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

Image from: http://www.hoyespharmacy.com/wp-content/uploads/2015/04/SI_StressBrain.png

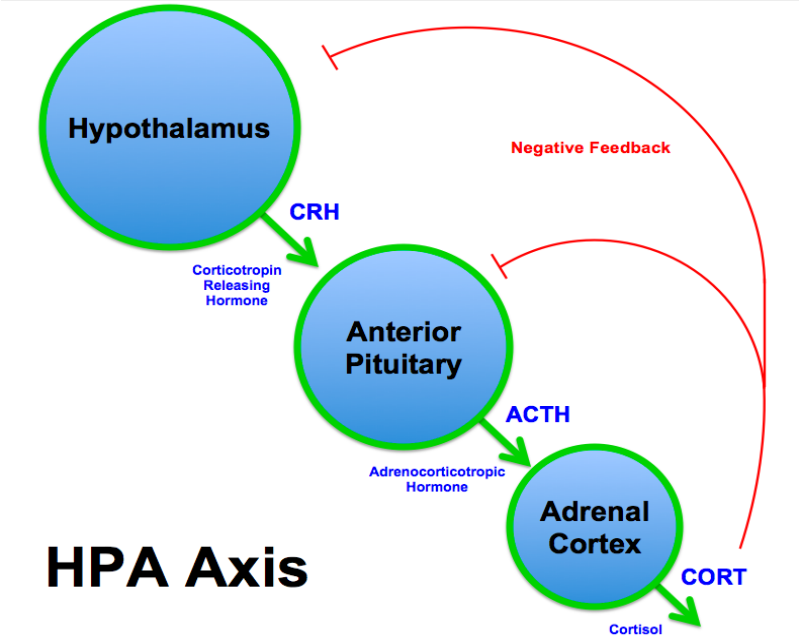
Stress Basics

- 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)



HPA Axis

Stress and Mental Health

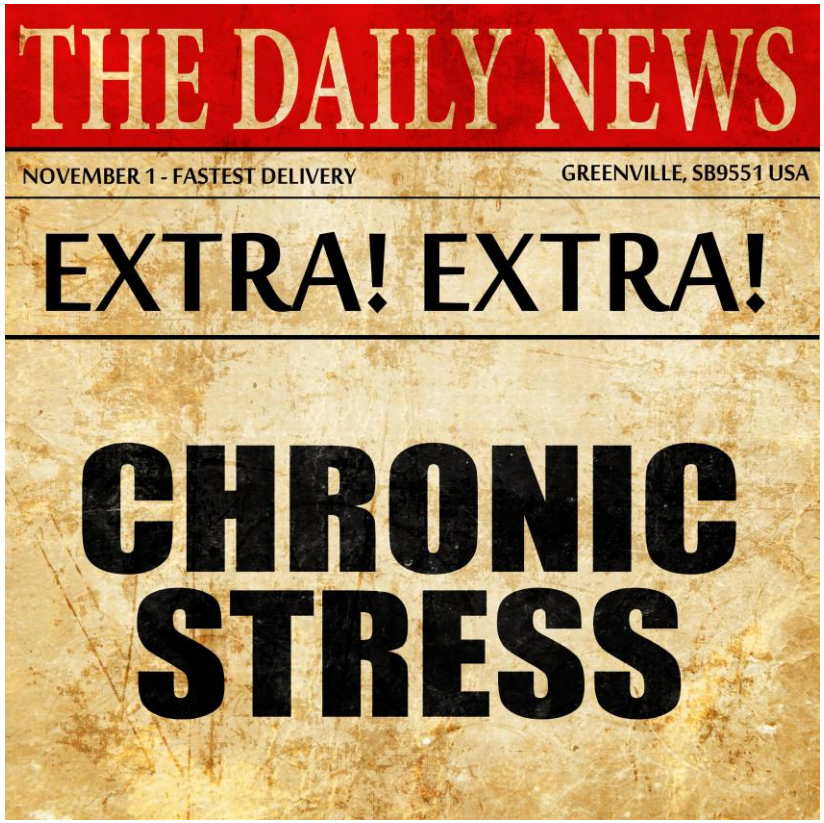
- Often intertwined.
- Stress functions as both an aggravator of mental illness, and the main cause of the disease (Asberg et al., 2010).

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)

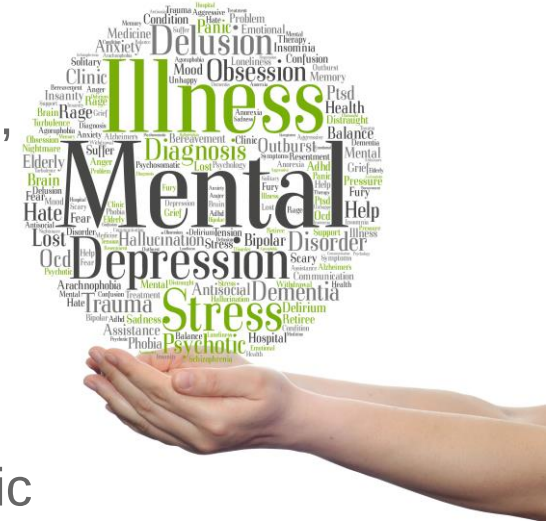


Stress and Mental Health

- 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)



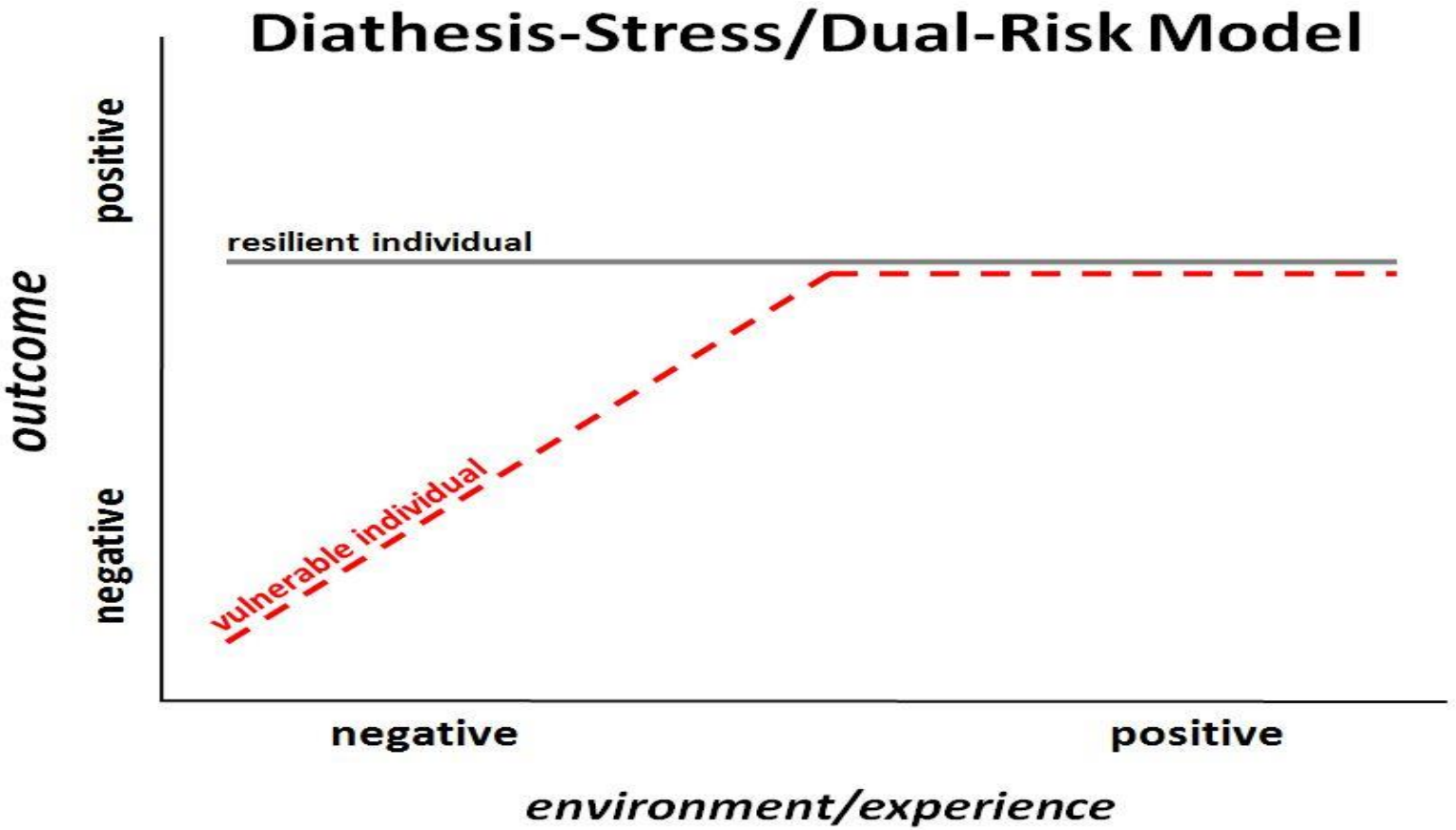
Stress and Mental Health

- 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



Stress and Mental Health

- Stress vulnerability model (Zubin & Spring, 1977)

