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MATERNAL SOCIAL STRESS EXACERBATES INSULIN RESISTANCE AND DYSLIPIDAEMIA IN ADULT MALE OFFSPRING OF GESTATIONAL DIABETIC RATS

СОЦІАЛЬНИЙ СТРЕС У МАТЕРІ ПОСИЛЮЄ ІНСУЛІНОРЕЗИСТЕНТНІСТЬ ТА ДИСЛІПІДЕМІЮ У ДОРОСЛИХ САМЦІВ, НАЩАДКІВ ЩУРІВ ІЗ ГЕСТАЦІЙНИМ ДІАБЕТОМ

Leshchenko Zh. A.
Candidate of Biological Sciences,
Senior Research Fellow at the
Department of Pathomorphology and
Genetics of Endocrine Diseases
State Institution "V. Danilevsky Institute
for Endocrine Pathology Problems
of the National Academy of Medical
Sciences of Ukraine"
Kharkiv, Ukraine

Лещенко Ж. А.
кандидат біологічних наук,
старший науковий співробітник
відділу патоморфології та генетики
ендокринних захворювань
Державна установа «Інститут
проблем ендокринної патології
імені В. Я. Данилевського
Національної академії медичних наук
України»
м. Харків, Україна

Insulin resistance is a major pathogenic factor contributing to metabolic disorders, including type 2 diabetes mellitus, obesity, and cardiovascular

diseases [1]. Increasing evidence supports the concept of developmental programming, whereby adverse intrauterine conditions predispose offspring to long-term metabolic dysfunction [2, 3]. Gestational diabetes mellitus is associated with an increased risk of insulin resistance and metabolic disturbances in offspring later in life [4]. In addition, maternal stress during pregnancy has been identified as an important modifier of metabolic programming through neuroendocrine and glucocorticoid-mediated mechanisms [3, 5]. However, the combined effect of maternal social stress and gestational diabetes on metabolic outcomes in offspring remains insufficiently characterized. The aim of this study was to evaluate the impact of maternal social stress on insulin resistance and lipid metabolism in adult male offspring of rats with gestational diabetes.

Materials and methods. Maternal social stress (MSS) was induced by transferring pregnant rats between social groups daily during gestational days 2–8. Gestational diabetes (GD) was induced by a single intraperitoneal injection of streptozotocin (45 mg/kg body weight) on gestational day 2. The maternal cohort included control (C), MSS, GD, and MSS+GD groups (n=25). Metabolic assessment was performed in male offspring (F1, n=32) at 90 days of age. An intraperitoneal glucose tolerance test (GTT; 3 g glucose/kg body weight) was conducted after overnight fasting. Fasting blood samples were analyzed for glucose, insulin (IRI), non-esterified fatty acids (NEFA), triglycerides (TG), and total cholesterol (TCh). Insulin resistance was evaluated using the Homeostasis Model Assessment (HOMA-IR), and insulin sensitivity was assessed using the Quantitative Insulin Sensitivity Check Index (QUICKI), which are validated indicators of metabolic dysfunction [6].

Results. Glucose tolerance was significantly impaired in offspring of GD mothers and was further worsened in MSS+GD offspring (AUC during GTT: 1022.7±19.3 and 1112.0±32.8 mmol/L/min, respectively, vs 640.7±8.0 mmol/L/min in controls; $p<0.001$). Plasma insulin levels and HOMA-IR were significantly increased in MSS+GD offspring compared with GD offspring (by 22% and 34%, respectively; $p<0.01$) and controls (by 140% and 292%, respectively; $p<0.001$), indicating pronounced insulin resistance [1, 4]. Maternal social stress was associated with reduced insulin sensitivity, as demonstrated by lower QUICKI values in MSS+GD offspring compared with GD offspring and controls ($p<0.001$). Total cholesterol and NEFA levels were significantly elevated in GD and MSS+GD offspring compared with controls ($p<0.001$), reflecting disturbances in lipid metabolism characteristic of metabolically programmed offspring [2, 7]. Maternal social stress further aggravated lipid abnormalities, contributing to increased triglyceride levels and enhanced metabolic dysfunction.

Conclusion. Maternal social stress during pregnancy exacerbates insulin resistance and promotes dyslipidaemia in adult male offspring of gestational diabetic rats. These metabolic alterations, including increased HOMA-IR, decreased insulin sensitivity, impaired glucose tolerance, and adverse lipid profile changes, confirm that maternal stress enhances the developmental programming effects of gestational diabetes [3, 5]. These findings highlight maternal stress as an important modifier of metabolic risk and contribute to understanding mechanisms underlying the intergenerational transmission of metabolic disorders [2, 4].

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