

## **FISH NUTRIENTS AND METHYLMERCURY IN EXPERIMENTAL MODELS**

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Fish are the source of important nutrients but are also the primary, if not the sole, source of human methylmercury exposure. This alone presents a dilemma, but one that is further confounded by the presence of conflicting results from major studies of fish-eating populations. Even the best epidemiological studies are correlational and cannot completely control for other important factors that can influence the key behavioral markers of hazard and benefit that derive from fish consumption. Experimental models provide the requisite control but they must be sensitive enough to detect the consequences of low-level exposures that most people experience.

Our group has conducted a series of studies in which rats were exposed to methylmercury (0, 40, or 400  $\mu\text{g}/\text{kg}/\text{day}$ ) during gestation or adulthood. Half of these animals consumed a purified diet containing low levels of selenium or, in separate studies, the n-3 polyunsaturated fatty acid, DHA. The other half consumed higher levels of these nutrients. The offspring of the pregnant rats were tracked through adulthood and aging. The animals exposed only as adults were also allowed to age. Highly advanced cognitive and motor endpoints were examined. Thus, we have information about developmental and adult-onset exposures to methylmercury and lifelong consumption of diets containing important fish nutrients.

Selenium, but not DHA, conferred substantial protection against neuromotor effects of adult-onset methylmercury exposure. By itself, selenium also showed benefits on motor tasks as the animals aged.

Developmental exposure to methylmercury, even at the lower exposure level, resulted in substantial and reproducible effects on a task (discrimination reversal) thought to model human executive function. Developmental exposures also enhanced sensitivity to the behavioral actions of drugs that act on the neurotransmitter, dopamine. No protection against methylmercury's developmental neurotoxicity was seen by either DHA or selenium, although both nutrients conferred benefits of their own. We conclude that selenium is neuroprotective against adult-onset methylmercury exposure and has some neural benefits of its own, especially in aging animals.