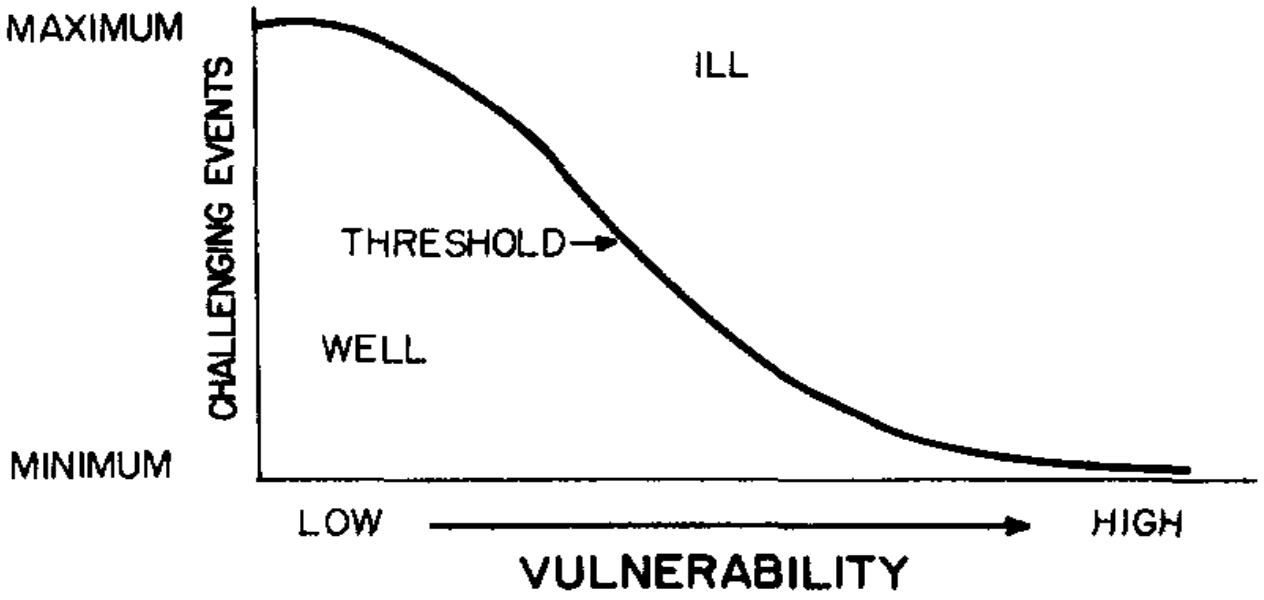


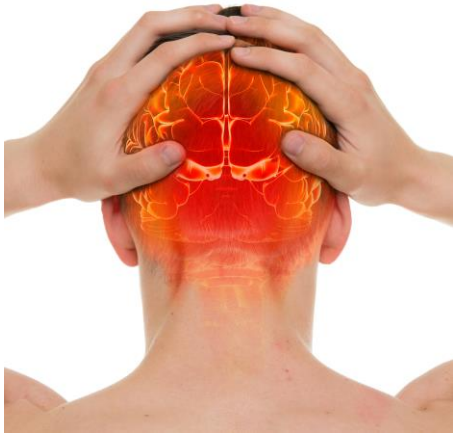
Figure 2. Relation between vulnerability and challenging events.

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., 19999)
  - Disruption of trophic/atrophic factors within neurons
- Polymorphisms in serotonin transporter (SERT)



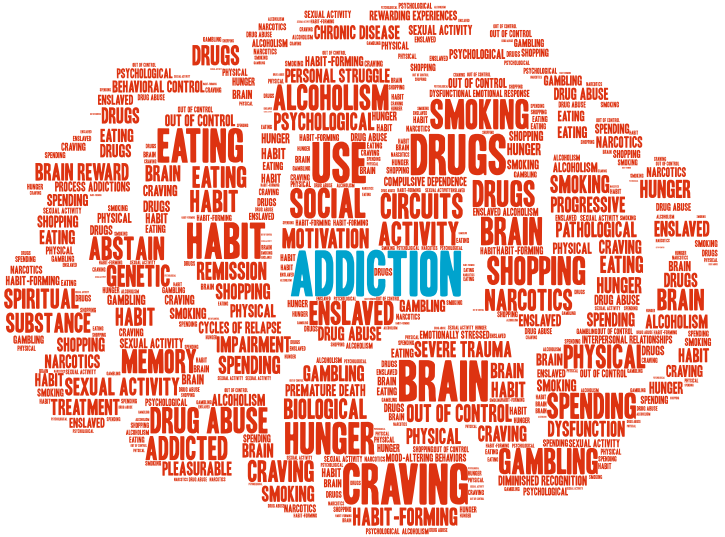
Stress and Mental Health

- 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

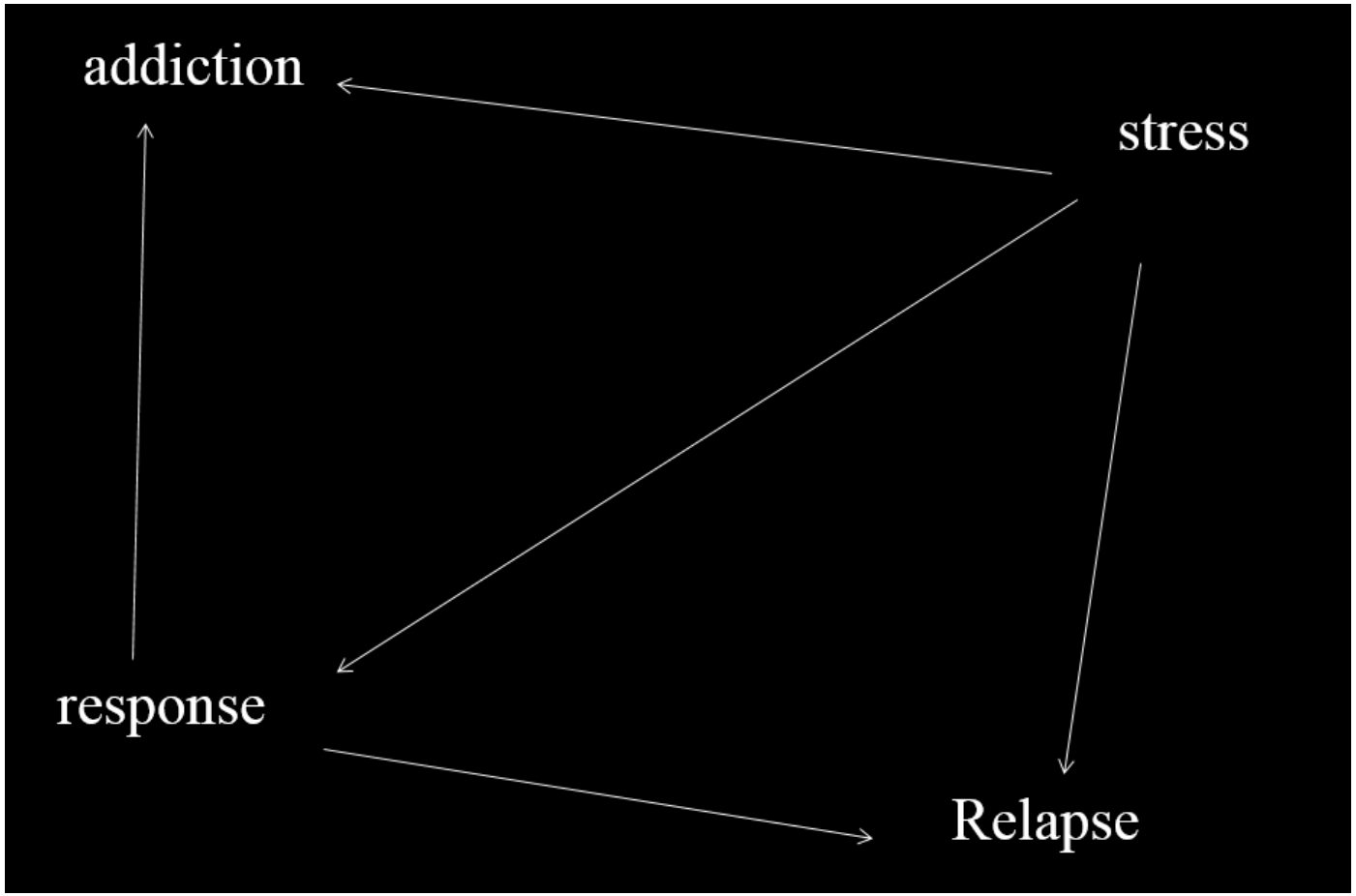
(Goh & Agius, 2010)

