Annotated Bibliography

Topic: Cortisol/ Stress

Flinn, M. V, Nepomnaschy, P. A., Muehlenbein, M. P., & Ponzi, D. (2011). hypothalamic-pituitary-adrenal axis development in humans. *Neuroscience and Biobehavioral Reviews*. doi:10.1016/j.neubiorev.2011.01.005

I. Evolutionary paradox: Since hormone response to stress has negative developmental and health consequences, why would NS have favored mechanisms that elevate stress hormone levels in response to psychosocial stimuli?

🡪 link stress response to neural plasticity that enables adaptation to dynamic social environment of the human child

II. Physiological mechanisms, developmental plasticity and adaptive function

* Chronic and traumatic stress can diminish health, bc resources are diverted away from important health maintenance systems (i.e. immune regulation) and (cortisol) can inhibit inflammatory responses, alter cytokine production and increase monocyte apoptosis.
* The ability to generate a variety of phenotypes from a single genotype in response to various environmental conditions is referred to as “phenotypic plasticity” (West-Eberhard, 2003).

The Importance of Phenotypic Plasticity and Life History Theory (fetal and early environmental programming)

Early preparation allows for improved specialization and economy of development; the sooner one can adjust development to suit future environments the better. In this way resources are not wasted maintaining abilities to respond to conditions that are unlikely to occur. The balance between predictability and specialization during development influences the ontogenetic trajectories of phenotypic plasticity. “Critical” or “sensitive” periods for environmental input involve this inherent temporal trade-off between the reliability of cues and the advantages of earlier specialization (Alexander, 1990; Mousseau et al., 2009; Shettleworth, 2010).

Possible adaptive/maladaptive functions of HPAA:

* Adaptive function of HPAA: homeostatic mechanisms of the HPAA system appear to be sensitive to exposure to high levels of corticotropin-releasing hormone (CRH) and adrenocrticotropin hormone (ACTH) and cortisol during development. Glucocorticoid receptors (GRs) are neurons in hippocampus and hypothalamus can be effected by excess levels of these, associated with exposure to trauma, which can then have deleterious health effects. \*\*If exposure to trauma was a common occurrence in an animals’ life history, this should be maladaptive, HOWEVER< if it provided useful environment about the future environment (food shortage, risk), then it could serve as a useful cue for the phenotype to adapt to the expected future environment.
* Possible maladaptation to novelty of chronic stress in social environments
* Selected to help enable acute responses to early social challenges (bully confrontation), and to facilitate modification during development (including learning)
* Function of the neuroendocrine stress response to guide adaptive neural reorganization, such as enhancing predator detection and avoidance mechanisms (Buwalda et al. 2005)
* The neurological effects from stress responses may underlie adaptation to short-term contingencies and guide long-term ontogenetic adjustments of emotional regulation and associated behavioural strategies.
* Temporary elevations in cortisol in response to social challenges = advantageous developmental effects involving long-term potentiation, synaptogenesis and neural reorganization. (useful when coping with unpredictable social environment)
* Evolutionary advantage would result if elevating stress hormones in response to social challenges (a) enhances specific acute mental functions, (b) regulates energetic resources used by the brain and (c) helps guide cortical remodeling.
* Selective pressures could have favored evolution of pathways that exchange info between HPAA and HPGA, leading to reproductive suppression when environmental conditions deteriorate (Nepomnaschy et. Al. 2004, 2006)
* How stress might be related to fetal outcomes: increase CRH causes increase in glucocorticoids and catecholamines, which reduces uterine blood flow, which may in turn restrict fetal growth and contribute to fetal hypoxia (hence, low birth weight, prematurity, poor neurologic outcomes) -> which is linked to increased HPAA reactivity in adults
* DHEAs

Female-specific HPAA responses

* In their research w. rural Guatemalan women, they found an intimate, hormonally-based connection between a woman expressing concerns, HPAA activation and reproductive supprsion: unfavorable circumstances avoiding reproduction could allow fems to focus resources on survival

**McDade et. al. 2012**

Chronic inflammation is potentially important pathway through which psychosocial stress increases risk for cardiovascular disease. Explores (through developmental, ecological perspective to consider whether microbial and nutritional environments in infancy alter patters of association between stressors and CRP.

* Elevated CRP associated with ^ risk of CVD (Ridker et al 1998), T2D (Pradham et al 2001)
* Parallel line: psychosocial stress positively associated with inflammation (Lutgendorf et al 1999, Maes et al 1999)
* Is inflammation pathway through which psychosocial stressors impacts diseases of ageing? (Black 2002)
* Perspective of ecology and evolutionary biology- it is important to look cross culturally, in regions that are not just over-nourished and “under-infected”, to adequately capture variation in determinants of inflammatory phenotypes and their consequence for disease (McDade 2003; Gurven 2008).

Aims of paper: (1) Does psychosocial stressors (perceived stress, childhood adversity) predict elevated CRP among young adults; Previously shown LBW associated with high CRP in young adults and high microbial exposure in infancy predict lower CRP. (2) Are psychosocial stressors and inflammation moderated by early environmental exposures.

Hypotheses: stressors will be positively associated with CRP for individuals with LBW or low microbial exposure in infancy; relationship between stressors and CRP will be attenuated or absent in individuals with HBW or high microbial exposure.

