

# Endocrine Disruption of the Neuro-immune Interface

Jamie DeWitt  
East Carolina University  
Brody School of Medicine  
[dewittj@ecu.edu](mailto:dewittj@ecu.edu)



# What is the neuro-immune interface?

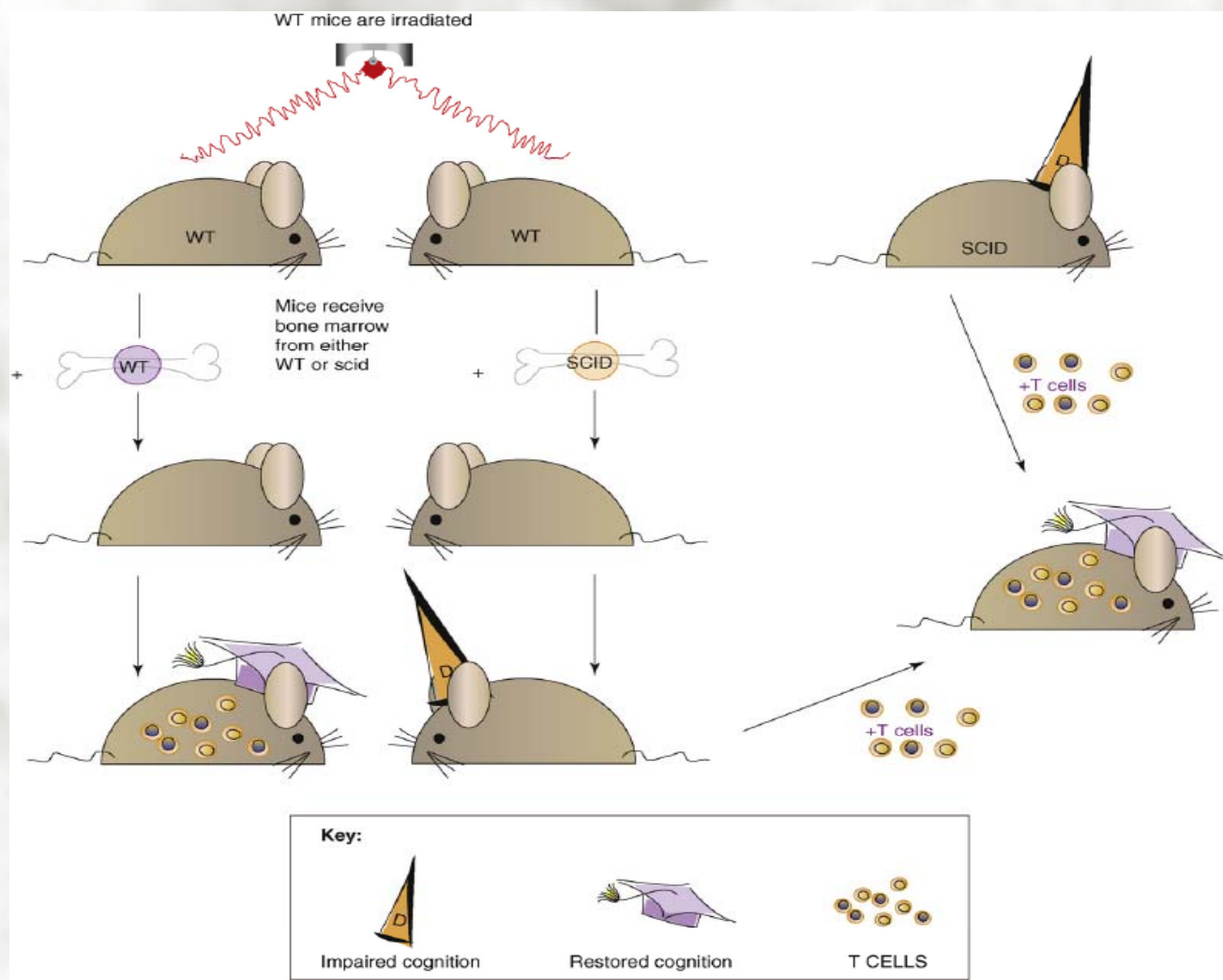
The interactions between the nervous and immune systems and the cross-regulatory impacts of these interactions on both immune and nervous system function.