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

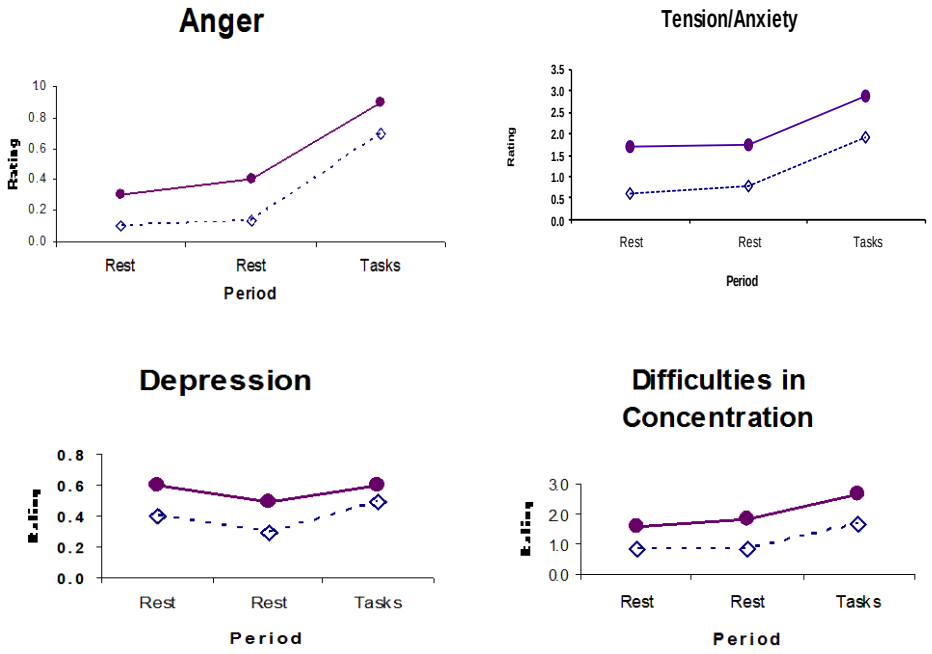


Stress and Substance Use

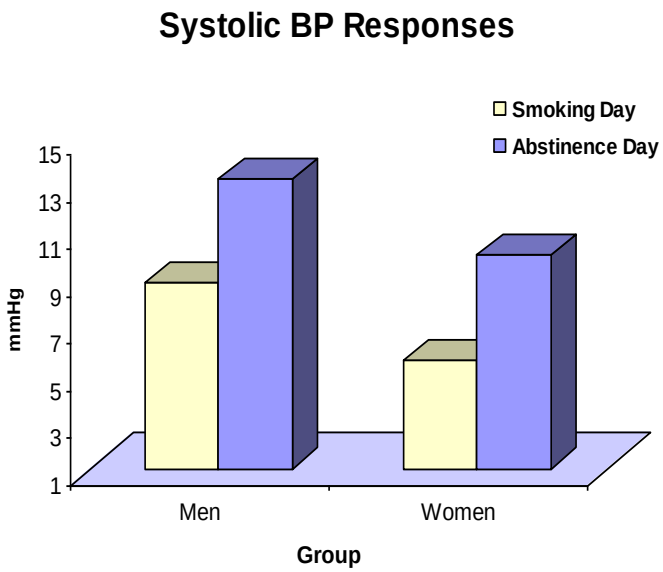
- Withdrawal stress psychobiology:
  - Define stress response patterns and alterations during smoking withdrawal in smokers and those attempting to quit.
  - Use stress-related biobehavioral measures to develop a model to predict smoking relapse

Stress and Substance Use

- Stress-like effects of withdrawal from smoking

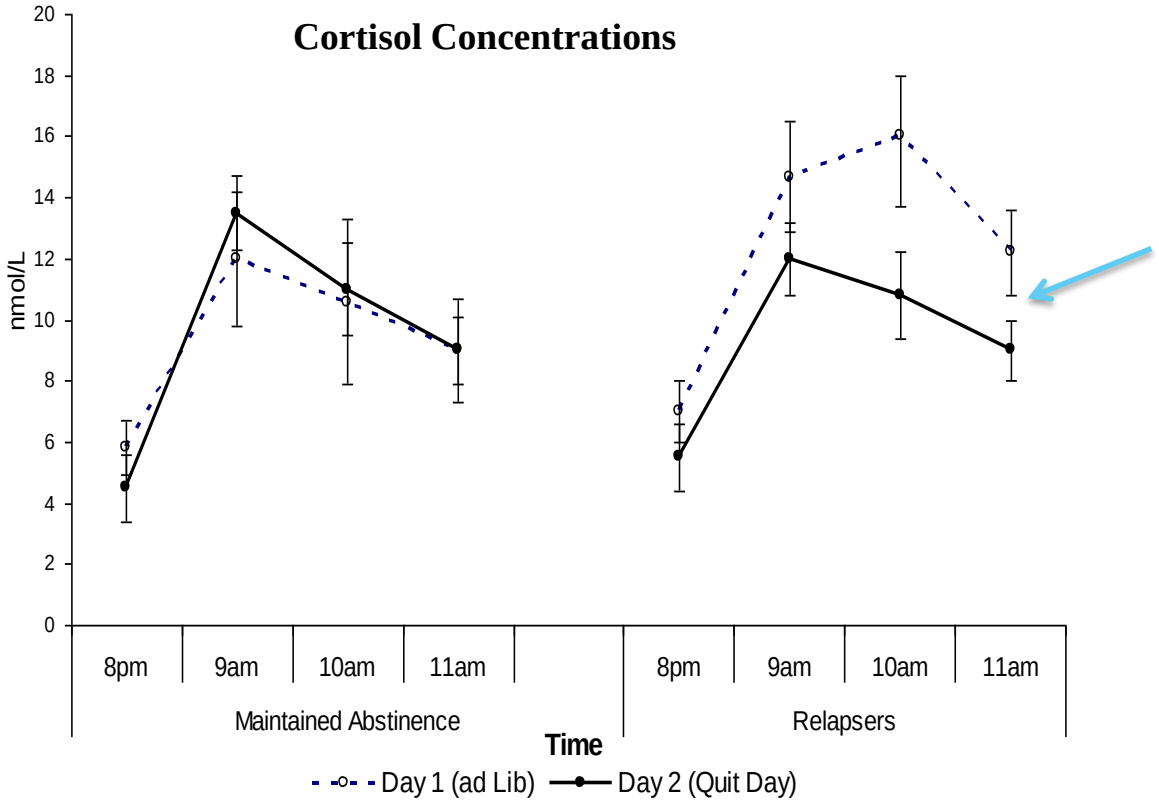


--- Smoking
— Abstinence



(al'Absi et al., 2002)

