Stress as a Risk Factor for Mental Health and Substance Use

Dr. Mustafa al’Absi, PhD
Sheena Potretzke, MS

Friday, February 10th 2017
Introductions

Dr. Mustafa al’Absi

- University of Minnesota- Duluth Medical School
  - Dept. of Family Medicine and Community Health
  - Dept. of Biobehavioral Health and Population Sciences
  - Max E. and Mary LaDue Pickworth Chair
  - Founding Director of the Duluth Medical Research Institute (DMRI)
Introductions

• Sheena Potretzke, MS
  – BS Neuroscience
  – MS Cognitive Neuroscience
  – Research Coordinator at the Minnesota Center for Chemical and Mental Health (MNCAMH)
Overview

- Stress basics
- Brief review of current research surrounding:
  - Stress and mental health
  - Stress and substance use
- Suggestions/options for clinicians in treating stress
- Questions

Stress Basics

• Stress is not a disease.

• Stress can lead to both physical and mental illness (Asberg et al, 2010; Anderson, 2004).
Stress basics

• Hypothalamic-pituitary-adrenal (HPA) axis
  • Neuroendocrine system (Malenka, Nestler & Hyman, 2009)
  • 3 endocrine glands:
    • Hypothalamus
    • Pituitary
    • Adrenal
  • Stress hormones:
    • Cortisol
    • Adrenaline
    • Corticotropin-releasing
    • Adrenocorticotropic hormone (ACTH)
Stress and Mental Health

- Often intertwined.

- Stress functions as both an aggravator of mental illness, and the main cause of the disease (Asberg et al., 2010).
Stress and Mental Health

- Stress-related illness:
  - Most common cause of long-term illness.
  - Diverse etiology and clinical presentation (Asberg et al., 2010)
Stress and Mental Health

• Stressful events → acute and post-traumatic stress disorder
• Chronis stress → variety of symptoms (Anderson, 2004), and cause illness (Asberg et al., 2010)
Stress and Mental Health

• Chronic fatigue syndrome (Asberg et al., 2010)
  • Prolonged stress without recovery
• 3 phases:
  – Prodromal
  – Acute
  – Recovery
Stress and Mental Health

- HPA axis hyper/hyposensitivity found in:
  - Schizophrenia (Goh & Agius, 2010)
  - Major Depressive Disorder (MDD) (Nestler et al., 2002; Asberg et al., 2010)
  - PTSD (Rasmusson, Vythilingam, & Morgan, 2003)
  - Psychosis (Pariante et al., 2004)
  - Bipolar mania (Goh & Agius, 2010)
  - Anxiety disorders (Goh & Agius, 2010)
  - Other stress-induced conditions, e.g. chronic fatigue syndrome (Asberg et al., 2010)
  - Addiction (al’Absi et al., 2005; al’Absi et al., 2004; al’Absi et al., 2014; al’Absi et al., 2003)
Stress and Mental Health

• Diathesis-stress model (Salomon & Jin, 2013):
  – Diathesis = predisposition or vulnerability for development of pathological state
  – Combination of predisposition and stressful event = pathological states or diseases (Zuckerman, 1999)
  – Stress defined by external events rather than subjective experience and reactions to event(s) (Monroe & Simons, 1991)
Stress and Mental Health

• Diathesis-stress model (continued):
  – Resilience
  • NOT the opposite of diathesis
Stress and Mental Health

Diathesis-Stress/Dual-Risk Model

outcome

positive

negative

negative

vulnerable individual

resilient individual

environment/experience

positive
Stress and Mental Health

• Stress vulnerability model (Zubin & Spring, 1977)

*Figure 2. Relation between vulnerability and challenging events.*
Stress and Mental Health

• Studies have demonstrated stress to predispose development of mental health problems in adulthood (Scott et al., 2012; Varese et al., 2012; Benjet et al., 2010; Kessler et al., 2010)
  – Potential causes:
    • Alterations in HPA axis
    • Abnormal immunological response
    • Changes in plasticity:
      – Cellular
      – Molecular
      – Epigenetic
Stress and Mental Health

• Intricate set of interactions involved in stress, namely persistently elevated cortisol, or hypercortisolemia, leading to: (Agius & Goh, 2010):
  – Increased CRF
  – Immune response
  – Impaired negative feedback of HPA axis
  – Neurodegenerative changes in hippocampus (Myint, 2009)
    • Hippocampal volume changes seen in:
      – Schizophrenia (Sumich et al., 2002)
      – Post-traumatic stress disorder (Felmingham et al., 2009)
      – Borderline personality disorder (Weniger et al., 2009)
      – Depression (Sheline et al., 1999)
    – Disruption of trophic/atrophic factors within neurons
• Polymorphisms in serotonin transporter (SERT)
Stress and Mental Health

• Similarities in response support a common pathway
  – Stress is mediated by HPA axis
  – Hypercortisolemia
    • Effect of hypercortisolemia:
      » Immune response (cytokines)
      » Imbalance of a/trophic factors