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

OR

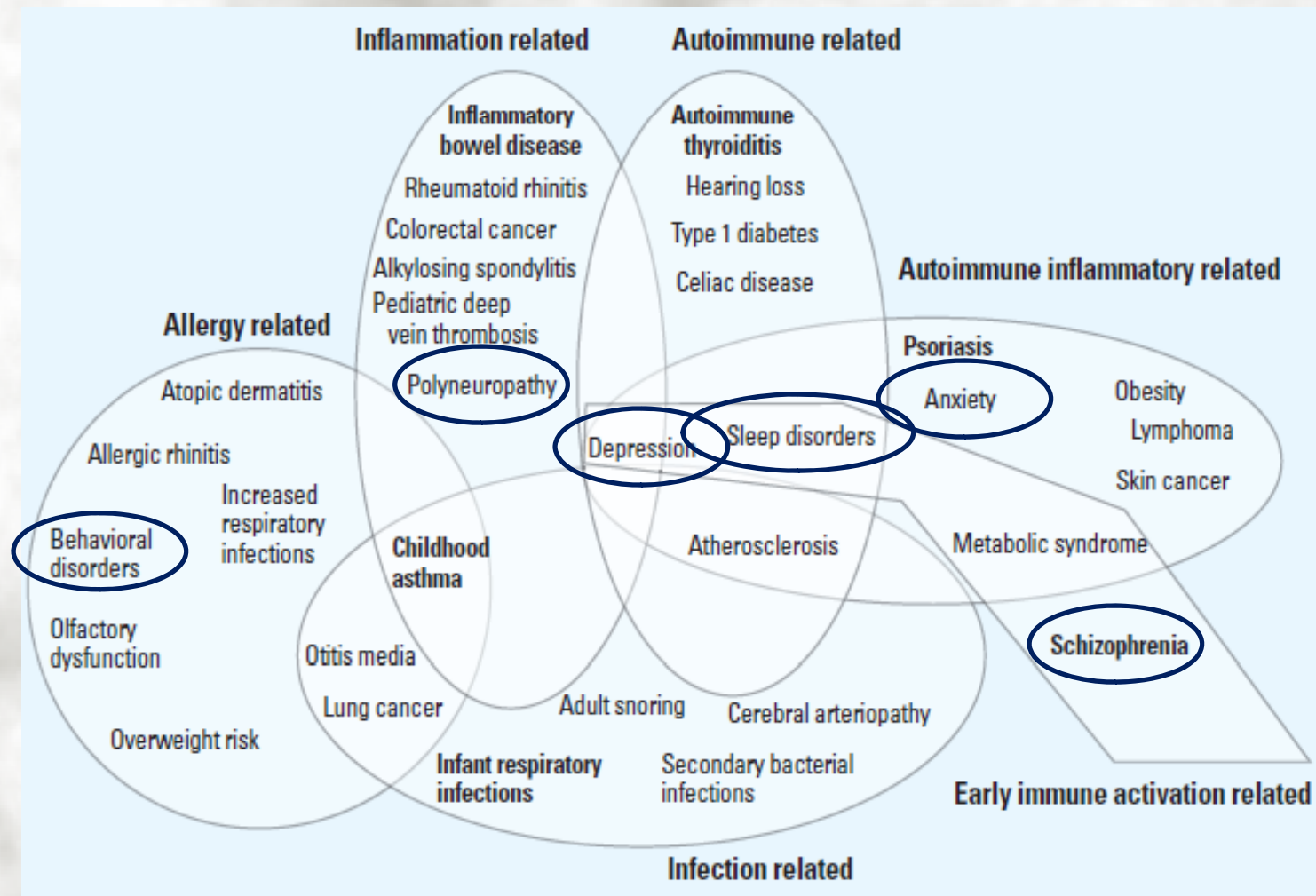
What the immune system does to the nervous system and what the nervous system does to the immune system and how they respond.