Stress and Substance Use

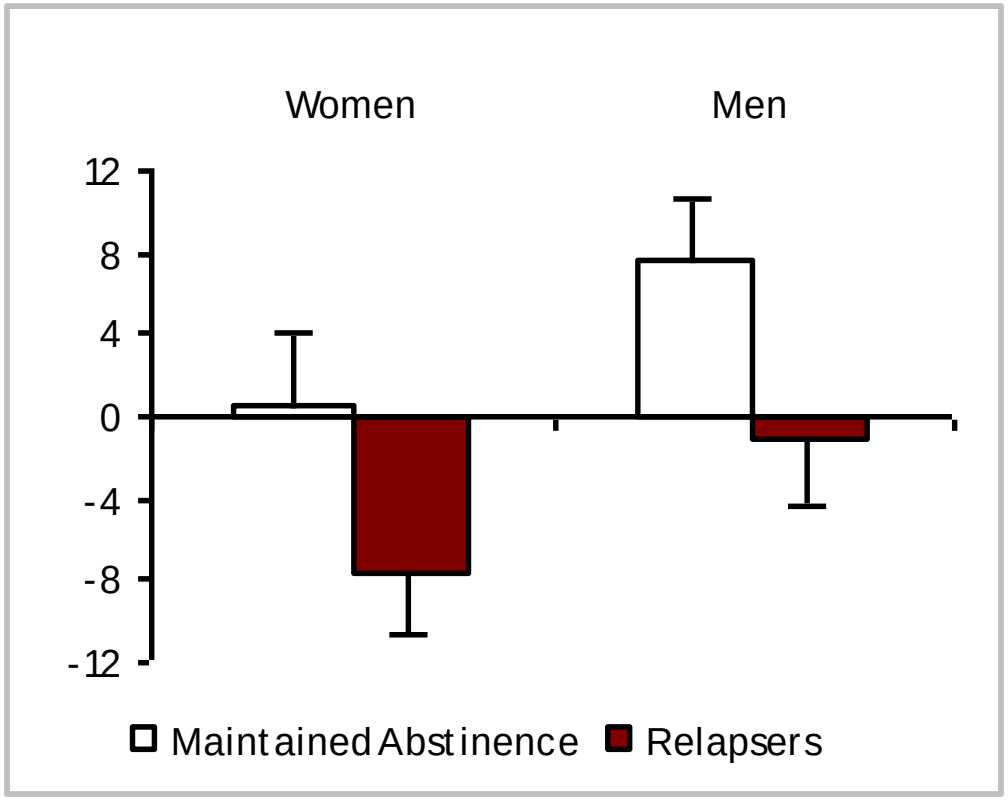


Steeper decline during the first morning of abstinence

(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

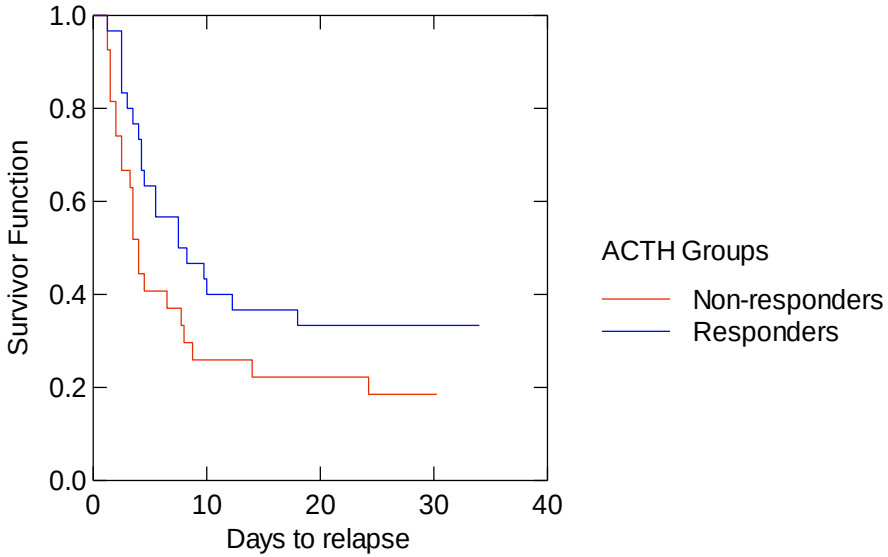


(al'Absi, Hatsukami, Davis, & Wittmers, 2004)

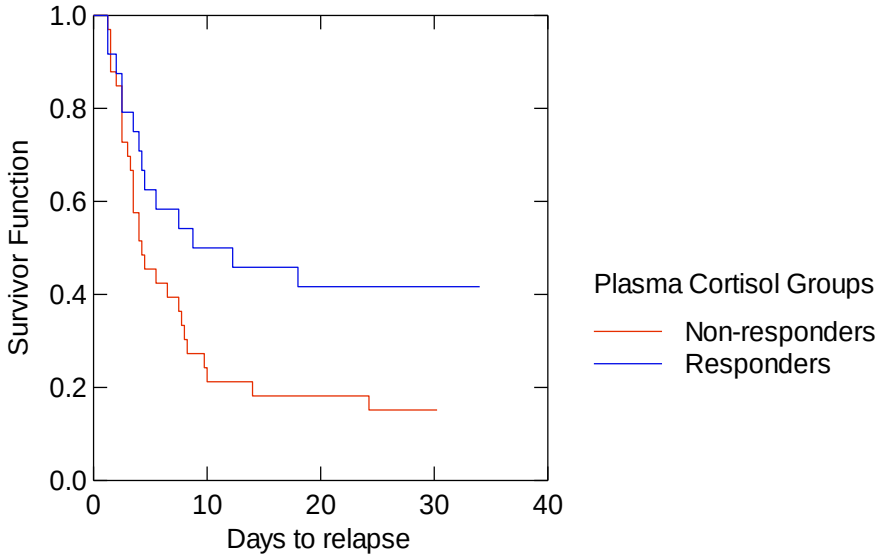
Stress and Substance Use

- 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.

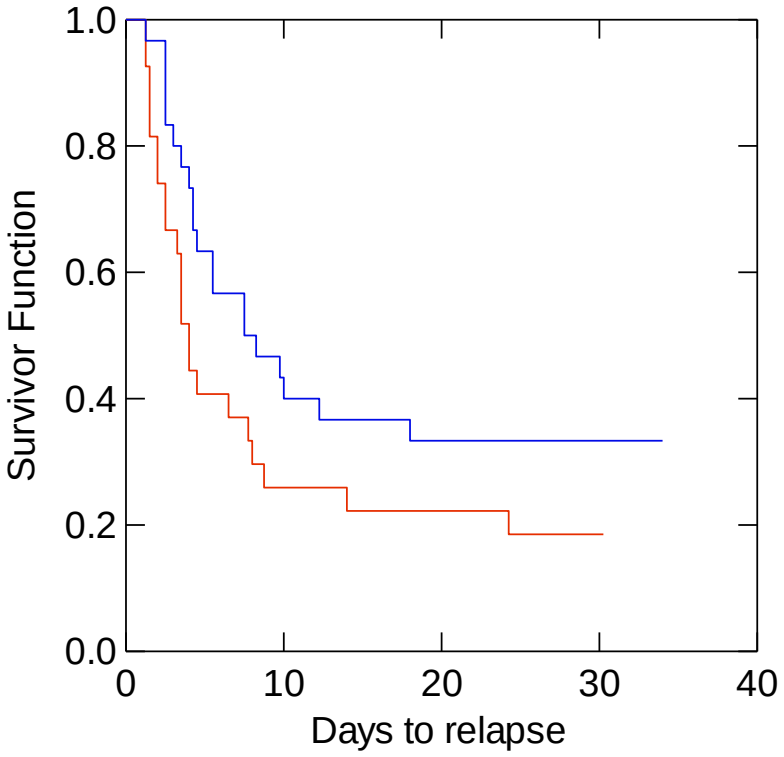


- Blunted cortisol response to stress associated with early relapse.



