Mind-Body Problem Solving: The Link Between Emotional and Physical Well-Being

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OHSU Psychiatry Grand Rounds
A little bit about me: **Sarina Saturn**

- The scientist formerly known as **Sarina Rodrigues**
- 1993: Entered neuroendocrinology research at OHSU
- 2003: PhD in Neuroscience at NYU: **Joseph LeDoux**
- 2005: Postdoctoral fellow at Stanford: **Robert Sapolsky**
- 2007: Postdoctoral scholar at UC Berkeley: **Dacher Keltner**
- 2009: Professordom: **Oregon State University, University of Portland**
A little bit about me: Sarina Saturn

- Cellular, molecular, and systemic mechanisms of emotions

**Personal:**
- Stress
- Fear
- Depression

**Social:**
- Empathy
- Compassion
- Moral Elevation
Stress Response

- Raw, primal, and amazingly strong
- Hardwired universal survival mechanism
- Similar rudimentary neurobiological architecture across species
Life or death situations
Everyday situations
Fun 😊

“STRESSED” is “DESSERTS” spelled backwards
A little stress....
Too much stress....
Stress is ESPECIALLY bad if it is:

• 1) Unpredictable
• 2) Uncontrollable
• 3) Chronic
• 4) Traumatic
Amygdala: Core of Emotional Circuitry

Name comes from the Greek word for “almond”
Amygdala

- Fear
- Stress
- Anxiety
- Prejudice
- Challenges
- Ambiguity
Release of stress hormones

- Pituitary
- Adrenal gland
- Kidney
- Cortex
- Medulla

Glucocorticoids
Epinephrine and norepinephrine

- Increase in cardiovascular tone
- Increase in blood pressure
- Mobilization of stored energy to muscle
- Transient enhancement of immunity
- Inhibition of costly, long-term processes such as growth and reproduction

Rodrigues, LeDoux, & Sapolsky (2009)
Annual Review of Neuroscience
Influence of Chronic Stress on Neurons in the **Amygdala**

**Control**

**Stress**

Rodrigues, LeDoux, & Sapolsky (2009)
*Annual Review of Neuroscience*

Vyas et al. (2002)
*Journal of Neuroscience*
Hippocampus

- Provides details about the context / environment to memories
Influence of Chronic Stress on Neurons in the Hippocampus

Vyas et al. (2002) 
*Journal of Neuroscience*

Rodrigues, LeDoux, & Sapolsky (2009) 
*Annual Review of Neuroscience*
Prefrontal Cortex

- Powerful inhibitory hold over the amygdala
- Higher-order cognitive processes
  - emotion regulation
  - complex associations
  - imagination
  - time travel
Influence of Chronic Stress on Neurons in the Prefrontal Cortex

Izquierdo et al. (2006) *Journal of Neuroscience*

Rodrigues, LeDoux, & Sapolsky (2009) *Annual Review of Neuroscience*
*Trends in Immunology.*
Stress and the Body

**BRAIN AND NERVES**
- Headaches, feelings of despair, lack of energy, sadness, nervousness, anger, irritability, increased or decreased eating, trouble concentrating, memory problems, trouble sleeping, mental health problems (such as panic attacks, anxiety disorders and depression)

**SKIN**
- Acne and other skin problems

**MUSCLES AND JOINTS**
- Muscle aches and tension (especially in the neck, shoulders and back), increased risk of reduced bone density

**HEART**
- Faster heartbeat, rise in blood pressure, increased risk of high cholesterol and heart attack

**STOMACH**
- Nausea, stomach pain, heartburn, weight gain

**PANCREAS**
- Increased risk of diabetes

**INTESTINES**
- Diarrhea, constipation and other digestive problems

**REPRODUCTIVE SYSTEM**
- For women-irregular or more painful periods, reduced sexual desire. For men-impotence, lower sperm production, reduced sexual desire

**IMMUNE SYSTEM**
- Lowered ability to fight or recover from illness
Stress and the Body

- Myofascial pain syndrome
- Fibromyalgia
- Chronic pelvic pain
- Vague symptoms
- Referred pain
- Autoimmune Disorders
Referred Pain

(a) Mechanism of referred pain

(b) Clinical map of referred pain

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Fighting Stress with **Resilience:**

*maintenance of high levels of positivity and well-being in the face of significant adversity*
Resilience:  

*the capacity for rapid recovery after negative events (hardship and trauma)*
Resilient People

- do experience negative affect, but it does not persist
- profit from the information provided by the negative affect
Resilient People

- capacity for meaning making in response to stressful events
Resilient People

• able to show rapid recovery in biological systems after exposure to a stressful event

- Amygdala
- Prefrontal cortex
- Stress hormones
- Immune system
- Recovery
- Disease progression
Resilience and Illness

![Bar graph showing the relationship between stress level and illness index for low and high hardiness.]
Resilient People

• protected from developing psychopathology

➢ Depression
➢ Anxiety / Panic
➢ Phobias
➢ PTSD
➢ Addiction
Build resilience with prosocial behaviors: actions that benefit others

- Social connectedness is the key to bouncing back

Keltner, Kogan, Piff, & Saturn (2014)
Annual Review of Psychology
People who perceive strong social support experience:

- Faster recoveries
- Fewer medical complications
- Lower mortality rates at any age
- Less distress in the face of terminal illness
Social isolation

- activation of a group of pro-inflammatory genes that help fertilize the development of cardiovascular disease, cancer, and neurodegeneration.
- downregulation of genes involved in the production of antiviral defenses and a particular type of antibody.

