Christopher La Tourette La Riche, MD, The Child is Father of the Man: Neurobiological Crossroads of Trauma, Addiction and Mood Disorders

LaRicheMD@gmail.com, Elements Behavioral Health Lecture, Winston-Salem, NC, March 2017
Heroin Overdose Deaths Exceed HIV Fatalities

The Countries That Imprison The Most People

Incarceration Rates in OECD Countries

Contextualizing Addiction as a Brain Disease

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Behavioral Health Lecture, Winston-Salem, NC, March 2017
Addictive Disorders as Circuit Disorders

Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Disruption in these circuits leads to the pathological pursuit of reward (by substance use) despite hazardous consequences.

(ASAM and NIDA)

Psychiatric vs Neurological Disease

Olds & Milner Discovered Rats will Lever Press to Receive Electrical Stimulation to Brain Regions

Neural Reward Circuits Important in the Reinforcing Effects of Drugs of Abuse

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Epigenetic Changes

The Neural Basis of Addiction: A Pathology of Motivation and Choice
Am J Psychiatry. 2005;162(8):1403-1413

Shared Neural Pathway for Reward

NALTREXONE

VIVITROL IS SHOWN TO HELP WITH OPIATES AND ALCOHOL IN:
- maintaining abstinence
- improving retention in treatment
- decreasing cravings
- preventing relapse

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Co-occurring Disorders (focus on Mood Disorders)

Epidemiology

Diagnosis

Past Year Addictive disorders, Mental illness (or both)

Past Year Treatment for both Co-occurring Patients in 2012

Coverage 2012

8.4 Million Adults with Co-occurring Mental Illness and Substance Use Disorder

Lifetime rates of alcoholism in major psychiatric disorders

12 months likelihood (ORs) of an additional SUD in Mania and Hypomania

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Hyper-hedonic Response to Reward in Bipolarity

People with Bipolarity evaluate Risk more in the Nucleus Accumbens than in Prefrontal Cortex

Shared Neural Pathway for Reward


Hyper-hedonic Response to Reward in Bipolarity

MoodCheck for Bipolarity (BSDS) Pies/Ghaemi

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MoodChech for Bipolarity (BSDS) Pies/Ghaemi

Is there a Link to Early Life Stress?

SO FAR:

- MOOD DISORDERS
- ADDICTIVE DISORDERS
- CO-OCCURRING DISORDERS
- NEUROBIOLOGY OF ADDICTION

The Adverse Childhood Experiences Study

The Adverse Childhood Experiences (ACE) Study

Summary of Findings:

- Adverse Childhood Experiences (ACEs) are very common
- ACEs are strong predictors of adult health risks and disease
- ACEs are implicated in the 10 leading causes of death in the U.S.

"I was actually stunned and I wept over what I saw."

-- ACE primary author Rob Anda, M.D.

Mechanisms by which Adverse Childhood Experiences Influence Health and Well-being Throughout the Lifespan

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ACE Score and Intravenous Drug Use

ACE Score and Impaired Childhood Memory

Adverse Childhood Experiences and Likelihood of > 50 Sexual Partners

ACE Score and Relation to Adult Homelessness

Risks Associated With Four or More Exposures of Childhood Trauma and Violence

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Adverse Childhood Experiences* Categories

Abuse of Child
- Recurrent sexual (statutory rape)
- Recurrent physical abuse
- Harassment, emotional abuse (or severe household member's emotional abuse)
- Mother treated violently
- General household violence
- Loss of parent (by death, by suicide, or by abandonment)

Neglect of Child
- Abandonment
- Child's basic physical and/or emotional needs unmet
- Child exposed to ACEs as the "heavy end" of abuse.

Trauma in (Child's) Household Environment
- ADDICTION IN HOUSEHOLD
- Parental separation or divorce
- Chronically depressed, emotionally disturbed or suicidal household member (MENTAL ILLNESS)
- Mother treated violently
- Imprisoned household member
- Loss of parent (by death, by suicide, or by abandonment)

Early Life Trauma and High-Risk Health Behaviors

Neurobiologic Effects of Trauma
- Disrupted normal brain and physical development
- Difficulty controlling anger, rage
- Hallucinations
- Depression
- Substance (habits)
- Anxiety
- Multiple (6+) somatic problems
- Sleep disturbance
- Memory problems
- Dissociation

Health Risk Behaviors
- Smoking
- Severe obesity
- Physical inactivity
- Alcoholism
- Drug abuse
- Suicide attempts
- Suicidal ideation
- Self harm
- Sexual promiscuity
- Multiple (6+) sex partners
- Repetition of original trauma
- Self injury
- Violence
- Eating disorders
- Sexually transmitted disease
- HIV/AIDS
- Homelessness
- Prostitution
- Delinquency, violence, criminal behavior
- Inability to sustain employment
- Compromised ability to parent
- Intergenerational transmission of abuse
- Long-term care of health, behavioral health, correctional, and social services

Long-Term Consequences of Unaddressed Trauma (ACEs)

Disease and Disability
- Ischemic heart disease
- Cancer
- Chronic lung disease
- Chronic emphysema
- Asthma
- Liver disease
- Diabetes
- Bone fracture
- Poor self-rated health
- Sexually transmitted disease
- HIV/AIDS

Serious Social Problems
- Homelessness
- Prostitution
- Delinquency, violence, criminal behavior
- Inability to sustain employment
- Compromised ability to parent
- Intergenerational transmission of abuse
- Long-term care of health, behavioral health, correctional, and social services

