The Pathophysiology of Stress (Chronic Stress is Bad) (Overwhelming Stress is Worse)

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Stress

- Emotional
- Environmental
- Physiological
- Stress is a condition or feeling experienced when a person perceives that "demands exceed the personal and social resources the individual is able to mobilize." (attributed to Richard S.Lazarus)
- "Stress is not what happens to you, but how you react to what happens
- "...we define stress as environmental conditions that require behavioral adjustment" (Benson, H. The Relaxation Response, 2000, pg. 41).
- Thus, change, good or bad, can induce a stress response. (Holmes and Rahe – Life Events Rating Scale)

Check your own Life Events Rating Scale at: http://www.mindtools.com/pages/article/newTCS_82.htm

Selected (of 43) Life Change Units

 Death of Spouse 	100
Divorce	73
 Jail term 	63
 Death of close family member 	63
Marriage	50
 Fired at work 	47
 Retirement 	47
 Gain of a new family member 	39
 Large mortgage or loan 	31
 Trouble with boss 	23
 Change in residence 	20
Vacation	13
 Christmas 	12
 Minor violations of law 	11

Holmes, TH & Rahe, RH, J Psychosomatic Research 11: 213-218, 1967 http://www.mindtools.com/pages/article/newTCS_82.htm

Instinct vs. Culture

The acute stress response was essential to survival in a time when human beings faced many physical threats





Instinct vs. Culture

Stresses of modern life are more likely to be chronic and often psychological and interpersonal. (e.g., Holmes & Rahe).

Unfortunately ... the body reacts to today's stresses as though it were still facing a real physical threat."



Some Major Avenues of Mind-Body Reciprocity

- Nervous System
- Endocrine System
- Immune System

Optimally, interaction of these systems maintains homeostasis and wellness

Stress-Induced Changes in the Nervous System

- Classical View of the Autonomic Nervous System
 - Parasympathetic
 - Rest and restoration
 - Sympathetic
 Fight or flight



The Parasympathetic Nervous System

- Integrates the 'rest & recreation' (feed & breed) response*
 - Release of acetylcholine
 - Decreased heart rate & blood pressure
 - Decreased respiratory rate and bronchial constriction
 - Decreased glycogen to glucose in liver
 - Pupillary constriction
 - Increased GI activity

*Also known as 'rest and restoration' or 'rest and RELAXATION' (emphasis added)

The Sympathetic Nervous System

- Integrates the 'fight or flight' response
 - Release of norepinephrine & epinephrine
 - Increased heart rate & blood pressure
 - Increased respiratory rate and bronchial dilation
 - Increased glycogen to glucose in liver
 - Increased pupil diameter
 - Decreased GI activity

Important: Sympathetic responses to acute stress normally dissipate quickly

The Fight or Flight Response



The Fight or Flight Response Dissipates Quickly



Sometimes Fight or Flight is not enough



The Autonomic Nervous System: But wait there's more!

- Parasympathetic
 - Rest and relaxation
- Sympathetic
 - Fight or flight

Freeze or feigned death



Where's the 'ol fight - flight' when you need it!

The Freeze or Feigned Death Response

"Tonic immobility is most useful when a slow-moving vulnerable organism ... is confronted with a lifethreatening situation involving mobile, large predators. Tonic immobility may enhance survival when a predator temporarily loosens its grip on captured prey under the assumption that it is indeed dead, providing the prey with an opportunity for escape. It is also a response that may be adaptive in humans when there is no possibility of escaping or winning a fight."

http://lauramcwilliams.wordpress.com/2009/11/30/the-freeze-response/

A New View of the Autonomic Nervous System: Polyvagal Theory

• Parasympathetic

'Mammalian' (myelinated) vagus Origin in the *nucleus ambiguus* (ventral) Fine tuning of daily life – especially social intx

'Reptilian' (unmyelinated) vagus Origin in the dorsal motor nucleus of the vagus Activated in perceived <u>life-threatening</u> danger

Porges (2011) The Polyvagal Theory, W.W. Norton

Activation of the Unmyelinated Vagus

Acute - extreme threat situations

Profound bradycardia

Freeze

Hypotension, fainting

Near death experience ?

Chronic – in perceived extreme threat

'The General Inhibition Syndrome ' Helplessness and avoidance

Persistent in post-traumatic stress disorder

Note: Activation of the reptilian vagus also inhibits the sympathetic nervous system and somatic muscles, inactivating fight or flight.



Some Stress-Induced Changes in Endocrine Function

- Increased cortisol, catecholamines
 & fatty acids
- Increased blood sugar (see above)
- Increased insulin (see above)
- Inc (LDL) cholesterol, (dec HDL)

Brindley et al. (1993) Metabolism 42: Supp1, 3-15

Homeostasis vs. Allostasis

- Homeostasis: balance of systems essential for life, pH, body temperature, [glucose], pO₂
- 'Allostasis': changes in the body that occur as a consequence of CHRONIC activation of homeostatic mechanisms (McEwen et al.)
 - Catecholamines
 - HPA axis
 - Cytokines
 - Etc.?

Stress and Development of Allostatic Load



Perception of stress is influenced by one's experiences, genetics, and behavior. When the brain perceives stress, physiologic and behavioral responses are initiated leading to allostasis and adaptation. Over time, allostatic load can accumulate, and the overexposure to neural, endocrine, and immune stress mediators can have adverse effects on various organ systems, leading to disease.