# The immune system can impact cognition

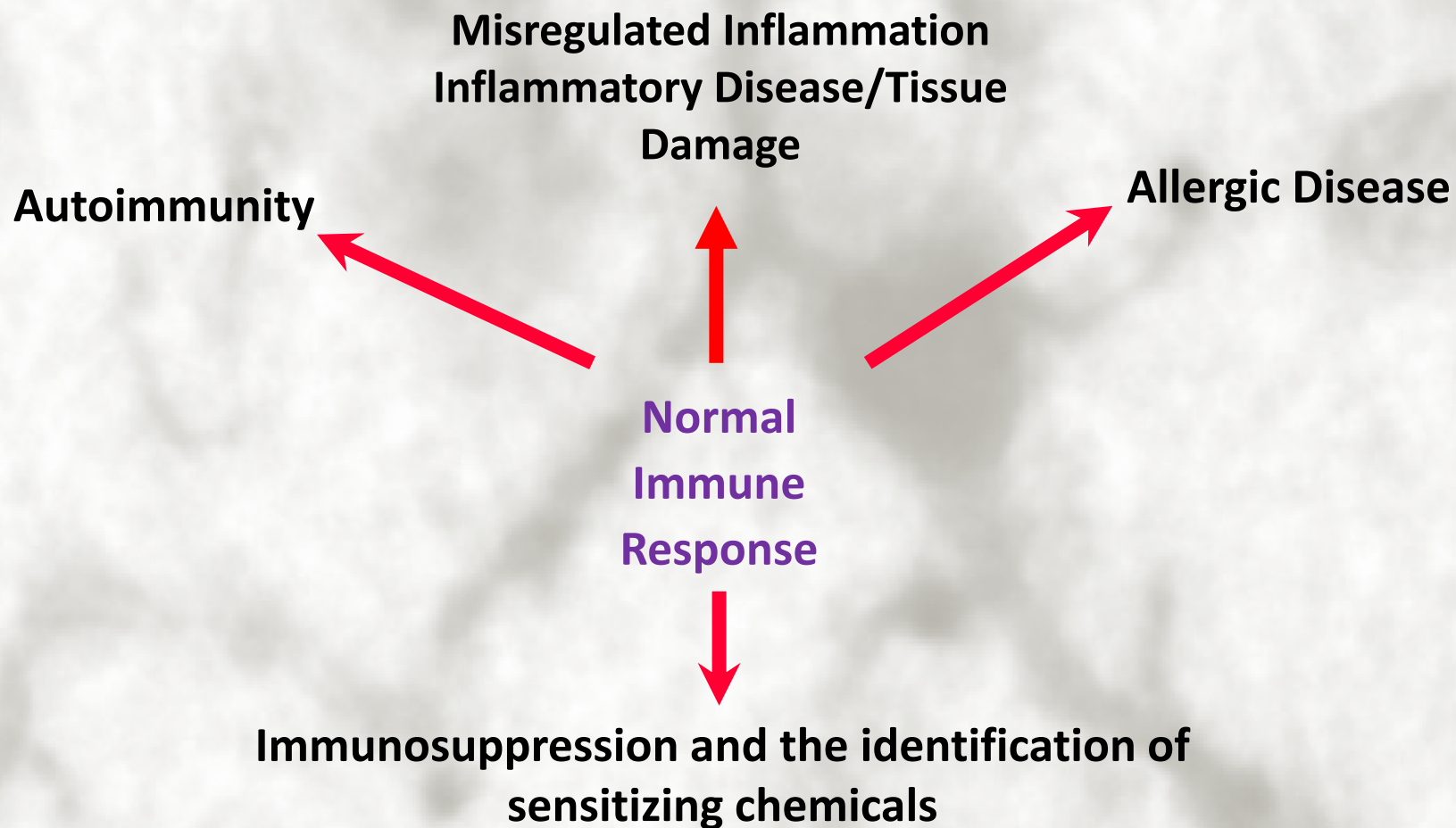


From: Kipnis, Derecki, Yang, and Scrable, *Trends in Immunology*, 2008.

