Prenatal exposure effects of repeated oral dose of domoic acid on neurobehavior in mice

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Domoic acid (DA) is an algal toxin which has been associated with significant neurotoxicity in human, non-human primates, rodents, and marine mammals. Developmental exposure to DA is believed to result in neurotoxicity that may persist into adulthood. DA is produced by harmful algal blooms of Pseudo-nitzshia and thus consumption of contaminated marine seafood is of potential concern. We evaluated oral exposures to DA during pregnancy in mice where exposures occurred during early neurodevelopment. Doses of 0 (vehicle), 1, or 3 mg/kg of DA were administered by gavage to C57BL/6 mice on gestational days 10 to 17. These doses represent human relevant exposures. The offspring were tested for persisting neurobehavioral consequences during neonate, adolescence and adulthood. DA did not induce dose related decreases in body weights of dams or offspring. Neurobehavioral tests revealed both dose and sex-related differences in several neurobehavioral measures including anxiety in elevated plus maze, walking patterns in CatWalk test, home-cage behaviors, and memory in the Morris water maze. This study demonstrated significant sex-specific and persistent neurobehavioral effects of repeated prenatal exposures to DA at low-dose levels that did not induce toxicity in dams. This study adds significant new information to the literature as most previous studies have focused on exposure routes/patterns with less relevant exposure pathways. (Supported by the Pacific Northwest Center for Human Health and Ocean Studies (NIH/NIEHS: P50 ES012762 and NSF: OCE-0434087, OCE-0910624 and 1128883))