McEwen (1998) N Engl J Med 338:171-179



Allostatic Overload: Wear and Tear on the Body Caused by Chronic Stress

- Decreased immune functions
- Hypertension
- Atherosclerosis
- Increase platelet reactivity
- Abdominal obesity
- Bone demineralization
- Atrophy of neurons in hippocampus and prefrontal cortex
- Increased activity of amygdala



Stress associated hormonal and neurohormonal changes

Henry and Wang (1998)

23:863-875

Psychoneuroendocrinology



A clinical allostatic load (AL) is associated with burnout and hypocortisolemic profiles in 'healthy' workers

Items in the AL index

cortisol c-reactive protein creatinine fibrinogen glycosylated haemoglobin insulin pancreatic amylase systolic and diastolic BP total cholesterol triglycerides waist-hip ratio

albumin dehydroepiandrosterone HDL cholesterol

Juster et al. (2011) Psychoneuroendocrinology 36: 797-805



Juster et al. (2011) Psychoneuroendocrinology 36: 797-805

Hypocortisolemic profiles in subject with high allostatic load index.



Figure 2 Mean (standard error bars) salivary cortisol levels (micrograms/deciliters) over two days as a function of allostatic load (AL) groups.



Figure 3 Mean (standard error bars) salivary cortisol levels (micrograms/deciliters) throughout the Trier Social Stress Test protocol as a function of allostatic load (AL) groups.

Juster et al. (2011) Psychoneuroendocrinology 36: 797-805

Stress-Induced Changes in Immune Function

• 'Eustress' (acute, physiologically adaptive)

 Increased delayed type hypersensitivity, associated with acute spikes in corticosterone and decreased leukocytes in blood (by movement to skin)

• 'Distress' (chronic, physiologically maladaptive)

 Decreased delayed type hypersensitivity, associated with chronically increased basal corticosterone and less decrease in blood leukocytes (i.e., less movement of leukocytes to skin)

Stress and Illness in Practice

- Review of audiotapes of primary care practice of patients with 'chronic-disease' (better, chronic illness)
- 439 interactions with 49 physicians
- Stress was by far the most time consuming topic.
- Nearly 60% of the discussions were not perfunctory but attempts to counsel or encourage behavior change in the patient

(It has been estimated that 70-80% of primary care visits involve an illness that is caused or augmented by stress)

Russell & Roter (1993) Am J Public Health 1993; 83: 979-982

Nortin Hader on NPR Oct 4, 2007 Medical care can change *what* you die of, but does not change much *when* you die

"We can capture about 80% of the mortal risk [of WHEN you die] by the answer to two questions:"

Are you comfortable in your socio-economic status?

Are you happy in your job?

Hadler (2004) The Last Well Person: How to Stay Well Despite the Health-Care System, McGill-Queen's University Press

Work-Related Stress and Illness

- 10,308 civil servants in the UK
- Work stress = poor work social support, high job demands, and low job control
- Associated with increased risk of BMI obesity (odds ratio, 1.73), and waist obesity (odds ratio, 1.61)
- Men were more likely than women to suffer the negative effects of job strain in terms of obesity; women did not experience a significant increase in waist obesity with stress.

Brunner et al. (2007) Am J Epidemiol 165:828-837

A Gender Difference in Stress Management?

- Female responses are more marked by a pattern of "tend-and-befriend."
- Nurturant activities designed to protect the self and offspring promote safety and reduce distress
- The tend-and-befriend pattern appears to draw on the attachment-caregiving system
- Neuroendocrine evidence suggests that oxytocin, in conjunction with female reproductive hormones and endogenous opioid peptide mechanisms, may be at its core

Taylor et al. (2000) Biobehavioral responses to stress in females: tend-and-befriend, not fight-or-flight, Psychol. Rev. 107: 411-429

The Tending Instinct

Fight or Flight may assure survival in the short term, but an individual is not likely to survive for long if he or she tries to go it alone. "Tend and befriend" is critical to our social nature and is vital to our survival as a species.

> Taylor (2002) The Tending Instinct: How Nurturing is Essential to Who we Are and How we Live, Henry Holt & Co.

In both males and females...

- Release of oxytocin is stimulated by non-noxious stimuli:
 - Touch, especially massage & consensual sexual activity
 - Warm temperature
 - Vibration
 - Electroacupuncture
 - Olfactory clues
 - Social interaction
- With repeated exposures release of oxytocin is highly conditionable
- Mental images of positive experiences may alter the physiological state; at least in part via oxytocin

Relaxation and positive social interaction; the linchpins of "Healing"



Uvnas-Moberg (1998) Psychoneuroendocrinology 23: 819-835

Is a deficiency of oxytocin function associated with autism spectrum disorder?

frontiers in	
PSYCHIATRY	

ORIGINAL RESEARCH ARTICLE published: 04 November 2011 doi: 10.3389/fpsyt.2011.00060



Oxytocin receptor gene associated with the efficiency of social auditory processing

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Magnitude of Stress and Cognitive Efficiency



Goleman (2006) Social Intelligence, the new science of human relationships, Random House

Management of Stress

- Many techniques most bring on the 'Relaxation Response' - typically, at least one technique 'clicks'
 - Exercise
 - Meditation
 - silent, focused, prayer, guided (imagery, progressive relaxation), active (yoga, shaking...)
 - Autogenics
 - Hypnosis
 - Mindfulness-based stress reduction (MBSR)

Summary: The BrainMindBody and Stress

- Interprets life situations as stressful, or not
- Modifies behavior that increases or decreases the allostatic load imposed by perceived stress
- Multiple mind/body techniques exist to manage and reduce stress – find what works for you!