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**EVOLIUCINĖ MEDICINA:
ŽMOGAUS RAIDOS PERSPEKTYVOS IR SVEIKATA
BESIKEIČIANČIOJE APLINKOJE**

**EVOLUTIONARY MEDICINE:
PERSPECTIVES ON HUMAN DEVELOPMENT AND HEALTH
CONSEQUENCES IN A CHANGING ENVIRONMENT**

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EFFECTS OF MATERNAL PHTHALATE EXPOSURE ON HIPPOCAMPAL STRUCTURE IN FIRST- AND SECOND-GENERATION MALE RAT OFFSPRING

Laurynas ORLA^{1,2}, Edita PAULIKAITE-BIVAINI¹, Evita SERIKOVAITE², Justina ALCAUSKAITE², Rasa AUKSTIKALNIENE¹, Violeta ZALGEVICIENE², Grita SKUJIENE¹

¹Institute of Biosciences, Life Sciences Center, Vilnius University, Vilnius, Lithuania

²Department of Anatomy, Histology and Anthropology, Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Vilnius, Lithuania

Contact e-mail: laurynas.orla@mf.vu.lt

Background and Aim: Di(2-ethylhexyl) phthalate (DEHP) and dibutyl phthalate (DBP) are endocrine-disrupting chemicals widely detected in Lithuanian surface waters that may impair neurodevelopment and increase the risk of neurological disorders later in life. Such effects may be particularly relevant to the hippocampus, a brain region essential for learning, memory formation, and emotional regulation, which is highly sensitive to environmental toxicants. The aim of this study was to evaluate the effects of DEHP and DBP exposure on hippocampal morphology in male offspring of the first (F1) and second (F2) generations derived from continuously exposed maternal lineages.

Materials and Methods: Female Wistar rats were assigned to six experimental groups: DEHP-200, DEHP-1000, DBP-100, DBP-500, a phthalate-mixture group (DEHP 200 + DBP 100 µg/kg/day), and a control group. Exposure began before mating and continued throughout pregnancy and lactation. Male offspring from F1 and F2 generations were euthanised after weaning. Brain sections were stained using the Cresyl Violet method. Hippocampal CA1 and CA3 region thickness and neuronal density were assessed using light microscopy. Statistical analysis was performed using one-way ANOVA.

Results: Maternal exposure to phthalates induced structural alterations in the hippocampus of male offspring in both the first (F1) and second (F2) generations. Significant reductions in neuronal density and thickness of the CA1 and CA3 regions were observed in male offspring from females exposed to higher DEHP and DBP doses. Lower DBP doses and the phthalate mixture also produced measurable changes in hippocampal morphology. Similar alterations were observed in both generations, suggesting that continuous maternal exposure to phthalates resulted in persistent hippocampal changes across generations.

Conclusions: Developmental exposure to DEHP and DBP during gestation and lactation adversely affects hippocampal structure in both F1 and F2 generations of rats in male offspring of both the F1 and F2 generations. The observed reductions in neuronal density and regional thickness suggest persistent neurotoxic effects of phthalates across multiple generations under continued maternal exposure.

Keywords: DBP, DEHP, hippocampus, neurotoxicity, phthalates