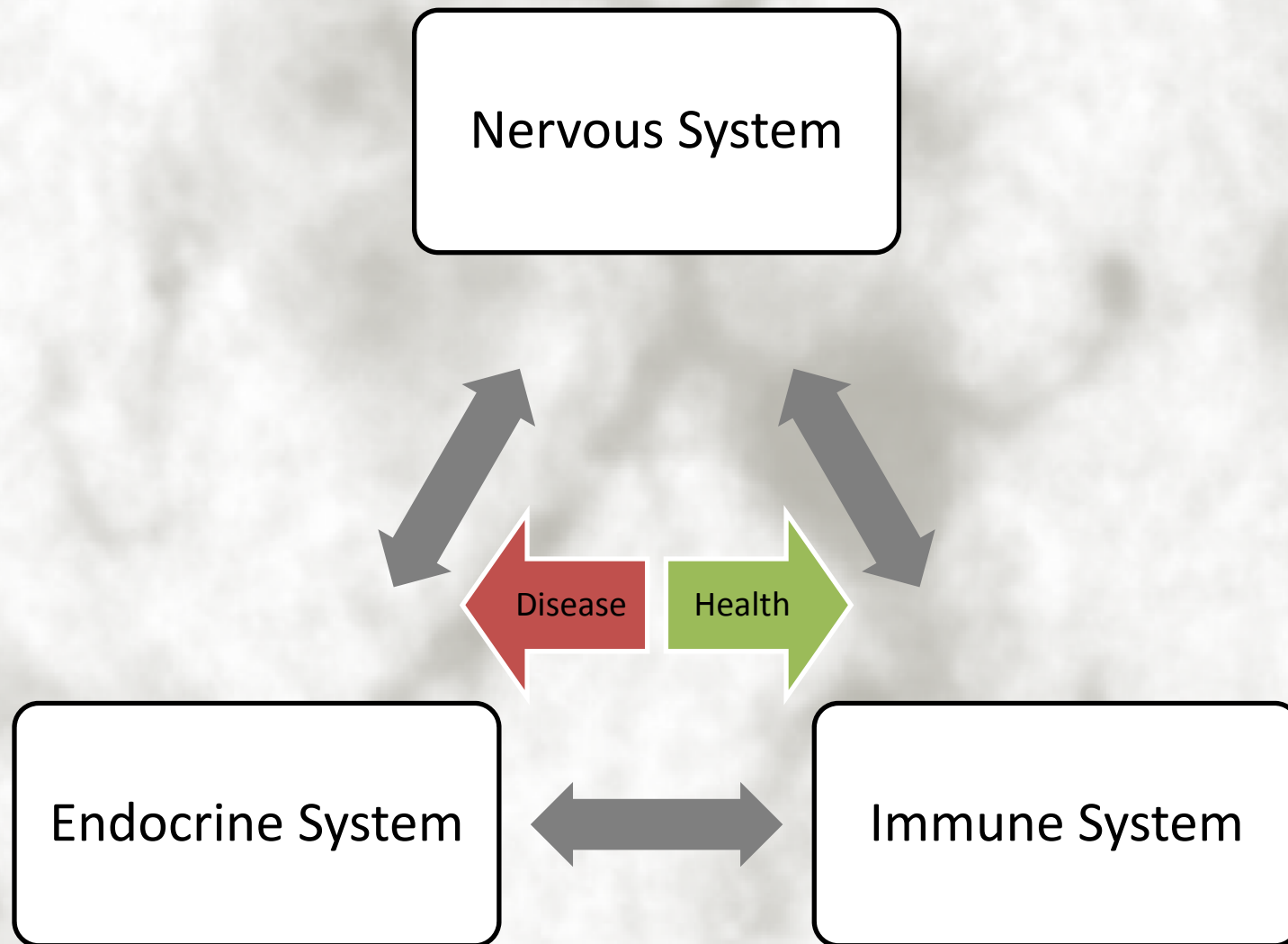
# Immune dysfunction underlies neurological diseases (?)

