

THE EFFECT OF MATERNAL HIGH-FAT DIET ON MORPHOLOGY AND INFLAMMATION OF OFFSPRING RETINA

Patricija Čepauskytė¹, Gintarė Urbonaitė¹, Neda Ieva Biliūtė¹, Guoda Laurinavičiūtė², Urtė Neniškytė^{1,3}

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

²Institute of Biomedical Sciences, Faculty of Medicine, Vilnius University, Lithuania

³VU-EMBL Partnership Institute, Life Sciences Center, Vilnius University, Lithuania

patricija.cepauskyte@gmc.stud.vu.lt

Aim: The standard diet in today's society consists of increased high fat content which contributes to the rising rates of obesity. Many studies indicate that maternal high-fat diet (mHFD) is the cause of systemic inflammation, potentially resulting in neurodevelopmental disorders of the offspring [1, 2, 3]. Female estrous cycle stages appeared to also have different response to inflammation [4, 5, 6]. In the context of inflammatory conditions, CD68 is used as a microglia activation marker that is often associated with immune cells of the central nervous system, including the retina [7]. Studies have shown that the retina is affected by diet consisting of high fat, however, there's little research done investigating its effects on the offspring retina [8]. This study aims to evaluate area changes of microglia and CD68 in the peripheral retina of mHFD offspring and assess how microglia and CD68 area depend on the stages of the estrous cycle.

Methods: Female C57Bl/6J mice from weaning to lactation were fed with control diet (CD, 10% fat) or high-fat diet (HFD, 60% fat). The offspring were weaned to CD. The eyeballs of the offspring were collected, fixed with 4% PFA, cryoprotected and sliced using cryotome. Microglia and activated microglia cells were labeled immunohistochemically using anti-RFP and anti-CD68 antibodies respectively, while cell nuclei were labeled with DAPI. The estrous cycle stages were determined by vaginal cytology in female offspring on the day of tissue collection (22 weeks old).

Results: We evaluated the area of microglia and CD68 in the peripheral retina and compared the measurements between the groups of offspring. mHFD significantly increased area of microglia and CD68 in female peripheral retina compared to maternal control diet offspring but had no significant effect on male retina. In addition, during evaluation of microglia area and CD68 area in microglia, alterations were observed in female offspring estrous cycle stages due to mHFD.

Conclusion: Our findings showed that mHFD had a gender-specific effect on the area of microglia and CD68 in offspring peripheral retina as well as revealed microglia and CD68 area changes in mHFD female offspring during estrous cycle stages.

Funding: This work was supported by the Science Promotion Fund of Vilnius University.

-
- [1] Maes M, Verkerk R, Bonaccorso S, Ombet W, Bosmans E, Scharpé S. Depressive and anxiety symptoms in the early puerperium are related to increased degradation of tryptophan into kynurenine, a phenomenon which is related to immune activation. *Life Sci.* 2002 Sep 6;71(16):1837-48. doi: 10.1016/s0024-3205(02)01853-2. PMID: 12175700.
 - [2] Oades RD, Myint AM, Dauvermann MR, Schimmelmann BG, Schwarz MJ. Attention-deficit hyperactivity disorder (ADHD) and glial integrity: an exploration of associations of cytokines and kynurenine metabolites with symptoms and attention. *Behav Brain Funct.* 2010 Jun 9;6:32. doi: 10.1186/1744-9081-6-32. PMID: 20534153; PMCID: PMC2900218.
 - [3] Kang SS, Kurti A, Fair DA, Fryer JD. Dietary intervention rescues maternal obesity induced behavior deficits and neuroinflammation in offspring. *J Neuroinflammation.* 2014 Sep 12;11:156. doi: 10.1186/s12974-014-0156-9. PMID: 25212412; PMCID: PMC4172780.
 - [4] Villa A, Vegeto E, Poletti A, Maggi A. Estrogens, Neuroinflammation, and Neurodegeneration. *Endocr Rev.* 2016 Aug;37(4):372-402. doi: 10.1210/er.2016-1007. Epub 2016 May 19. PMID: 27196727; PMCID: PMC4971309.
 - [5] Chang RC, Shi L, Huang CC, Kim AJ, Ko ML, Zhou B, Ko GY. High-Fat Diet-Induced Retinal Dysfunction. *Invest Ophthalmol Vis Sci.* 2015 Apr;56(4):2367-80. doi: 10.1167/iovs.14-16143. PMID: 25788653; PMCID: PMC4407693.
 - [6] Lee JJ, Wang PW, Yang IH, Huang HM, Chang CS, Wu CL, Chuang JH. High-fat diet induces toll-like receptor 4-dependent macrophage/microglial cell activation and retinal impairment. *Invest Ophthalmol Vis Sci.* 2015 May;56(5):3041-50. doi: 10.1167/iovs.15-16504. PMID: 26024088.
 - [7] Choudhary M, Malek G. CD68: Potential Contributor to Inflammation and RPE Cell Dystrophy. *Adv Exp Med Biol.* 2023;1415:207-213.
 - [8] Clarkson-Townsend DA, Douglass AJ, Singh A, Allen RS, Uwaifo IN, Pardue MT. Impacts of high fat diet on ocular outcomes in rodent models of visual disease. *Exp Eye Res.* 2021 Mar;204:108440. doi: 10.1016/j.exer.2021.108440. Epub 2021 Jan 11. PMID: 33444582; PMCID: PMC7946735.