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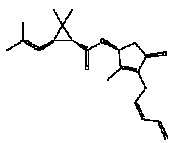
Deltamethrin, a Pyrethroid Insecticide, Increases Dopamine Transporter Levels and Locomotor Activity

OVERVIEW

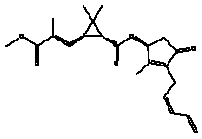
It is imperative to understand the extent to which exposure to insecticides affect the nervous systems of mammals. Since the majority of insecticides are neurotoxicants and the insects targeted for eradication share similar target sites for toxicity as non-target organisms, there is significant risk for damage to non-target organisms.

Subtle changes in neurochemistry induced by low-level exposure can have a critical impact on normal neurochemical and behavioral function. It is therefore essential to evaluate the impact of lower doses of insecticides on non-target organisms to determine the possible neurotoxic effects that may be occurring in the environment.

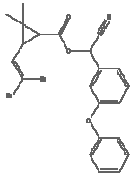
Pyrethroid insecticides are of particular interest because of their widespread use. These compounds are utilized in foggers, sprays, shampoos, and insect-repellant clothing. Here, we demonstrate that exposure to deltamethrin, a synthetic derivative of pyrethrin, increases the levels of a key protein involved in maintaining dopamine homeostasis. This protein is the dopamine transporter, and it is important because regulating dopamine is vital for voluntary movement, reward detection, and spatial learning.



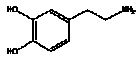
Pyrethrin I



Pyrethrin II



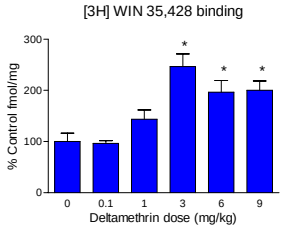
Deltamethrin



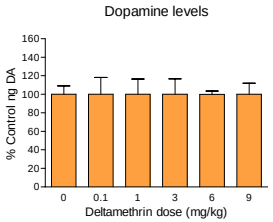
Dopamine

RESULTS

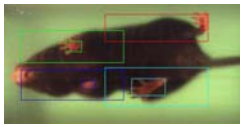
BINDING



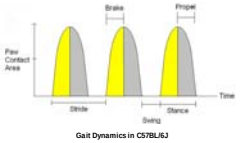
HPLC - ECD



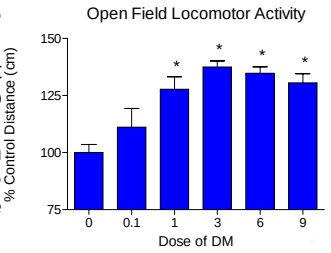
GAIT ANALYSIS

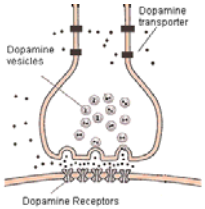


TreadScan software

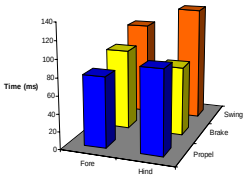


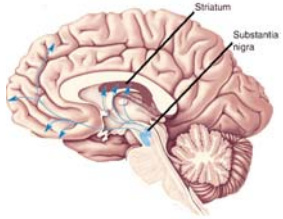
LOCOMOTOR ACTIVITY



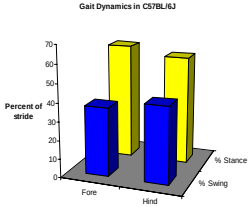


Dopamine Synapse





Nigrostriatal Dopamine System



APPROACH

The research plan combines molecular, neurochemical, and behavioral studies to elucidate the changes caused by pyrethroid exposure. Nigrostriatal neurons will be evaluated for changes in neurochemistry, using high-performance liquid chromatography coupled to electrochemical detection, radioligand binding & uptake, and immunoblotting. Additionally, real-time PCR will be used to determine effects on the dopamine system at the molecular level. Behavior measures tested will be open-field locomotor activity and gait analysis, both utilizing sophisticated video tracking software to maximize data collection.

DISCUSSION

These results demonstrate that exposure to deltamethrin increases the levels of the dopamine transporter, as measured by binding and immunoblotting. This phenomenon is correlated with an increase in the basal locomotor activity. The dopamine system appears to be particularly sensitive to the effects of deltamethrin since we observed no change in [^{3}H]nisoxetine binding to the norepinephrine transporter and [^{3}H]paroxetine binding to the serotonin transporter. The total levels of dopamine, norepinephrine, and serotonin were not changed in the striatum. Future studies will be focused on determining what other changes have occurred in the dopamine synapse, including the sensitivity of the postsynaptic dopamine receptors. Animals exposed to deltamethrin are currently being evaluated by gait analysis to determine if the changes in the dopamine system are correlated to changes in motor behavior.

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