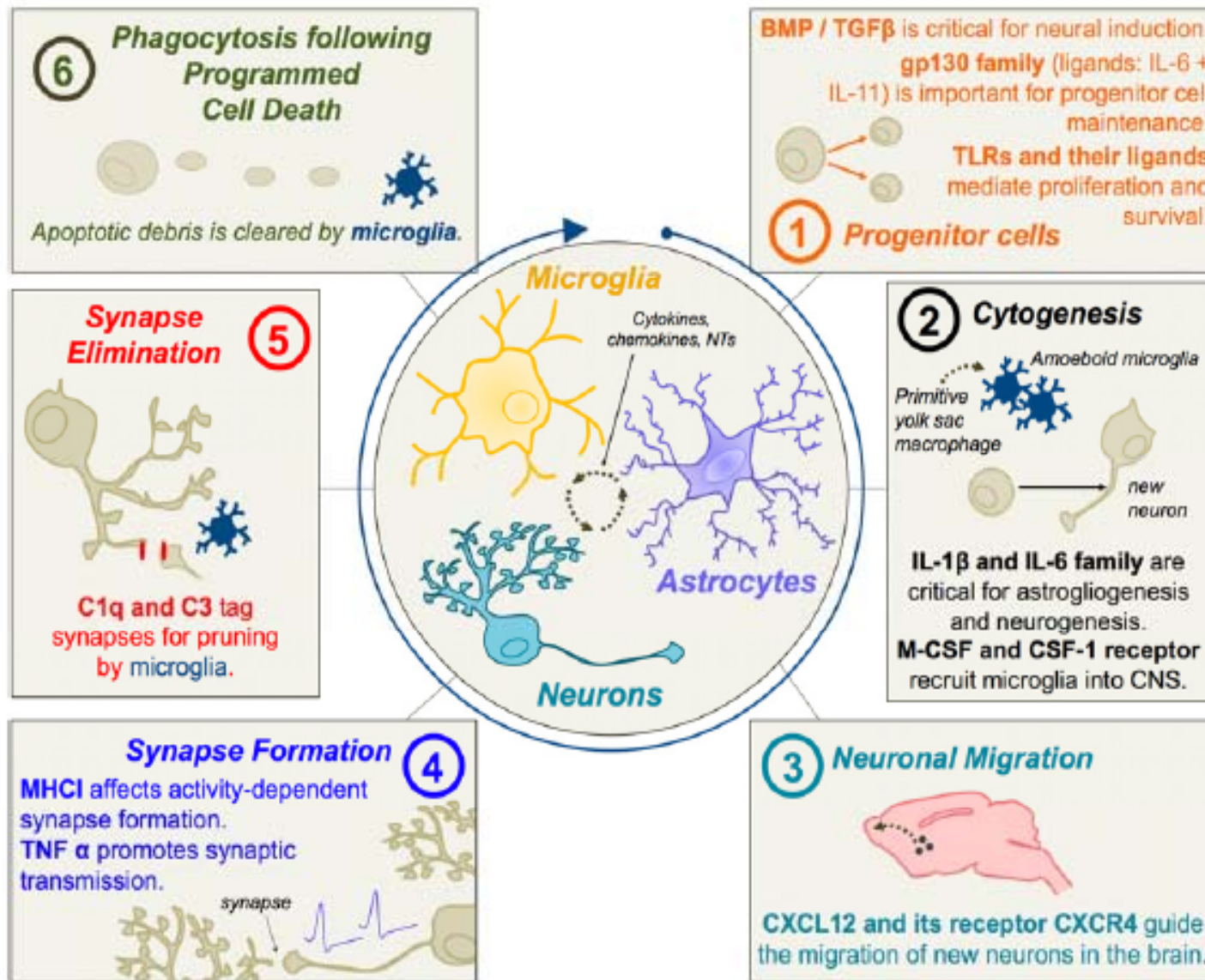


# Immune dysfunction can arise during development



# But what about the endocrine system and EDCs?





# An example: Brain sex development

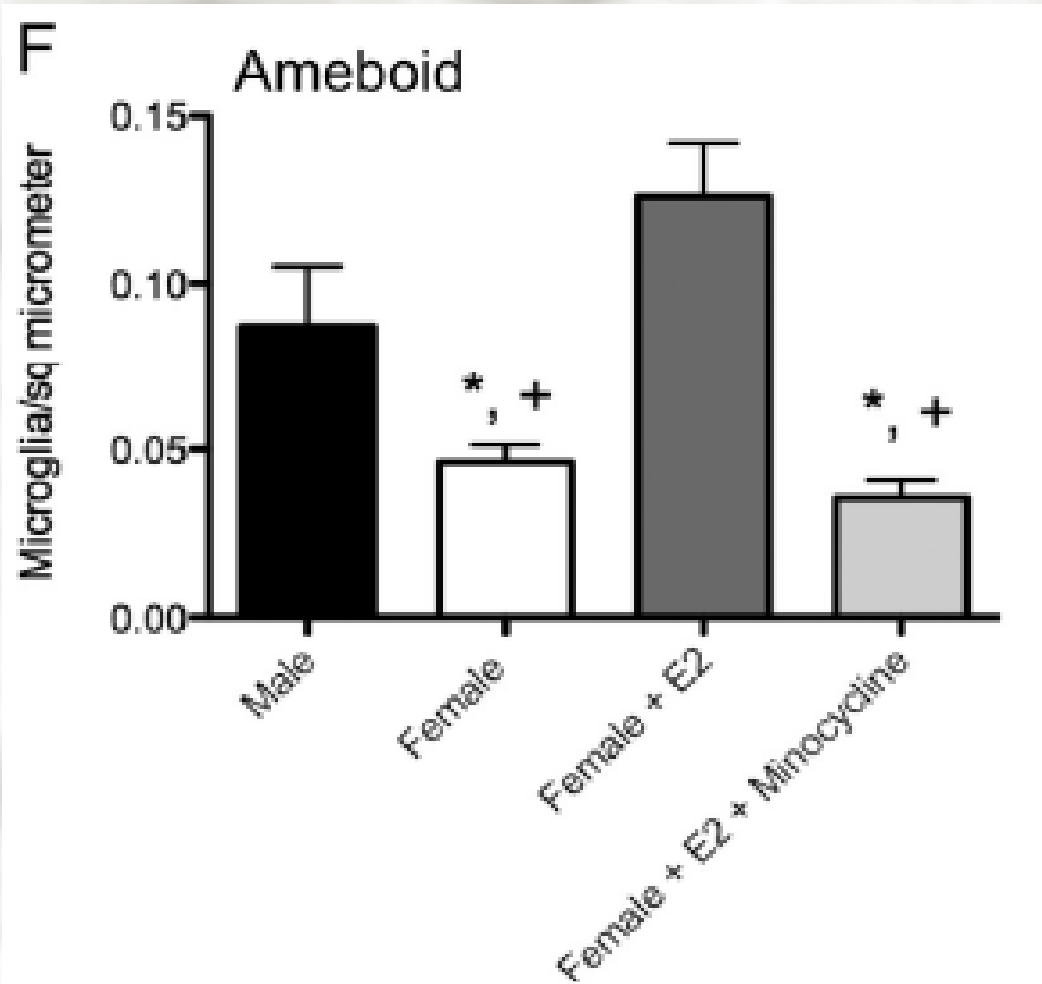
Microglia (cells of the immune system) respond to a postnatal surge of testosterone (a hormone that is converted to estrogen in the brain) to masculinize dendritic spines on neurons (nervous system).