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

M. al'Absi / International Journal of Psychophysiology 59 (2006) 218–227

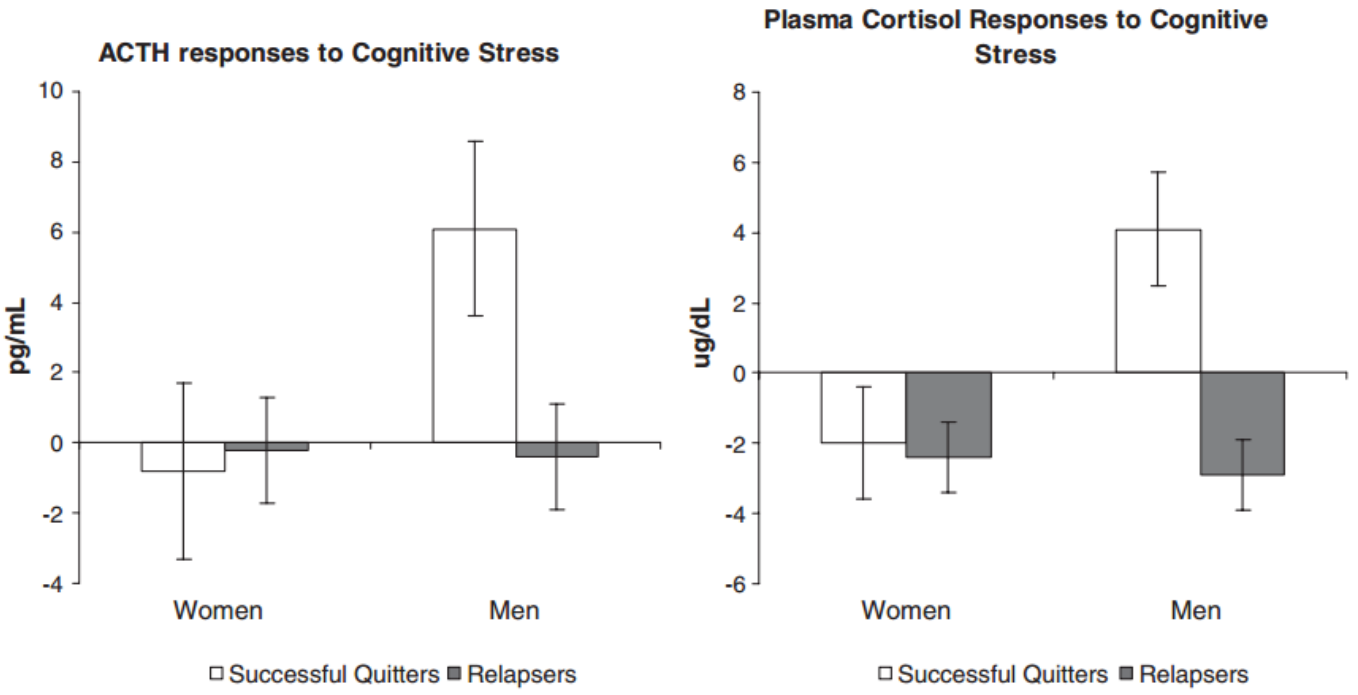
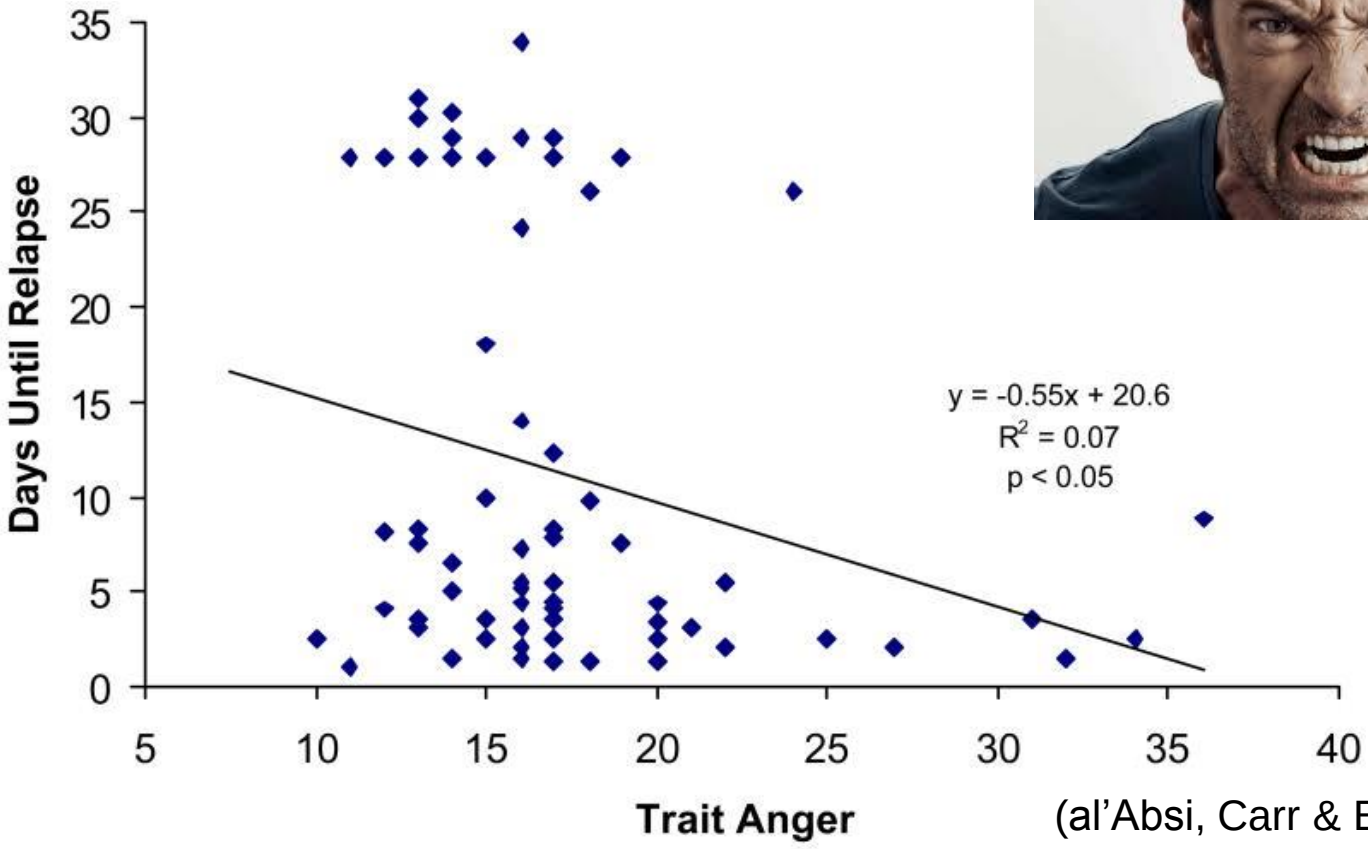


Fig. 2. Mean adrenocorticotropic hormone (ACTH; top figure) and plasma cortisol (bottom figure) responses to the cognitive stressor.

