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"Clinical, biochemical and genetic correlates of affective temperment, depressive symptoms and the performance of prefrontal cortex in obese population."

Obesity is a disease associated with complications like depressive disorders, cognitive deterioration and impaired carbohydrate metabolism. Studies show that genes involed in the dopaminergic neurotransmission have significant role in the development of obesity. Dopamine is a putative factor connecting obesity with depression or cognitive deterioration. Still literature lacks information about correlations between dopaminergic gene polymorphisms and cognitive performance, affective temperament or sex. Also no studies investigated the role of affective temperament on glycemic control in obese with carbohydrate disorders.

Therefore, I established subsequent objectives of the series of publications:

1. The evaluation of correlations between dopaminergic genes polymorphisms and the executive functions in obese population.
2. The analysis of correlations between dopaminergic genes polymorphisms and affective temperament in obese population.
3. The analysis of correlations between affective temperament and biochemical parameters of glycemic control in obese with concurrent type 2 diabetes mellitus (T2DM), impaired glucose tolerance(IGT)/impaired fasting glucose (IFG).
4. The analysis whether sex differs the results of executive functions measured with Wisconsin Card Sorting Tes (WCST).

First analysis consisted of 248 obese persons (179 femals, 69 males). The evaluation of the prefrontal cortex function (executive functions) was performed with WCST. Genetic analysis included gene polymorphisms: *COMT*Val158Met, *DAT1* and *DRD4*.

Second study enrolled 245 obese subjects (178 females, 67 males). Following gene polymorphisms were evaluated: *COMT*Val158Met, *DAT1* and *DRD4*. To assess affective temperament, we utilized Temperament Evaluation of Memphis, Pisa, Paris and San Diego autoquestionnaire (TEMPS-A).

The third study enrolled 185 obese subjects (146 females, 39 males). After performing oral glucose tolerance test (OGTT), subjects were divided into three groups: obese people with T2DM, obese with IGT/IFG, and obese non-diabetic patients. Then, we evaluated affective temperament with TEMPS-A. For the assessment of glycemic control, the level of glycolated hemoglobin A1c

(HbA1c) was measured from the sample of peripheral blood.

Results of the first analysis show positive correlations between *COMT* Met/Met and Met/Val polymorphisms and better results in WCST, but after further analysis those results did not maintain statistical significant. In the group of males, subjects with *DAT1* 10/10 and 10/9 obtained less non perseverative errors compared to 9/9 homozygotes. Females who are over 45 yo and have *DRD4* L-allele gained better results of WCST_1st. We also observed significant differences between men and women regarding executive functions measured with WCST.

Obtained results suggest that dopaminergic transmission determined by dopaminergic genes polymorphisms affects the performance of prefrontal cortex. Observed dfferences in cognitive performance between men and women may result from estrogens, which may modulate dopaminergic neurotransmission.

In the second study, we observed correlations between polymorphism of *COMT* Met/Val and irritable and cyclothymic dimensions of affective temperament. Both *DAT1* and *DRD4* did not show any significant correlations with TEMPS-A. Obtained results indicate, that dopaminergic transmission modulated by *COMT* may be associated with greater susceptibility to the development of affective disorders linked with irritable and cyclothymic dimensions.

Results of the third analysis did not show any significant differences of affective temperament between obese subjects with carbohydrate disorders and non-diabetic ones. T2DM and IGT/IFG groups showed significant correlations between affective temperament and fasting plasma glucose and HbA1c values. Obese with T2DM showed positive correlation betwen anxious