## 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

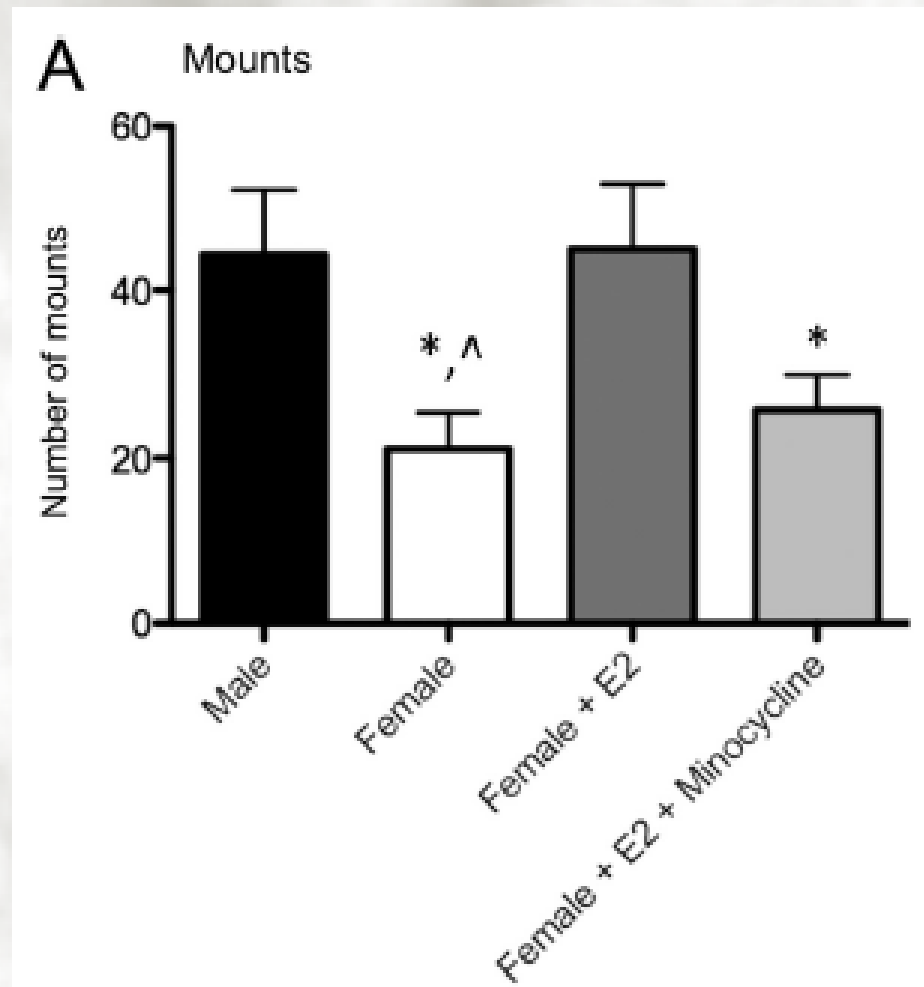


## An example: Brain sex development



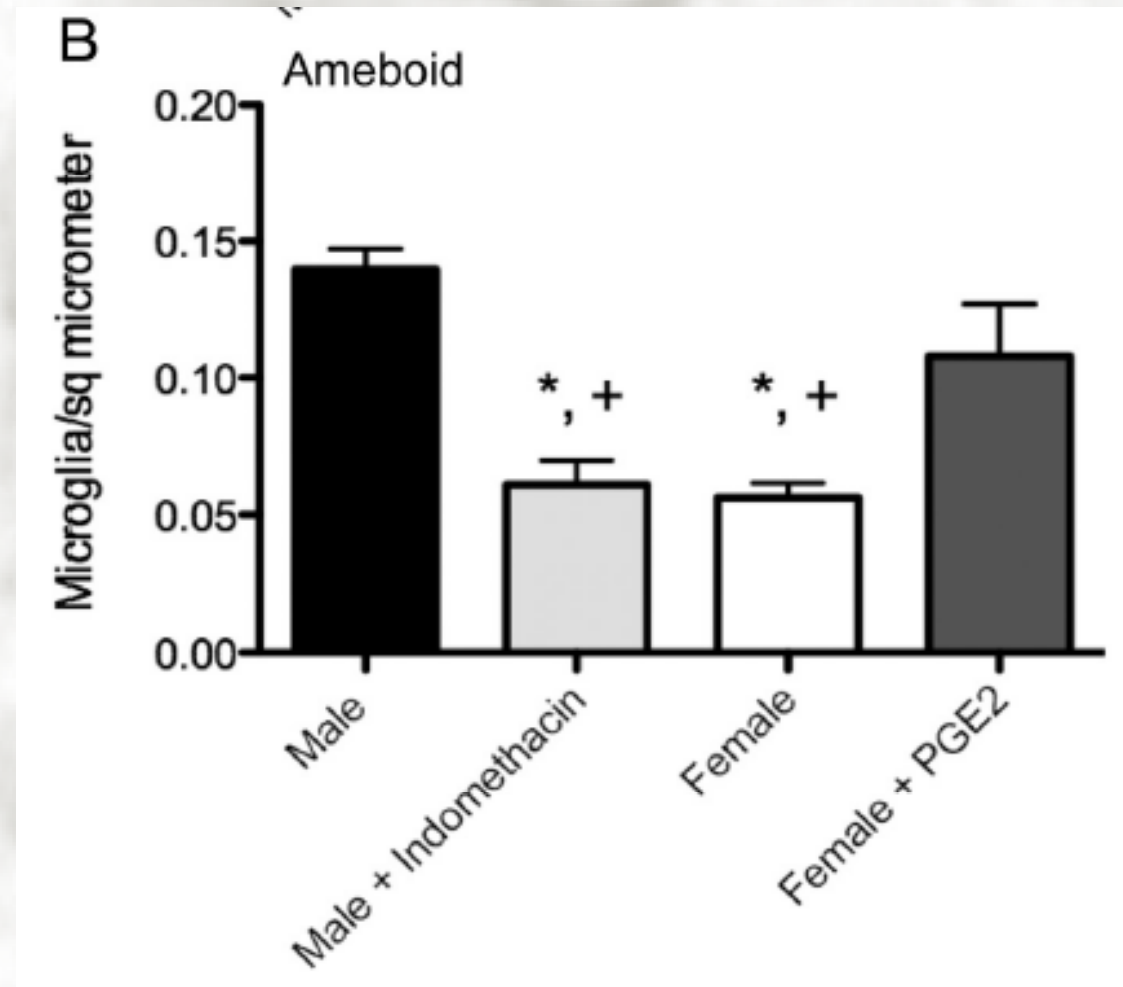
From: Lenz, Nugent, Haliyur, and McCarthy, *The Journal of Neuroscience*, 2013.

# An example: Brain sex development



From: Lenz, Nugent, Haliyur, and McCarthy, *The Journal of Neuroscience*, 2013.

