken together, these data suggest that social isolation could induce an alteration of the main pathways of energy homeostasis in fat tissue. In particular, the observed increase of visceral fat might be, at least in part, mediated by an increase of adipogenesis, and a decrease of thermogenesis. Our results provide new insights in the relationship between the responses to a chronic psychosocial stressor and the development of metabolic dysfunctions. Thus, it is likely that stress-induced psychotic subjects might be inherently predisposed to metabolic abnormalities, and that visceral obesity might occur as a treatment-unrelated illness trait.

Kajimura et al., (2010). *Cell Metab*. 11(4):257-62.