Stress and Substance Use

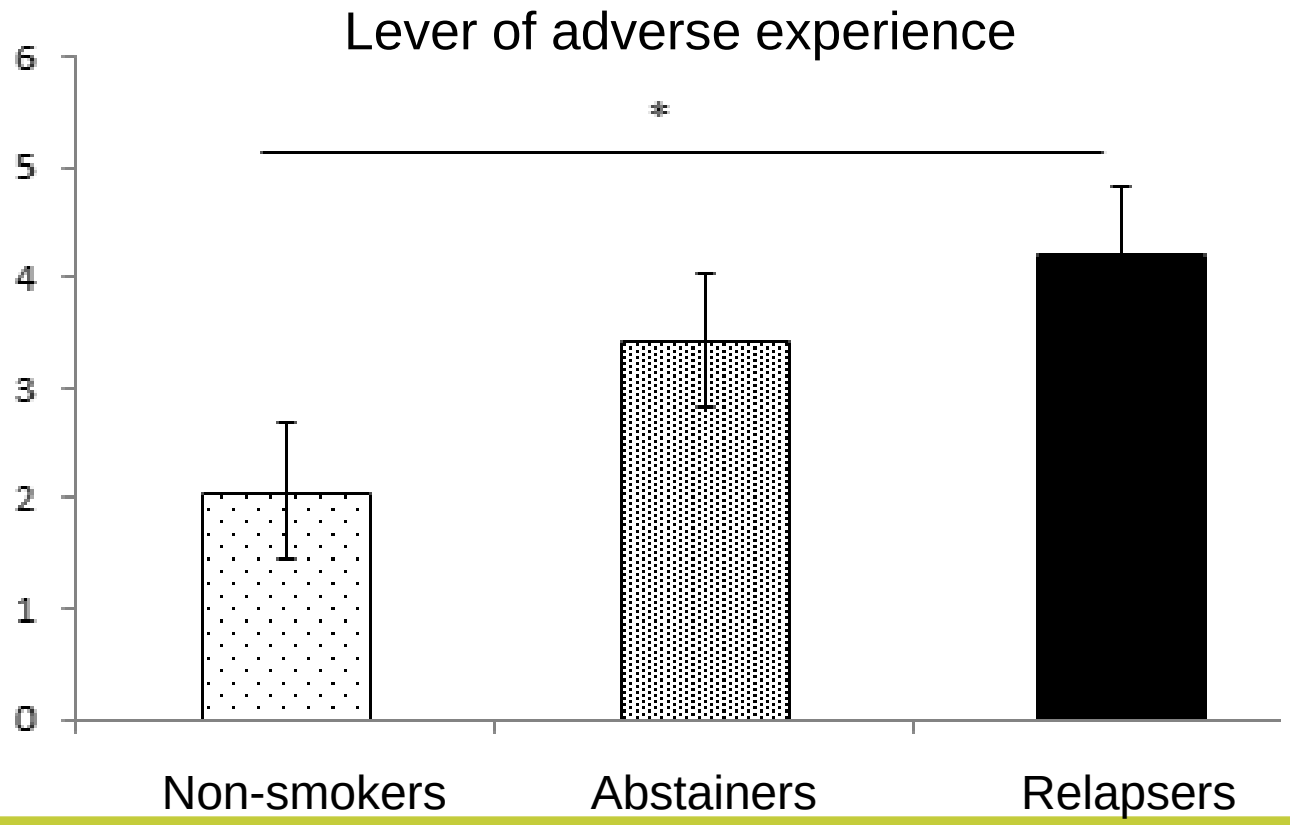
- Emotional dispositions



(al'Absi, Carr & Bongard, 2007)

Stress and Substance Use

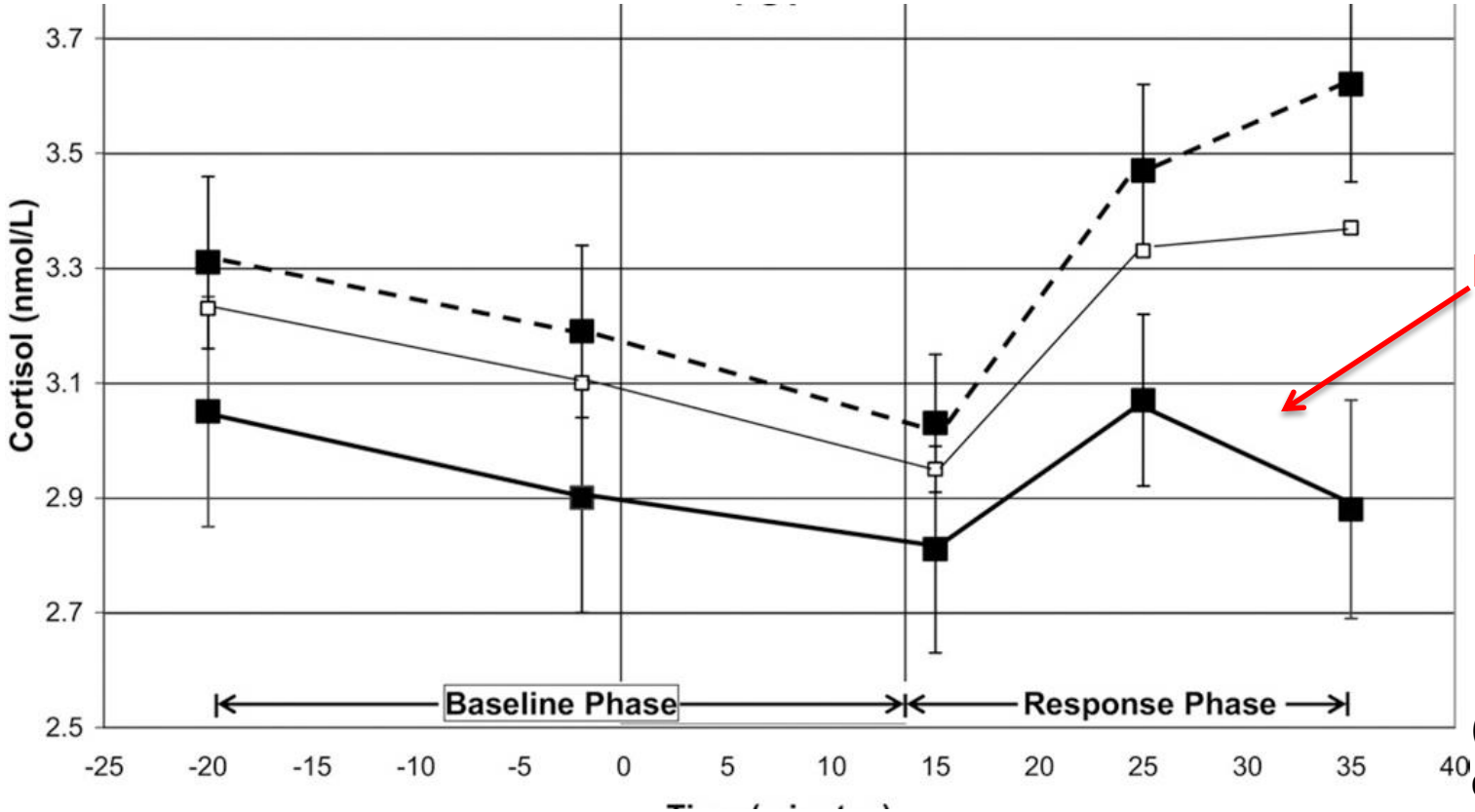
- Life adversity



(Lemieux, Olson, Nakajima, Schulberg, & al'Absi, 2016)

Stress and Substance Use

- Life adversity



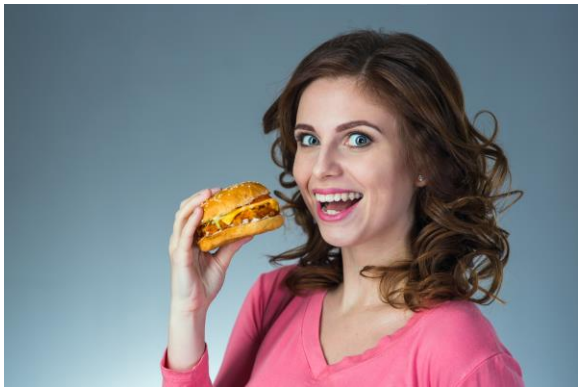
(Ouellet-Morin et al., 2011)

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?

