National Institute of Environmental Health Sciences

Superfund Research Program

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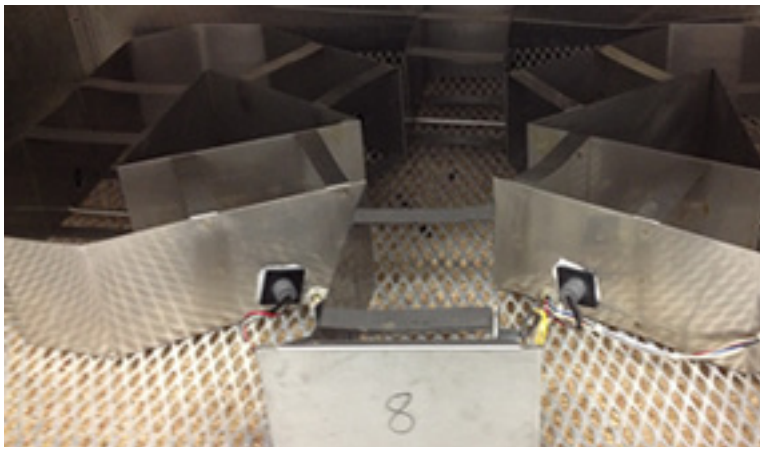
Combined Exposure to Glucocorticoids and Chlorpyrifos Influences Neurobehavioral Development

Prenatal glucocorticoid treatment, used to speed up the development of a preterm infant's lungs, has the potential to worsen the outcome of later exposures to toxins, according to findings by the Duke University Superfund Research Program (SRP). The study in rats, led by Ed Levin, Ph.D., and Ted Slotkin, Ph.D., explored how exposure to glucocorticoids, a type of steroid, before birth changes the effect of the insecticide chlorpyrifos on behavioral development. The findings have implications concerning the interaction of maternal stress, which increases prenatal glucocorticoid exposure, and susceptibility to later toxicant exposure.

At Duke, researchers are exploring how glucocorticoid treatment makes the developing brain more sensitive to later exposures to organophosphates, such as chlorpyrifos, the most widely used class of insecticides. Glucocorticoids are the consensus treatment for preventing respiratory distress syndrome in neonates born prior to 34 weeks of gestation. Recent studies have shown that excess levels of glucocorticoids during pregnancy can produce neurodevelopmental disorders in children.

Understanding co-exposure

Researchers exposed pregnant rats to dexamethasone, the most commonly used glucocorticoid for preterm labor, during the stage of prenatal brain development in which glucocorticoid therapy is typically given. They then exposed offspring to chlorpyrifos after birth. The study in rats included four treatment groups: unexposed, dexamethasone alone, chlorpyrifos alone, and dexamethasone followed by chlorpyrifos. The scientists performed tests on the offspring to assess behavioral activity, emotional response, and movement.



Scientists placed each of the test animals in a maze with a figure 8 shaped path (shown above) and measured their locomotor activity. The testing system evaluates the exploratory behavior of the test animal and assesses when it becomes familiar with its environment. (Photo courtesy of Ed Levin)

For some behaviors, treatment of either chlorpyrifos or dexamethasone caused small but similar changes compared to unexposed rats. When rats were exposed to both chemicals, the effects on these behaviors became much larger. Behavioral abnormalities previously shown to be caused by neonatal chlorpyrifos exposure were worsened in animals that received prenatal dexamethasone treatment.

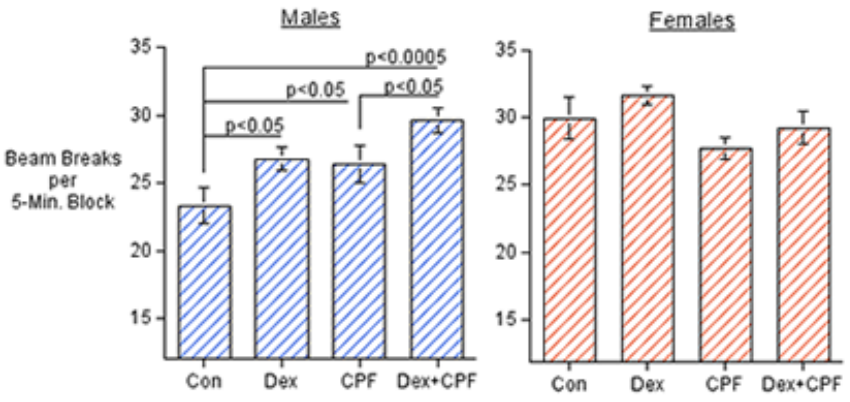
According to the study authors, the combined exposures to dexamethasone and chlorpyrifos not only cause long-term neurochemical changes, as previously reported by the research group,[1] but also cause long-term functional behavioral impairments. Researchers saw differences in a spectrum of behavioral functions including cognition, emotional response, and spontaneous behavior.

Behavioral changes by sex

For some behaviors where rats normally have a sex difference in performance, the combined treatment either eliminated or reversed the sex difference.

Previous work by Levin and Slotkin in animals has shown that developmental exposure to chlorpyrifos interferes with sexual differences of behavioral performance.[2] The new study indicates that this, too, is likely to be enhanced in subjects exposed to prenatal glucocorticoids.

According to the authors, these results reinforce the idea that an individual's "chemical history" may be just as important as genetic differences in determining later susceptibility to environmental toxicants. The findings also have important implications for understanding the effects of maternal stress and the use of specific drugs in preterm labor on child development.



Rats were tested on their activity level in the figure 8 maze. The mean activity for unexposed males was significantly lower than unexposed females (Con). All of the treatments significantly increased activity in males. With co-exposure to dexamethasone (Dex) and chlorpyrifos (CPF) there was a significantly worsened effect of CPF on the males and no longer a normal difference in activity between sexes. (Photo courtesy of Ed Levin)

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For more information, please refer to the following source:

Levin ED, Cauley M, Johnson JE, Cooper EM, Stapleton HM, Ferguson PL, Seidler FJ, Slotkin TA. 2014. Prenatal dexamethasone augments the neurobehavioral teratology of chlorpyrifos: Significance for maternal stress and preterm labor. Neurotoxicology and Teratology 41:35-42. doi: 10.1016/j.ntt.2013.10.004

[1]Slotkin TA, Card J, Infante A, Seidler FJ. 2013. Prenatal dexamethasone augments the sex-selective developmental neurotoxicity of chlorpyrifos: implications for vulnerability after pharmacotherapy for preterm labor. Neurotoxicology and Teratology 37:1-12. doi: 10.1016/j.ntt.2013.02.002

[2]Levin ED, Addy N, Nakajima A, Christopher NC, Seidler FJ, Slotkin TA. 2001. Persistent behavioral consequences of neonatal chlorpyrifos exposure in rats. Developmental Brain Research 130:83-89. doi: 10.1016/S0165-3806(01)00215-2