Endocrine Disruption of the Neuro-immune Interface

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What is the neuro-immune interface?

The interactions between the nervous and immune systems and the cross-regulatory impacts of these interactions on both immune and nervous system function.

--M.J. Carson in *Molecular Mechanisms and Consequences of Immune and Nervous System Interactions*

OR

What the immune system does to the nervous system and what the nervous system does to the immune system and how they respond.
The immune system can impact cognition

Immune dysfunction underlies neurological diseases (?)

Immune dysfunction can arise during development

- Autoimmunity
- Allergic Disease
- Normal Immune Response
- Immunosuppression and the identification of sensitizing chemicals

Misregulated Inflammation
Inflammatory Disease/Tissue Damage

But what about the endocrine system and EDCs?

Nervous System

Endocrine System

Disease

Health

Immune System
An example: Brain sex development

Microglia (cells of the immune system) respond to a postnatal surge of testosterone (a hormone that is converted to estrogen in the brain) to masculinize dendritic spines on neurons (nervous system).

Microglia Are Essential to Masculinization of Brain and Behavior
Lenz KM, Nugent BM, Haliyur R, and McCarthy MM
The Journal of Neuroscience, 2013, 33:2761–2772
An example: Brain sex development

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Brief summary of the Lenz et al. (2013) study:

- Females given estrogen or prostaglandins postnatally, have masculinized microglia.
- Females given estrogen postnatally have masculinized sexual behavior as adults.
- When microglial activity is blocked, this masculinization of microglia and sexual behavior in females is prevented.
- Males given a drug that blocks prostaglandin synthesis have feminized microglia.

THEREFORE, hormone disruption during this sensitive early postnatal period can impact adult sexual behavior.
An example: Brain sex development

But what happens during *prenatal* development?

When males receive high doses of estrogen *prenatally*, they have feminized genitalia and hypermasculinized adult sexual behavior (K. McCoy, unpublished data).

![Figure 1](image)

*Figure 1.* Males given E for three days embryonically (E13.5-16.5) have hypermasculinized reproductive behavior relative to males given a corn oil control embryonically.
An example: Brain sex development

We propose that prenatally, exposure to EDCs can change how the immune system responds to postnatal hormones, leading to changes in brain development and adult sexual behavior.
An example: Brain sex development

THEREFORE, hormone disruption during this sensitive *prenatal* period can impact *adult* sexual behavior.

As we learn more about how brain sex develops and how the endocrine, immune, and nervous systems interact, we find more and more complex critical windows of developmental exposure.

End game: more research into the basic science of development is required before we can even begin to understand the extent to which exposure to EDCs may impact development.
Collaborators

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Thank you!