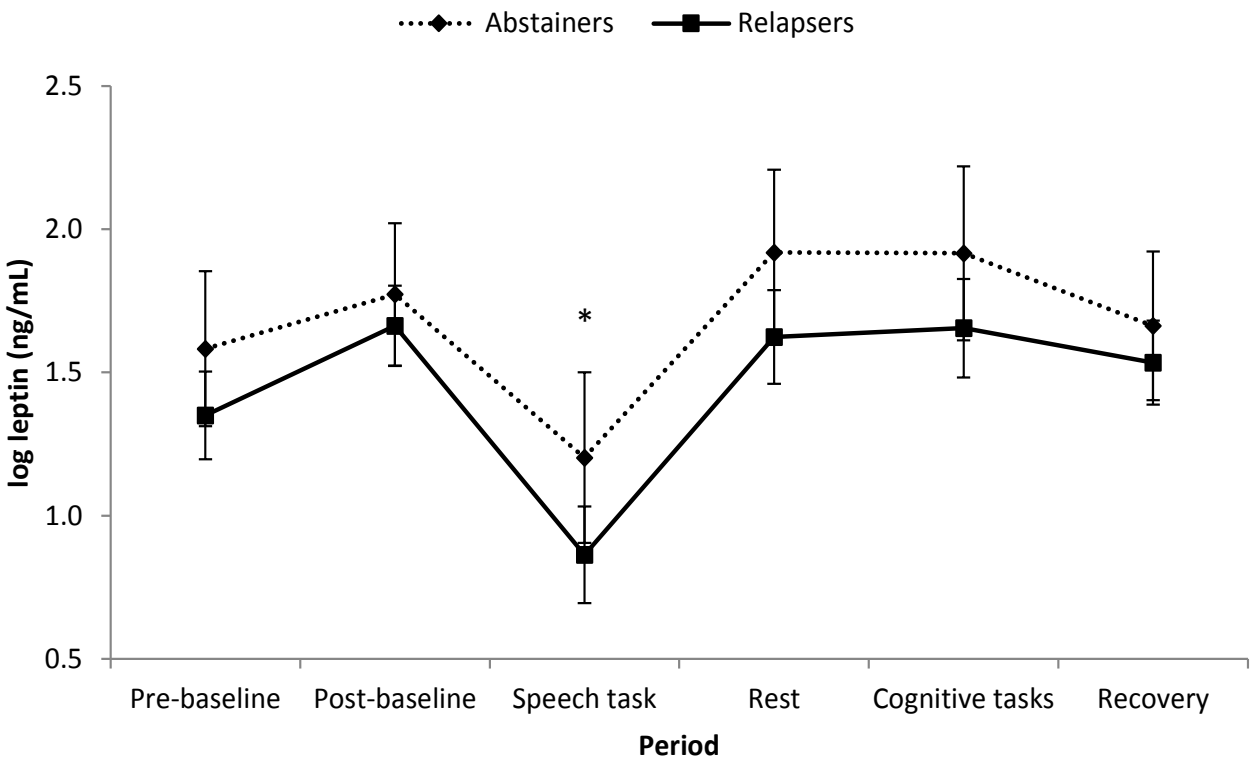


Stress and Substance Use

- 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

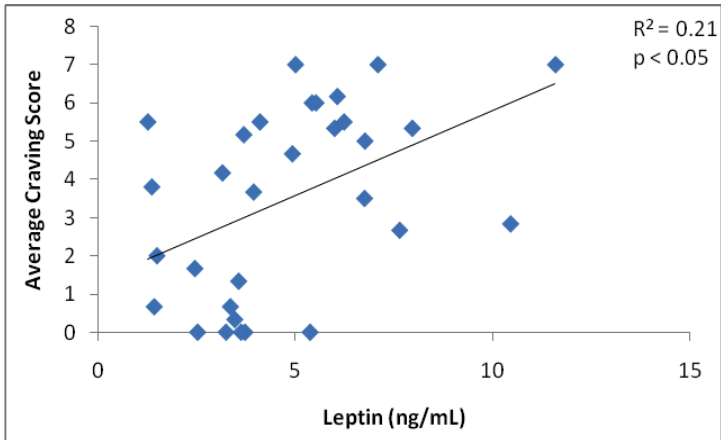


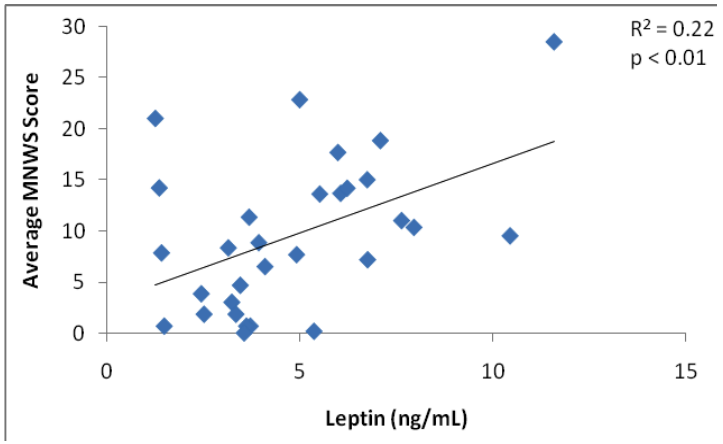
(Potretzke, Nakajima, Cragin & al'Absi, 2014)

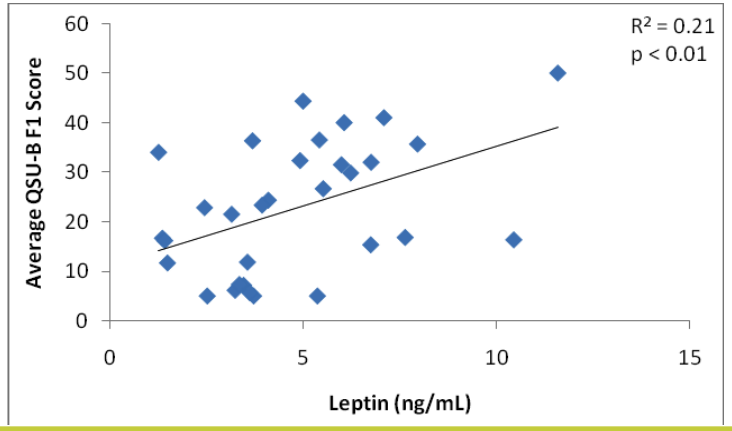
Stress and Substance Use

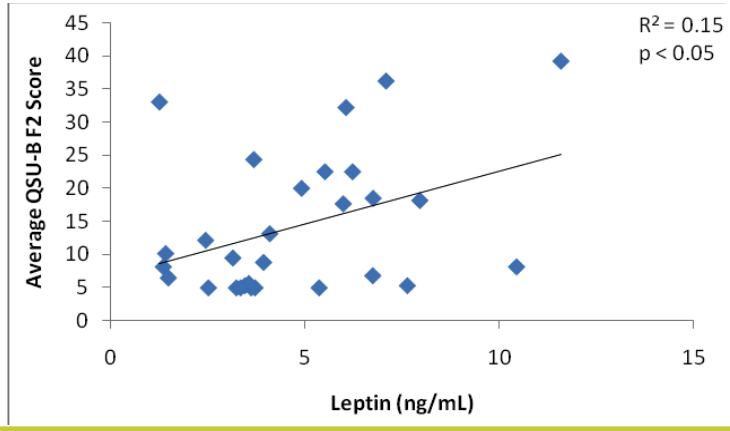
- Leptin as a marker for stress and craving

(Potretzke, Nakajima, Cragin & al'Absi, 2014)



