Vitamina B1-tiamina - VITAMIN B1-Thiamine

Zhang H, Lu T, Feng Y, Sun X, Yang X, Zhou K, Sun R, Wang Y, Wang X, Chen M.
A metabolomic study on the gender-dependent effects of maternal exposure to fenvalerate on neurodevelopment in offspring mice.
Sci Total Environ. 2020 Mar 10;707:136130. doi: 10.1016/j.scitotenv.2019.136130.

Background: The general population is widely exposed to fenvalerate. However, the effects of maternal exposure to fenvalerate on neurodevelopment in offspring and the underlying metabolic mechanism are largely unknown.
Methods: Pregnant mice were exposed to fenvalerate for 11 consecutive days. The forced swimming test (FST) was performed in 35 day-old offspring to investigate the effects of fenvalerate on neurobehavioral responses. Blood serum free T4 and free T3 concentrations were measured using commercial ELISA. Blood and thyroid samples were used for metabolomic analyses with UPLC Q-Exactive. The expression levels of neurotransmitter metaolite receptors were determined in the frontal cortex of offspring using real-time PCR.
Results: The immobility time, free T4 and free T3, and expression levels of Htr1a and Htr2a were statistically changed in offspring male mice. Metabolomic analysis revealed that the pentose phosphate pathway, starch and sucrose metabolism, glutamic acid metabolism were the key changed pathways in the blood, and thiamine metabolism was the key changed pathway in the thyroid.
Conclusion: Prenatal exposure to fenvalerate affected neurodevelopment in male offspring mice both via the changed abundances of metabolites involved in glycolysis related metabolism and medium-chain fatty acid metabolism, and the changes in 5-HT receptor expression.

Fan Y, Qin Y, Chen M, Li X, Wang R, Huang Z, Xu Q, Yu M, Zhang Y, Han X, Du G, Xia Y, Wang X, Lu C.
Prenatal low-dose DEHP exposure induces metabolic adaptation and obesity: Role of hepatic thiamine metabolism.
J Hazard Mater. 2020 Mar 5;385:121534. doi: 10.1016/j.jhazmat.2019.121534. Epub 2019 Oct 28. PMID: 31706747;

Di-(2-ethylhexyl)-phthalate (DEHP) is a ubiquitous environmental pollutant and is widely used in industrial plastics. However, the long-term health implications of prenatal exposure to DEHP remains unclear. We set out to determine whether prenatal DEHP exposure can induce metabolic syndrome in offspring and investigate the underlying mechanisms. A mouse model of prenatal DEHP exposure (0.2, 2, and 20 mg/kg/day) was established to evaluate the long-term metabolic disturbance in offspring. The mice were profiled for the hepatic metabolome, transcriptome and gut microbiota to determine the underlying mechanisms. Thiamine supplementation (50 mg/kg/day) was administered to offspring to investigate the role of thiamine in ameliorating metabolic syndrome. Prenatal exposure to low-dose DEHP (0.2 mg/kg/day) resulted in metabolic syndrome, including abnormal adipogenesis, energy expenditure and glucose metabolism, along with dysbiosis of the gut microbiome, in male offspring. Notably, hepatic thiamine metabolism was disrupted in these offspring due to the dysregulation of thiamine transport enzymes, which caused abnormal glucose metabolism. Prenatal low-dose DEHP exposure caused life-long metabolic consequences in a sex-dependent

manner, and these consequences were be attenuated by thiamine supplementation in offspring. Our findings suggest low-dose DEHP exposure during early life stages is a potential risk factor for later obesity and metabolic syndrome.

Takeda T, Matsuo Y, Nishida K, Fujiki A, Hattori Y, Koga T, Ishii Y, Yamada H.
α-Lipoic acid potentially targets AMP-activated protein kinase and energy production in the fetal brain to ameliorate dioxin-produced attenuation in fetal steroidogenesis.
J Toxicol Sci. 2017;42(1):13-23.

Our previous studies demonstrated that treating pregnant rats with dioxins, including 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), targets the pituitary expression of luteinizing hormone (LH) to attenuate testicular steroidogenesis in fetuses, resulting in the imprinting of sexual immaturity of the offspring after reaching maturity. Furthermore, we found that although TCDD disturbs the tricarboxylic acid (TCA) cycle in the fetal hypothalamus, maternal co-treatment with α-lipoic acid (α-LA), a cofactor of the TCA cycle, restores a TCDD-produced reduction in the LH-evoked steroidogenesis as well as the TCA cycle activity in fetuses. However, the mechanism underlying the beneficial effect of α-LA remains to be fully elucidated. To address this issue, we compared the effect of α-LA with that of thiamine, another cofactor of the TCA cycle. As with α-LA, supplying thiamine to dams exposed to TCDD alleviates the reduced level of not only hypothalamic ATP but also pituitary LH and testicular steroidogenic protein in fetuses. However, thiamine had a much weaker effect than α-LA. In agreement with ATP attenuation, TCDD activated AMP-activated protein kinase (AMPK), a negative regulator of LH production, whereas the supplementation of α-LA allowed recovery from this defect. Furthermore, α-LA restored the TCDD-produced reduction in the pituitary expression of the receptor for gonadotropin-releasing hormone (GnRH), an upstream regulator of LH synthesis. These results suggest that α-LA rescues TCDD-produced attenuation during fetal steroidogenesis due not only to facilitation of energy production through the TCA cycle but also through suppression of AMPK activation, and the pituitary GnRH receptor may serve as a mediator of these effects.

Yildirim A, Zhang J, Manzetti S, van der Spoel D.
Binding of Pollutants to Biomolecules: A Simulation Study.
Chem Res Toxicol. 2016 Oct 17;29(10):1679-1688.

A number of cases around the world have been reported where animals were found dead or dying with symptoms resembling a thiamine (vitamin B) deficiency, and for some of these, a link to pollutants has been suggested. Here, we investigate whether biomolecules involved in thiamin binding and transport could be blocked by a range of different pollutants. We used in silico docking of five compound classes (25 compounds in total) to each of five targets (prion protein, ECF-type ABC transporter, thi-box riboswitch receptor, thiamin pyrophosphokinase, and YKoF protein) and subsequently performed molecular dynamics (MD) simulations to assess the stability of the complexes. The compound classes were thiamin analogues (control), pesticides, veterinary medicines, polychlorinated biphenyls, and dioxins, all of which are prevalent in the environment to some extent. A few anthropogenic compounds were found to bind the ECF-type ABC transporter, but none binds stably to prion protein. For the riboswitch,

most compounds remained in their binding pockets during 50 ns of MD simulation, indicating that RNA provides a promiscuous binding site. In both YKoF and thiamin pyrophosphokinase (TPK), most compounds remain tightly bound. However, TPK biomolecules undergo pollutant-induced conformational changes. Although most compounds are found to bind to some of these targets, a larger data set is needed along with more quantitative methods like free energy perturbation calculations before firm conclusions can be drawn. This study is in part a test bed for large-scale quantitative computational screening of interactions between biological entities and pollutant molecules.