Results:

* Parental absence marginally assoc with low PSS
* Prenatal nutrition and microbial exposure not assoc w parental absence or PSS
* Perceived stress lower for ppl born in dry season
* High exposure to animal feces signif associated with lower CRP
* PSS predicted elevated CRP for LBW indiv, PSS – assoc with CRP in HBW indiv

\*\*High levels of microbial exposure promote the development of effective anti-inflammatory regulatory networks that reduce sensitivity to the potentially pro-inflammatory effects of psychosocial stressors.

Infectious exposure during sensitive periods of immune development (when are these sensitive periods?) are important for establishing anti-inflammatory pathways, thereby reducing sensitivity to potentially pro-inflammatory stimuli such as psychosocial stress.

Stress and Reproductive Function (Wing, J. C., & Sapolsky, R. M. (2003))

Stress-induced suppression of reproduction in hares due to predation risk and food scarcity led to 10 year cycle in rabbit abundance.

Suppression in females:

1. Disruption in ovulatory cycles
   1. Inhibition of GnRH (gonadotropin-releasing hormone release) 🡪 decreased sensitivity of pituitary gonadotropes to stimulatory effects of GnRH 🡪 greatly reduced amount of luteinizing hormone (LH). At ovary-level: decreased responsiveness to LH (likely bc glucocorticosteroid-induced decreases in LH receptor number). == results in extra long follicular stage, and more irregular cycle.
2. Impairment of uterine maturation
   1. Decrease in progesterone due to stress. (progesterone primes the uterus way for implantation durint luteal phase)
   2. Stress-induced secretion of prolactin antagonizes the anabolic effects of progesterone in the uterus.
3. Inhibition of proceptive and receptive behaviors.
   1. Stress-induced decreases in oesterogen 🡪 loss of libido
   2. Stress-induced suppression of adrenal androgens (that would increase proceptive and receptive behavior)

Suppression in Males

1. Inhibition of hormones of the gonadal axis
   1. Same as in females
2. Impairment of erectile function
   1. Parasympathetic and sympathetic activation of ANS (autonomic nervous system)—para- tone is prereq for erection and transition to symp- mediates ejaculation. (stress can block ability to get erection and cause premature ejaculation)
3. Damping of proceptive and receptive behavior

Maintenance of reproductive function during stress

(see Table 1 Wing and Sapolsky 2003)

Resistance to stress response may be adaptive in highly competitive (“tournament”) species (i.e. Olive baboons)

* During stress, the SNS tone is greater in dominant individuals- which enhances testosterone secretion and can have the effect of vasodilating the testicular parenchyma, which increases blood flow to the testes and thus absolute amounts of LH delivered.

Neuroendocrine mechanisms underlying resistance of gonadal function to stress

* Perturbation may not be viewed as stressor (and thus not initiate response)
  + Subjective perception greatly influence events stressfulness (i.e. you create the world in which you live)
  + Psychological filters are malleable. Stressors are less so if an person feels they have control. i.e. a fat bird in good condition might not perceive food restriction as stressful as a skinny bird in poor condition.
  + Stressor may provoke secretion of glucocorticosteroids that exert inhibitory effects on gonadal axis.

Szyf et al 2008: Social Environment and the Epigenome

Main argument: epigenetic changes in methylation patterns can occur beyond developmental stages, even in mature cells, such that methylation patterns can change throughout life, allowing for a platform through which the environment could sculpt the genome and affect phenotype throughout life.

* They model mechanisms for alteration in DNA methylation in adult tissues (proposing that the DNA methylation machinery remains active throughout life)
* Epigenetic programming by maternal care
  + DNA methylation, histone acetylation, and transcription occupancy bear the memory of maternal behavior.
* Programming in the hippocampus by maternal care early in life is reversible later in the adult
* Mechanisms linking maternal care and epigenetic reprogramming
* Not evident that normal environmental changes can impact methylation patterns on par with pharmaceutical interventions.

**Early Experience and the Development of Stress Reactivity in Regulation in Children: Loman and Gunnar 2010**

Early Life Stress model

* Lack of caregiving experienced early in life (parental nurturance) results in chronic stress in the infant.
  + Chronic stress biases the development of threat and stress responses: over-activity of response systems may impact the development of prefrontal regulatory systems (which also increase risk of attention- and emotion- regulatory problems):: increasing vulnerability to stressors throughout life
* Stress-Response system
  + This regulatory system is highly plastic during childhood, but becomes less so (more canalized) as child develops. Til what age? (3-5 yrs are critical time period)
  + Hypocortisolism- low early morning cortisol levels have been found in studies of children experiencing conditions of chronic deprivation and neglect (Gunnar and Vazquez, 2001)
* Threat-response system
* Animal Models
  + Rodent studies- parental care BOTH buffers and regulates basal activity of the axis, and influences development of stress- and threat- responses systems (i.e. meythlation of glucocorticoid receptor gene- Meaney and Szyf 2005).
  + Adverse parental care increases CRH-1 receptor expression, increasing sensitivity to fear—stress organizing effects of CRH over time (Sanchez 2001)

**Brain of Stress: How the social environment gets under the skin: McEwen 2012**

As the brain ages, it loses its resilience (ability to recover from stress-induced changes, and changes from isolation or unhealthy lifestyles)

In cases with Type 2 Diabetes, decreased hippocampal size has been reported (which may be important because of it’s ability to take up and respond to insulin, insulin-like growth factor-1, ghrelin and leptin.

Active Calibration Model: individuals adapt to particular environments and experiences to achieve reproductive success; however, these adaptations to one context may be maladaptive to another environment, and as such may predispose them to poor health