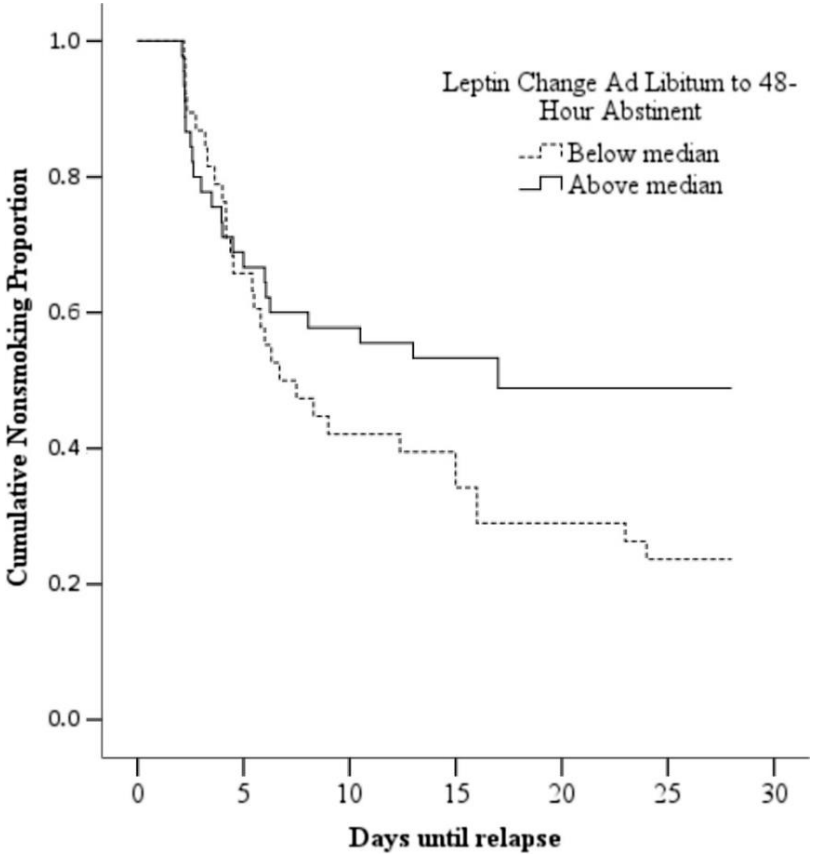






Stress and Substance Use

- Decline in leptin concentrations from ad libitum to abstinence



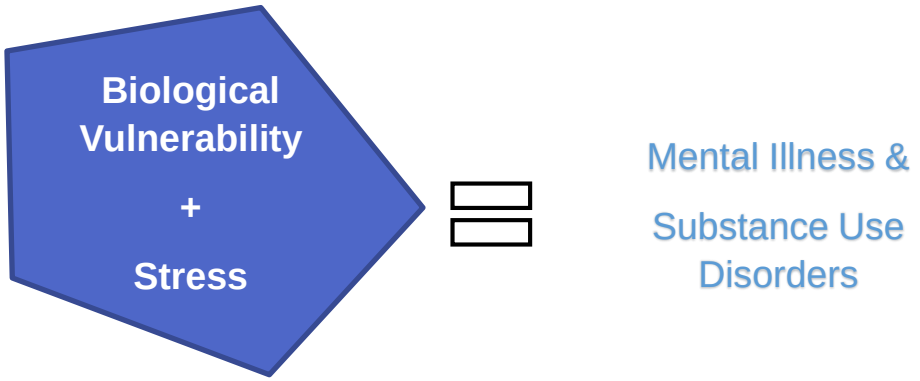
(Lemieux, Nakajima, Hatsukami, Allen & al'Absi, 2015)

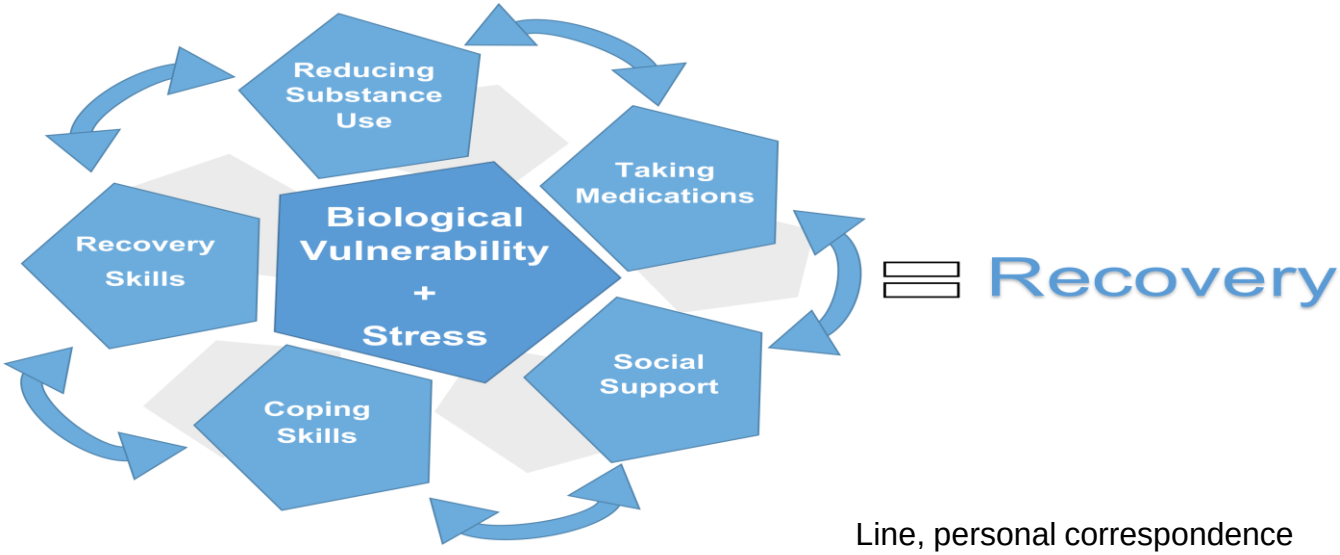
Stress and Substance Use

- 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



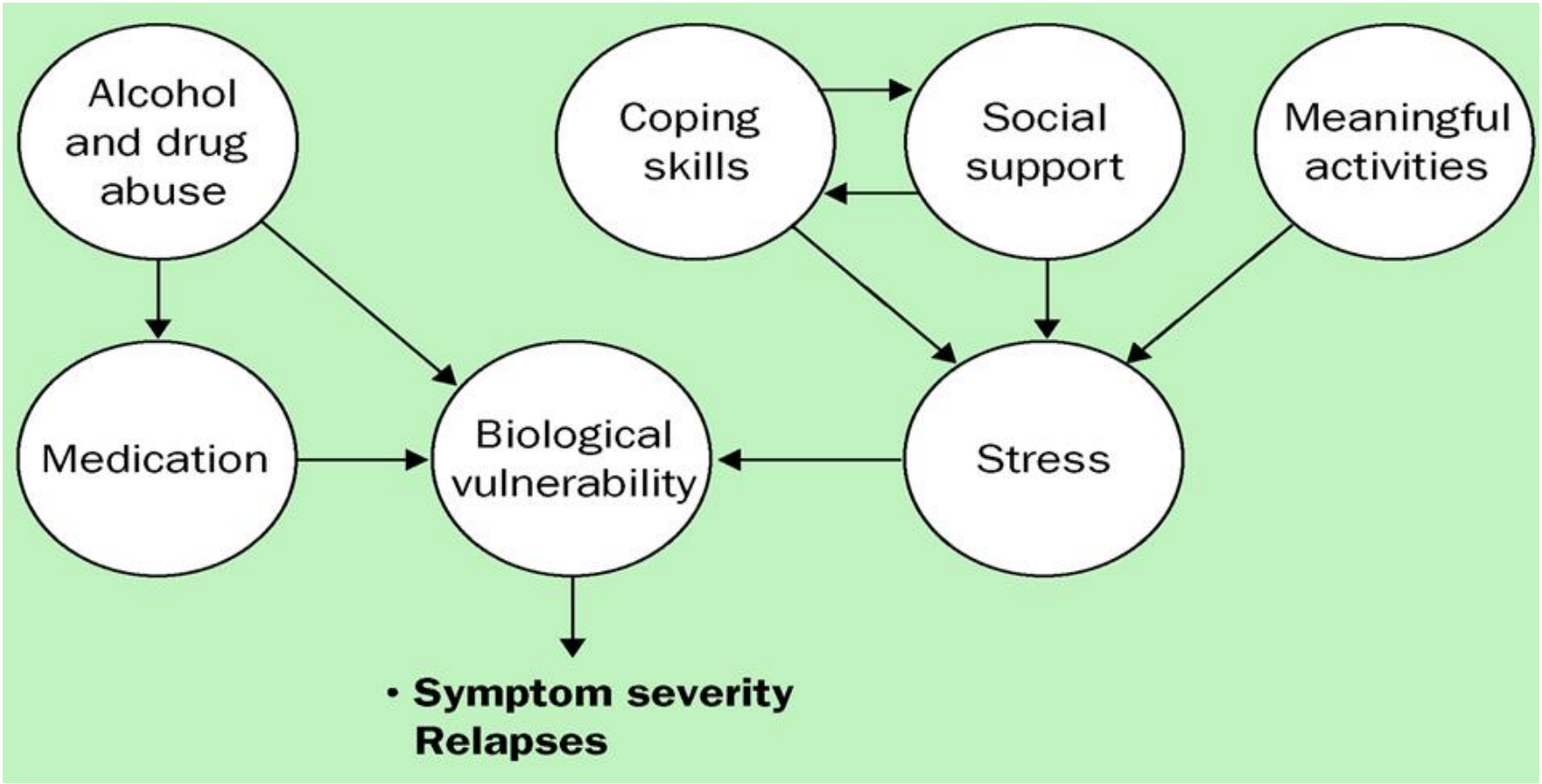


Line, personal correspondence

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



Substance Abuse and Mental Health Services Administration. Illness Management and Recovery: Practitioner Guides and Handouts. HHS Pub. No. SMA-09-4462, Rockville, MD: Center for Mental Health Services, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services, 2009.

Questions

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