THE EFFECTS OF PERINATAL EXPOSURE TO BDE47 ON ACCUMULATION, CEREBRAL GENE EXPRESSION AND NEUROBEHAVIOURAL DEVELOPMENT IN MICE

Haave M[1,2], Folven KI[1], Carroll T[3], Glover C[1,a,], Heegaard E[4], Brattelid T[1], Hogstrand C[3] & Lundebye AK[1]

[1] National Institute of Nutrition and Seafood Research (NIFES), P.O. box 2029 Nordnes, N-5817, Bergen, Norway; [2] Department of Biology, University of Bergen, P.O. box 7803, N-5020, Bergen, Norway;[3] Nutritional Sciences Division, King's College London, Franklin-Wilkins Building, 150 Stamford Street, London, SE1 9NH, UK; [4] Norwegian Forest and Landscape Institute, Fanaflaten 4, N-5244 Fana, Norway; [a] Present address: University of Canterbury, Christchurch, New Zealand.

Abstract

Nutrients commonly present in seafood, such as long chain omega-3 fatty acids, are known to be beneficial for brain development. Effects of maternal exposure to 2,2',4,4' tetra-bromo diphenylether (BDE47) was investigated, alongside the potential ameliorating impact of seafood nutrients, through assessment of neurobehaviour and gene expression in brain and liver. Developing mice were exposed during gestation and lactation via dams dosed through casein- or salmon-based feed with low background contamination, spiked with BDE47. Two concentrations were used: a low level (6µg/kg feed) representing an environmentally realistic concentration; and a high level (1900µg/kg feed), representing a BDE47 intake much higher than expected from frequents consumption of contaminated seafood. Experimental groups were similar with respect to reproductive success, growth and physical development. Minor, transient changes in neurobehavioural metrics were observed in groups given the highest dose of BDE47. No significant differences in behaviour or development were seen on postnatal day18 among maternally exposed offspring. Accumulation of BDE47 in pups reflected the BDE47 dose consumed by the dams, however, the pups of dams exposed to salmon-based diets had significantly lower BDE47 accumulation in liver, brain and adipose tissues than pups of the casein-fed dams. Cerebral gene-expression investigated by microarray analyses and validated by RT-qPCR showed low fold changes for all genes, despite dose-dependent accumulation of BDE47 in brain tissue. The gene for glutamate ammonia ligase was upregulated compared to control in the casein-based high BDE47diet, without further demonstrated impacts on downstream synaptic transmission. The study supported a previously observed regulation of *Igfbp2* in brain with BDE47 exposure. Genes for hepatic metabolic enzymes were not influenced by BDE47. In conclusion, the potential neurotoxic effects and neurobehavioural aberrations after perinatal exposure to high levels of BDE47 were not readily observed in mice pups with the present experimental exposure regimes and methods of analysis. Nevertheless this study highlights the importance of effects of nutrition in relation to toxicology.