Reproductive Neurobiology Research

CORE CONCERNS AND COMPETENCIES

What is the relationship between reproductive biology and the brain? Researchers at the Cummings School of Veterinary Medicine at Tufts are looking at a number of aspects of this question. Their answers, based in the intersection between neuroscience and behaviors around pregnancy, may have major implications for women's health, child development, and social well-being. Using animal models, primarily rats and mice, they are looking at physiological and chemical changes in the brain and gene-environment interactions as they relate to both normal and abnormal behaviors in the context of reproduction and lifelong health.

The research approach of the Reproductive Neurobiology Group bridges the gap between basic and clinical research in an effort to establish new understandings of how the biology of the brain and the reproductive experiences of females impact their and their offsprings' mental health and the successful rearing of young. Whereas a central focus of this research is to establish what is normal in terms of physiology and neurobiology, there are strong linkages to mental and other health topics. Among the avenues being pursued are:

- **Neurobiology of Parental Care:** This research is designed to investigate whether certain hormones affect changes in mood or behavior around the time of birth or the early postpartum period. The implications of this research include a better understanding of mood disorders such as postpartum depression and also of how the brain regulates anxiety after giving birth. Work in the area of hormone-brain interactions has shown that female rats that have experienced pregnancy are likely to be less anxious in the short term and more anxious in the long term than their counterparts that did not. Applications of this research could extend to the use and dosing of psychotropic and pain medications as prescribed to women with or without reproductive experience as well as men.

- **Hormonal Regulation of Maternal Behavior:** Tufts researchers are looking at how the experience of being a mother changes brain sensitivity to hormones. Injections of the hormone prolactin, which is crucial for lactation, directly into specific neural sites of inexperienced female rats stimulate maternal care. Moreover, once females have raised young, their neural sensitivity to prolactin increases in regions of the brain that regulate maternal care. Current research is aimed at understanding the underlying mechanisms that mediate prolactin's and other neurochemicals' actions on the brain and behavior.

- **Neurogenesis during Pregnancy:** New neurons are generated in the brains of mice and rats during pregnancy. Tufts researchers are trying to understand what the functional significance is of this gestational neurogenesis. Building on the finding that mothers display a rapid reestablishment of maternal care months following an initial postpartum experience, Tufts researchers are exploring the possibility that new neurons being produced during pregnancy are integrated into the olfactory system and are involved in the formation of "maternal memory." Hence, a mother starts to identify or link certain smells associated with the postpartum period with the young.

- **Transgenerational Consequences of Drug Addiction:** By exposing rats to morphine before pregnancy, researchers are investigating a possible link between drug use during adolescence and effects on opiate sensitivity in the next generation. Compelling findings show that the offspring of laboratory animals may be affected by drug-induced changes in the mother's brain or endocrine system that occurred weeks before gestation commenced and the mother gave birth to the affected young.

Reproductive Neurobiology CONTINUED

- **Genetic Modeling Related to Autism and Mood Disorder:** Reproductive success is tied to one's social behavior, which develops under the influence of genes and environmental conditions. Using genetic tools, researchers at the Cummings School have successfully manipulated the activity of specific genes in the mouse brain, which leads to significant changes in a mouse's social behaviors. Such changes can also be induced by modifications in the early social experience of mice. Analyses of chromatin modifications and gene expression reveal that the social brain appears to be plastic, responding to both gene and behavioral therapies by chromatin remodeling and expression reprogramming. This research contributes to our understanding of how brain sex differences are modified by sex hormones and/or sex chromosomes and can differentially affect the relative impact of genes in males and females in conditions like autism and mood disorders.

- **Links to Cancer Research:** Some of the findings show long-term changes in hormone secretion as well as in hormone receptor expression both in the brain and in memory tissue and in the liver among females who have experienced pregnancy. Further study could explore whether there is a link between reproductive experience and females' susceptibility to cancer or immune function. This includes research on whether certain hormones are associated with cell proliferation and possibly tumor growth.

SELECTED PRINCIPAL INVESTIGATORS

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FUNDING SOURCES

- National Institutes of Health
- National Institute of Child Health and Human Development
- National Institute on Drug Abuse
- National Science Foundation

TECHNICAL CAPABILITIES

Animal Surgery (Rodents)
- Catheterization
- Gonadectomies
- Stereotaxic
- Subcutaneous Implant Devices

Behavioral Testing
- Activity (computerized chambers)
- Aggression
- Anxiety (elevated plus maze)
- Maternal Behaviors
- Prepulse Inhibition

Biochemical Techniques
- Chromatin Immunoprecipitation assays (ChIP)
- High-pressure Liquid Chromatography (neurotransmitters)
- Hormone Assays (Elisa & radioimmunoassay for proteins, peptides & steroids)
- Microarrays
- Polymerase Chain Reactions (PCR)
- Western Blots

Microscopy
- Florescence Microscopy
- *In situ* hybridization histochemistry
- Light and Dark Phase
- Tissue Sectioning (Cryostat)