

**Department of Pediatrics
COLLEGE OF MEDICINE**

**SUMMER RESEARCH OPPORTUNITIES
FOR UNDERGRADUATE WOMEN**

APPLICATION DEADLINE: March 2, 2009

The Department of Pediatrics is pleased to offer the following research project for the summer of 2009. Interested students are urged to contact the faculty member(s) directing the project that most interests them. By contacting the faculty member, you can discover more about the project, learn what your responsibilities will be and, if possible, develop a timetable for the twelve-week research period.

EFFECTS OF DRUGS OF ABUSE ON THE BRAIN AND BEHAVIOR

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PROJECT DESCRIPTION

Dr. Vorhees' laboratory is investigating the effects of drugs of abuse on brain and behavior in collaboration with the adjoining laboratory of Dr. Michael Williams. The drugs currently investigated are methamphetamine and MDMA ('ecstasy').

We know that methamphetamine given during early development to rats at a stage analogous to human third trimester, leads to learning and memory impairments in the offspring when tested as adults and that these effects are irreversible, and as far as we currently know are irremediable. Methamphetamine also causes a significant and prolonged release of the stress hormone corticosterone and reduces levels of the neurotransmitter serotonin. Although methamphetamine reduces the neurotransmitter dopamine in adult brain, in the developing brain this effect is absent. To test the role of corticosterone, we adrenalectomized rats before treating them with methamphetamine. Unfortunately, this caused exaggerated reductions of brain serotonin once methamphetamine treatment began. In order to resolve this problem, we adrenalectomized the rats and then placed the adrenals back in the abdominal cavity. This technique allows the adrenals to engraft to surrounding organs spontaneously. We showed experimentally that such replaced adrenals reattach and regain partial function (about 20% of normal). This allows adrenal output but dampens the response such that methamphetamine induced only a fraction of the corticosterone release seen in intact rats. Equally important, the

partial adrenal function prevented the methamphetamine-induced exaggerated serotonin reduction seen in adrenalectomized rats. With this revised approach, we treated a group with replaced adrenals + methamphetamine and tested them as adults. Methamphetamine-treated offspring, with or without autotransplantation, were impaired. This showed that the drug-induced increase in corticosterone release is not the cause of the long-term learning impairments. This summer we are planning experiment to test the role of serotonin in the mechanism of methamphetamine-induced learning impairments by blocking the effect of methamphetamine on serotonin release by pretreating rats with a selective serotonin reuptake inhibitor (SSRI).

In addition, experiments on the adult cognitive effects of methamphetamine are planned as are experiments on the developmental effects of MDMA.

Students will primarily be involved in testing rats in a series of procedure to assess spatial and path integration learning, as well as locomotor activity, latent inhibition, acoustic startle reactivity, and anxiety. Students will work with other summer students and technicians, as well as graduate students and postdoctoral fellows.