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Dietary lecithin effects on the behavior, brain metabolism, mitochondrial and cellular structure of the neurons in mice

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Motivation and Aim: Nowadays lecithin is widely used as a neuroprotective and hepatoprotective drug, a dietary supplement and is the often component of food production as an emulsifier. Therefore, the overall dose of lecithin in the modern human diet can be very high. Previously, we have shown that chronic intestinal inflammation in *Muc2*-knockout mice induces behavioral changes along with the substantial increases of the phospholipids content in intestinal epithelial cells, particularly, phosphatidylcholine, phosphatidylserine, and phosphatidic acid [1, 2]. It is known that phospholipids perform a whole range of molecular and cellular functions, and changes in their metabolism correlate with diseases and the course of chronic inflammatory processes [3]. Animals given the same phospholipid mixture with food have shown similar behavioral changes [4]. Also, our data demonstrate impaired mitochondrial function in intestinal cells of such animals [1, 5]. Soy lecithin consists up to 70 % of the similar phospholipids mixture: phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol and phosphatidic acid. Here we investigate the effects of soy lecithin administration on the behavioral patterns, brain cells and metabolism in laboratory mice.

Methods and Algorithms: Long-term feeding of C57BL/6 mice: pregnant females, starting from the third week of pregnancy, received standard food with the addition of soy lecithin (35 g per 1 kg, Solgar Inc. USA). The offspring also continued to receive lecithin in the same doses until behavioral testing. Short-term lecithin feeding: males received a soy lecithin with food (35 g per 1 kg) for four weeks before testing. Behavioral tests: assessment of anxiety, autistic-like behavior; social test; test for discrimination between social and non-social odor stimuli. Untargeted metabolomics analysis in mice brain samples: LC-MS/MS analysis of the metabolites composition (Waters Aquity UPLC/Q-Exactive HF-X (Thermo Scientific)) in brain samples was performed in Advanced Mass Spectrometry Core Facility of Skolkovo Institute of Science and Technology Metabolomics. Transmission electron microscopy (TEM) analysis was performed on ultrathin sections of hypothalamus, amygdala, and frontal cortex of mice brain at the Center for microscopy analysis of ICG SBRAS (FWNR-2022-0015).

Results: As a result of experiments on long-term and short-term feeding of healthy C57BL/6 laboratory mice with soy lecithin, significant deviations in social behavioral patterns were revealed. In particular, animals did not distinguish between the odor of a female and a male, while their discrimination of non-social odors was normal. At the

same time, in the test with two intruders (female and male), animals after lecithin feeding did not demonstrate normal preference towards the female. In addition, perinatal, rather than short-term feeding of lecithin resulted in changes in stereotypic behavior. These behavioral changes were accompanied by changes in a number of metabolites levels identified by LC-MS analysis in the brain of experimental group of animals. TEM analysis revealed substantially altered structure of mitochondria in hypothalamus and amygdala regions of brain in animals with long-termly administered soy lecithin: the density of the matrix increases, and internal structures degrade forming empty space inside the mitochondria. In addition, synaptic vesicles were found to be of irregular size and shape, and the synaptic cleft formed a wider than normal brush-like structure. In experimental animals, high rate of the apoptosis of neurons and glial cells, as well as cellular membranes degradation, was more often observed.

Conclusion: Our results indicate a significant effect of lecithin supplementation on brain function, metabolism and cellular structure of neurons in laboratory mice. Further studies of the effects of the lecithin and dietary phospholipids, as well as their metabolic regulatory capacity on the brain functions regulation of may provide a new level in understanding the role of metabolic compounds in the gut-brain axis.

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