

Stress During the Critical Periods: A Programming Dilemma With Windows for Manipulation Brian A. Smith Advised by: Professor Patricia O'Hara and Dr. Richard Aronson

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Stress and the HPA Axis

•Stress is a condition in which the organism senses a challenge to physical or mental stability that leads to altered activities of body systems to meet that challenge.

•The hypothalamic-pituitary-adrenal axis is a major stress effector system in which release of chemicals in the hypothalamus of the upper brainstem effects release of corticotropin (ACTH) from the pituitary gland, and the ACTH stimulates release of steroid hormones from the adrenal cortex, such as cortisol.

Critical Periods

•A "critical period" is a developmental window of susceptibility during which the brain goes through different programming effects.

Multiple critical periods exist, from prenatal to neonatal

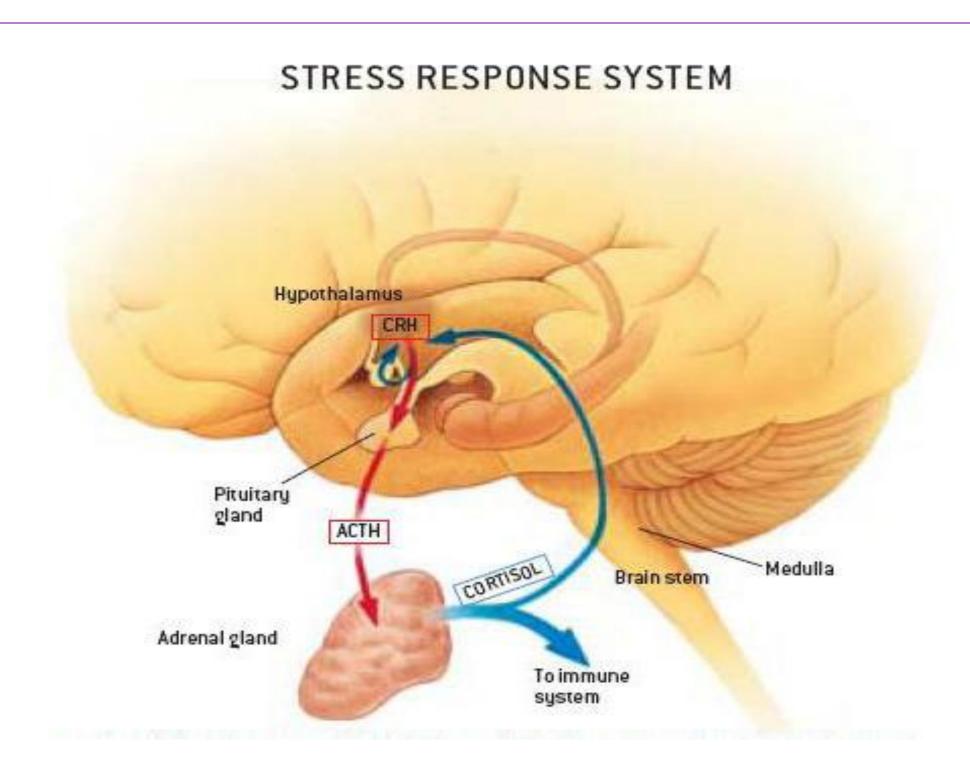
 Identifying developmental processes affected during this window may lead to therapeutic

At-Risk Pregnancies

- Physicians may be able to assess who is at risk for transmission of stress
- Prevention of stress during critical periods
 - This may solve the environmental stress factors
- Utilization of neonatal handling
 - This may solve the both environmental and genetic stress factors

targets or biomarkers that can predict neurodevelopmental diseases

- This could be extremely beneficial in at-risk pregnancies
- Maternal care can affect neonatal health
 - Mothers with increased HPA axis response to stress exhibit lower quality maternal care, resulting in potential for future health problems for offspring



Courtesy: Max Planck Institute for Human Cognitive and Brain Sciences

Neonatal Handling

•What is "neonatal handling?"

Short-term (can be daily) separation of offspring from the mother

•Neonatal handling is a frequent occurrence in modern childbirth

> Vitals are checked to make sure newborn is in good health

•This handling can have different health effects

- Neonatal handling reverses behavioral abnormalities induced by prenatal stress
- Neonatal handling also permanently alters HPA axis function, behavior, and body weight

Public Health

- Prenatal and neonatal stress are highly intertwined in public health problems
 - Low socioeconomic status creates more stress
- Hospitals with fewer resources may not be able to be as vigilant with at-risk pregnancies
- How does one reverse the effects of stress during the first few years of life?
 - Early education, peer support groups, health education, etc.
 - These resources need to be available to everyone
- Focusing on the prevention of prenatal and neonatal stress during critical periods is synonymous with the prevention of adult diseases and disorders

Prenatal Stress

•Prenatal stress results in both physical and behavioral health problems later in life

e.g. Cardiovascular disease, depression, autism •Maternal stress can affect the fetus' long-term health

Direct environmental and epigenetic transmission •Paternal stress can also affect the fetus' long-term health

Indirect environmental and direct epigenetic transmission

•Maternal care can affect neonatal health

Mothers with increased HPA axis response to stress exhibit lower quality maternal care, resulting in potential for future health problems for offspring



A form of neonatal handling, circa 1960s. **Courtesy: Canadian Medical Association Journal**

Conclusion

•Both maternal and paternal stress play vitals roles in the health of the fetus and neonate •Prenatal and neonatal stress can cause long-term health effects, but understanding how this happens can lead to prevention and treatment •A focus on public health solutions can lead to the elimination of fetal-oriented diseases and disorders

References:

Barker, D.J.P. (1994) The fetal origins of adult disease. Fetal and Maternal Medicine Review 671-680. Goldstein, D.S. (2006) Adrenaline and the inner world. Baltimore: Johns Hopkins University Press. Maccari, S. and Morley-Fletcher, S. (2007) Effects of prenatal restraint stress on the hypothalamuspituitary-adrenal axis and related behavioral and neurobiological alterations. Psychoneuroendorcinology 32(Suppl 1):S10–S15.

Morgan, C. and Bale, T. (2011) Early prenatal stress epigenetically programs dysmasculinization in secondgeneration offspring via the paternal lineage. J Neurosci 31(33):11748-11755. Wakshlak, A. and Weinstock, M. (1990) Neonatal handling reverse behavioral abnormalities induced in rats by prenatal stress. Physiology & Behavior 48:289-292.