## An example: Brain sex development



## An example: Brain sex development

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

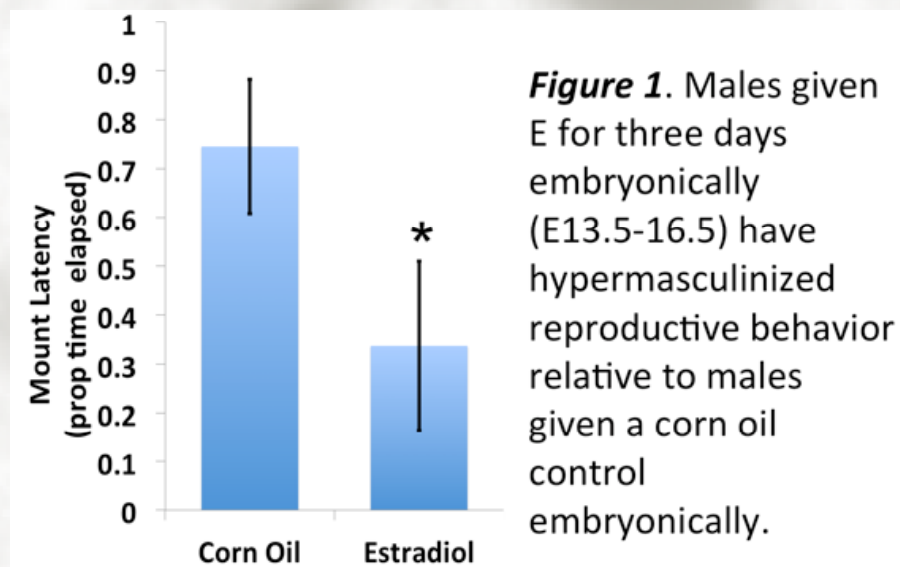
- Females given estrogen or prostaglandins postnatally, have masculinized microglia.
- Females given estrogen postnatally have masculinized sexual behavior as adults.
- When microglial activity is blocked, this masculinization of microglia and sexual behavior in females is prevented.
- Males given a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

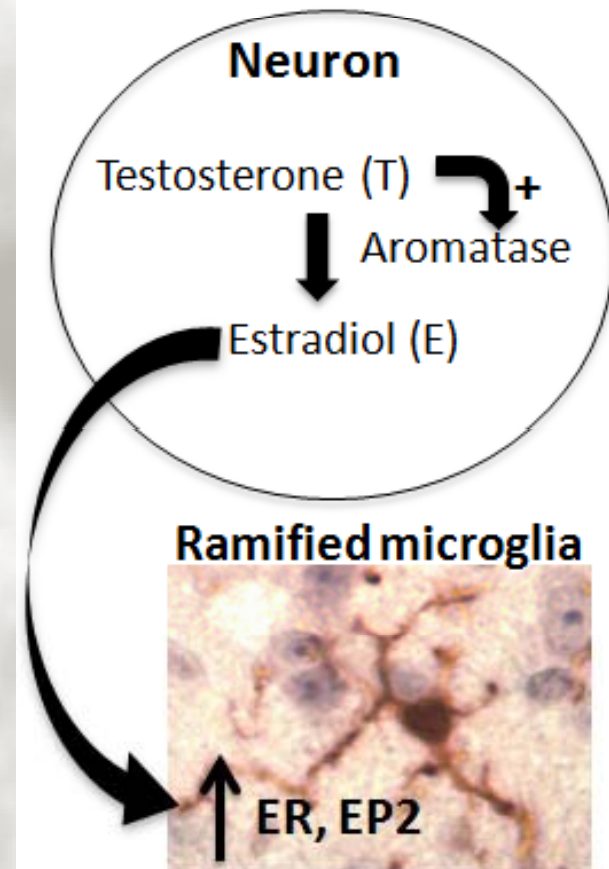
When males receive high doses of estrogen *prenatally*, they have feminized genitalia and hypermasculinized adult sexual behavior (K. McCoy, unpublished data).



# 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.

## *Embryonic programming*



## 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.

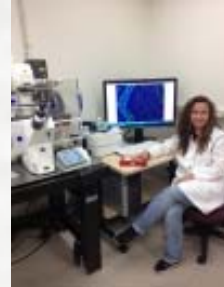
End game: more research into the basic science of development is required before we can even begin to understand the extent to which exposure to EDCs may impact development.

# Collaborators



Dr. Rod Dietert, Cornell University

Dr. Krista McCoy, East Carolina University



Thank you!