Table 1. ACE-Related Odds of Having a Physical Health Condition

<table>
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<tr>
<th>Health Condition</th>
<th>0 ACEs</th>
<th>1 ACEs</th>
<th>2 ACEs</th>
<th>3 ACEs</th>
<th>4+ ACEs</th>
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<tbody>
<tr>
<td>Arthritis</td>
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<td>14%</td>
<td>15%</td>
<td>16%</td>
<td>23%</td>
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<tr>
<td>Asthma</td>
<td>100%</td>
<td>17%</td>
<td>17%</td>
<td>17%</td>
<td>21%</td>
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<tr>
<td>Cancer</td>
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<td>11%</td>
<td>10%</td>
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</tr>
<tr>
<td>COPD</td>
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<td>13%</td>
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<tr>
<td>Diabetes</td>
<td>100%</td>
<td>11%</td>
<td>12%</td>
<td>15%</td>
<td>19%</td>
</tr>
<tr>
<td>Heart Attack</td>
<td>100%</td>
<td>11%</td>
<td>12%</td>
<td>17%</td>
<td>22%</td>
</tr>
<tr>
<td>Heart Disease</td>
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<td>13%</td>
<td>12%</td>
<td>16%</td>
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<tr>
<td>Kidney Disease</td>
<td>100%</td>
<td>13%</td>
<td>11%</td>
<td>15%</td>
<td>20%</td>
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<tr>
<td>Stroke</td>
<td>100%</td>
<td>14%</td>
<td>13%</td>
<td>16%</td>
<td>22%</td>
</tr>
<tr>
<td>Vision</td>
<td>100%</td>
<td>16%</td>
<td>16%</td>
<td>19%</td>
<td>24%</td>
</tr>
</tbody>
</table>

Advanced Children's Experience in Iowa: A New Way of Understanding Lifelong Health

Family Policy Council 2012

Family Policy Council 2012
POSSIBLE MECHANISMS

Theories of Depression

**Monoamine Hypothesis:**
Functional defect of Neurotransmitters (biogenic amines SER, NE, DA) evidenced by efficacy of Tricyclic antidepressants, MAO Inhibitors, SRIs

**Neuroendocrine/Chronic Stress Hypothesis:** Hypothalamic-Pituitary-Adrenal dysfunction and dysregulation of CRF-Cortisol circulation

**Inflammatory Hypothesis:** Immuno-mediated changes contribute to depression, including pro-inflammatory cytokines and cytokine-signaling pathways

ACE Study

- [www.cdc.gov/nccdphp/ace](http://www.cdc.gov/nccdphp/ace)
- [www.acestudy.org](http://www.acestudy.org)
- [www.acestoohigh.com](http://www.acestoohigh.com)

KEY ABBREVIATIONS

1) The Hypothalamus-Pituitary-Adrenal Axis is also called the (Adrenal Stress Axis)

HPA AXIS
2) The BIOCHEMICAL CASCADE that creates Cortisol is:

CRF \rightarrow ACTH \rightarrow CORTISOL

THE SIGNATURE OF STRESS
A traumatic experience elicits an immediate physiological response, and has long-term effects on the brain.

During stressful situations, the pituitary gland in the brain releases neurohormones.

In response, the adrenal glands release adrenaline and Cortisol.

Adrenaline induces quick, fight-or-flight responses.

Cortisol elicits long-lasting stress responses and shuts down the release of neurohormones.

CRF/HPA AXIS LINKS WITH LOCUS CERULEUS/ NORADENERGIC CIRCUIT CAUSING “FIGHT OR FLIGHT” RESPONSE

STRESS

Acute Stress (the fight or flight response) involves immediate stress hormones, energy allocation, and cardiovascular function.

Chronic stress suppresses immune systems, endocrine, gastrointestinal, and cardiovascular function.

KEY ABBREVIATIONS

CRF - Corticotropin-Releasing Factor
ACTH - Adrenocorticotropic Hormone

Hypothalamus-Pituitary-Adrenal Axis

Hughes (2012) Nature
Adapted from: McEwan B (2012), Protective and damaging effects of mediators of stress and adaptation
Summary: Stress Circuity and Depression

- Depression and the HPA axis: same depressed patients have hyperactive HPA axis, including stress cortisol or catabolism
- showroom coping, which may be related to HPA dysregulation, genetic susceptibility, and/or diminished cognitive function
- Depression, stress, and serotonin-dopamine neurotransmitter activity
  - HPA axis associated with specific symptoms of depression in certain brain regions
  - Serum cortisol levels and the dopamine to norepinephrine ratio: the presence of low dopamine/norepinephrine ratios is associated with severe, atypical depression, higher levels of anxiety, and abnormal triglyceride metabolism

Depression, stress, and endophenotypes: biobehavioral syndromes

- Reduced frontal activation in major depression patients
- Depression, low cortisol
- Increased aggression in non-depressed controls

Genetics

Early Adverse Life Events

Current Life Stress

CRF

Behavioral Effects

Addiction

Depression

Anxiety

Biological Effects

HPA Axis Activation

ANS Activation

Depressed adults showed equal response to antidepressant and psychotherapy

Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma

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IS THERE ANOTHER LINK BETWEEN A.C.E. AND LATER-LIFE:

- MOOD DISORDERS?
- ADDICTIVE DISORDERS?

CORTICAL THICKNESS

Measuring Cortical Thickness

Cortical Thickness after Childhood Sexual Abuse

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Cortical Thickness after Childhood Sexual Abuse in Women

Cortical Thinning in the Genital Sensory Cortex

Protect [the child] against processing the abusive experience at a sensory level but may be implicated in the development of (future) behavioral problems

“...gives to airy nothing a local habitation and a name.”

—Shakespeare, A Midsummer Night’s Dream

Thank you!

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