• Differences (schizophrenia, bipolar disorder, PTSD, depression):
  – Different neurotransmitters
    • E.g. Dopamine in schizophrenia vs. serotonin and noradrenaline in depression
  – Some neurotrophic factors specific
    (Goh & Agius, 2010)
Stress and Substance Use

• Stress is an established, key risk factor for both the development of addictive disorders and relapse of addictive behaviors (Sinha and Jastreboff, 2013).
Stress and Substance Use

- Addiction
- Response
- Stress
- Relapse
Stress and Substance Use

• Withdrawal stress psychobiology:
  – Define stress response patterns and alterations during smoking withdrawal in smokers and those attempting to quit.
  – Use stress-related biobehavioral measures to develop a model to predict smoking relapse
Stress and Substance Use

- Stress-like effects of withdrawal from smoking

---

**Anger**

**Depression**

**Tension/Anxiety**

**Difficulties in Concentration**

**Systolic BP Responses**

---

Smoking

---

Abstinence

---

( al’Absi et al., 2002)
Stress and Substance Use

Cortisol Concentrations

Steeper decline during the first morning of abstinence

(al’Absi, Hatsukami, Davis, & Wittmers, 2004)
Stress and Substance Use

- Association of blunted awakening response with early relapse- also with intense craving and withdrawal symptoms

(al’Absi, Hatsukami, Davis, & Wittmers, 2004)
Stress and Substance Use

- Disruption of the stress response is associated with increased risk for relapse (al’Absi, Hatsukami, & Davis, 2005)

- Blunted ACTH response to stress associated with early relapse.

- Blunted cortisol response to stress associated with early relapse.
Stress and Substance Use

- Blunted ACTH response to stress associated with early relapse.

(al’Absi, Hatsukami, & Davis, 2005)
Stress and Substance Use

- Stress and relapse: consideration of modifiers
  - Individual differences
    - Sex differences
    - Emotional dispositions
  - Situational factors
    - Life adversity
    - Use of multiple substances
Stress and Substance Use

• Sex differences

*Fig. 2. Mean adrenocorticotropic hormone (ACTH; top figure) and plasma cortisol (bottom figure) responses to the cognitive stressor.*
Stress and Substance Use

- Emotional dispositions

\[ y = -0.55x + 20.6 \]

\[ R^2 = 0.07 \]

\[ p < 0.05 \]

(al’Absi, Carr & Bongard, 2007)
Stress and Substance Use

- Life adversity

Lever of adverse experience

(Lemieux, Olson, Nakajima, Schulberg, & al’Absi, 2016)
Stress and Substance Use

- Life adversity

(Ouellet-Morin et al., 2011)
Stress and Substance Use

- Psychosocial stressors increase smoking as well as the risk for smoking relapse (Cohen and Lichtenstein, 1990; Shiffman et al., 1996).
- A reduced HPA stress response following 24-48 hours of withdrawal predicts early relapse of cigarette smoking at one month (al’Absi et al., 2005; al’Absi et al., 2004; al’Absi et al., 2014; al’Absi et al., 2003).
Stress and Substance Use

- Stress, smoking, and appetite regulation
  - Does blunted response to stress predict changes in appetite, dietary intake, weight, and smoking relapse?
Stress and Substance Use

• Stress has been shown to be related to both subjective craving and appetite hormones such as leptin and ghrelin associated with craving for cigarettes (Potretzke et al., 2014; Potretzke, 2017 unpublished manuscript).
Stress and Substance Use

- Leptin as a marker for stress and craving

(Potretzke, Nakajima, Cragin & al’Absi, 2014)
Stress and Substance Use

- Leptin as a marker for stress and craving

(Potretzke, Nakajima, Cragin & al’Absi, 2014)
Stress and Substance Use

- Decline in leptin concentrations from ad libitum to abstinence

(Lemieux, Nakajima, Hatsukami, Allen & al’Absi, 2015)
Stress and Substance Use

• Models to orient research in the context of addiction:
  – What does a blunted stress response mean?
  – Is it a cause or an effect?

• Hypotheses:
  – Long-term exposure to substances may produce changes in multiple brain circuitries.
  – Changes in key central nervous system (CNS) emotion and cognitive substrates leading to dysregulated stress response.
  – Psychosocial stress and early adversity may prime the brain to be sensitive to substance exposure (vulnerability)
  – Subsequent exposure to stress → maintenance of substance use and relapse
Stress and Mental Health and Substance Use

- New stress vulnerability model

Line, personal correspondence
Implications for clinicians

• Evidence-based treatments
  – Stress vulnerability model:
    • Illness Management and Recovery (IMR), Integrated Illness Management and Recovery (I-IMR) and soon to be Enhanced Illness Management and Recovery (E-IMR)
  – Mindfulness-based stress reduction/relapse prevention
    • Integrated Coping Awareness Therapy (I-CAT)
Stress and Mental Health

Questions

• Please feel free to e-mail any additional questions to: Sheena Potretzke
  potre005@umn.edu