Cole et al., Genome Biology, 2007

Lonely

Integrated

Inflammation

Immunoglobulin G₁ production
Type I interferon antiviral response
Low SES
Social loss / anticipated bereavement
Post-traumatic stress
Cancer diagnosis
Social threat
Loneliness
Social instability
Chronic stress
Low social rank
Caregiving for seriously ill
Depression
Early life low SES

Across a wide variety of other types of adverse life circumstances, we see the same general pattern of increased inflammatory gene expression and reduced activity of interferon and antibody genes.
This conserved transcriptional response to adversity (CTRA) is characterized by increased expression of genes involved in inflammation (e.g., proinflammatory cytokines such as IL1B, IL6, IL8, and TNF) and decreased expression of genes involved in type I IFN antiviral responses (e.g., IFI-, OAS-, and MX-family genes) and IgG1 antibody synthesis.

primary cellular mediators of these dynamics.
How not to live
How should we live?

What is the nature of true happiness?

Hedonic

One perspective suggests that happiness comes from accumulating lots of happy experiences – happiness can best be gained through the pursuit of happiness.

Eudaimonic

True happiness comes from not from pursuing happy experiences for the self but rather from dedicating oneself to the happiness of others, or the betterment of the world.
How often do you feel **happy**?
How often do you feel **satisfied**?

Short Flourishing – Hedonic

Life has **direction** and **meaning**?
Grow and become a **better person**?

Short Flourishing – Eudaimonic

How often do you feel **sad**?
How often do you feel **depressed**?

CES-D
hedonic and eudaimonic well-being appear to be similarly effective ways of being happy

Fredrickson et al., 2013 PNAS
plot the gene expression profiles for people with high levels of hedonic well-being, we see a very different story, with low levels of antiviral and antibody genes, and high levels of inflammatory gene expression.
at the level of psychology, hedonic and eudaimonic well-being are experienced quite similarly

at the level of immune cell genomes, hedonic and eudaimonic are experienced very differently

Steve Cole @ UCLA
Other-Oriented Living and Longevity

• **Volunteers live longer** than nonvolunteers, but this is only true if they volunteer for other-oriented, not self-serving, reasons.

Konrath et al., 2012 *Health Psychology*
Compassion Fatigue

Egoistic helping
• Empathic distress
• Consumption of our own discomfort
• Leads to BURNOUT
• Self-focused

Altruistic helping
• Empathic concern
• Taps into our restful and soothing caregiving system
• Creative & invigorating
• Other-focused
The Prosocial Nervous System

Keltner, Kogan, Piff, & Saturn (2014)
Annual Review of Psychology
Dopamine and Prosocial Behavior

- processing of self-relevant rewards as well as:
  - Charitable acts
  - When altruistic choices prevail over selfish ones
  - Cooperation
  - Fairness
  - Compassion meditation

Keltner, Kogan, Piff, & Saturn (2014)
Annual Review of Psychology
Serotonin and Prosociality

KEY FOR:
• Mood attunement
• Overall well-being
• Cooperation
• Fairness
• Affiliation
• Moral judgment
Oxytocin and Prosociality

• Oxytocin supports affiliative behavior in a variety of species
  ▪ pair-bond formation
  ▪ parental care
  ▪ bio-behavioral synchrony
Oxytocin and Prosocial Behavior

- In humans, intra-nasal administration of oxytocin increases:
  - generosity
  - trust
  - eye gaze
  - ability to infer the affective mental state of others

- Natural oxytocin levels relate to:
  - parent-child bonding behaviors
  - feelings of romantic love and trust
  - empathy and subsequent generosity towards strangers
  - bonding with pets
Oxytocin has potent physiological anti-stress effects:

- modulates stress hormone levels
- inhibits cardiovascular responses to stress
- lowers amygdala responses to emotional stimuli
What causes individual differences?

• GENETIC PREDISPOSITION
  - Genetic variations of our neurochemical systems can have a profound impact on neurochemistry
Polymorphisms
“many forms”
Variety is the Spice of Life

• This world would be VERY boring if we all looked, acted, and felt the same!
Neurochemical polymorphisms

• **Serotonin system**
  - social sensitivity and emotional reactivity

• **Dopamine system**
  - reward-related behaviors
**Oxytocin Receptor**

- Distributed throughout the body and the brain:
  - heart
  - hypothalamus, amygdala
  - medullary structures regulating vagal control of the heart
  - regions of the spinal cord that regulate the autonomic nervous system, especially the parasympathetic branch
How is a polymorphism (rs53576) of the oxytocin receptor related to stress reactivity?
Stress Reactivity: Physiological

- Startle paradigm: white noise bursts presented through headphones
- Average heart rate during a fear-potentiated startle anticipation task (vs. baseline)
Stress Reactivity: Startle Anticipation Heart Rate

Rodrigues et al. (2009)
Proceedings of the National Academy of Sciences
Stress Reactivity Scale

We used items that measure negative-emotion reactivity in stressful situations, emergencies, and crises, rather than baseline negative affect. This unidimensional scale measures a general factor of stress reactivity.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pearson Correlation</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resilience</td>
<td>-0.52**</td>
<td>Sinclair &amp; Watson, 2004</td>
</tr>
<tr>
<td>Rumination</td>
<td>0.52**</td>
<td>Trapnell &amp; Campbell, 1999</td>
</tr>
<tr>
<td>Perceived stress</td>
<td>0.59**</td>
<td>Cohen et al., 1983</td>
</tr>
<tr>
<td>Emotion Reappraisal</td>
<td>-0.28**</td>
<td>Gross &amp; John, 2003</td>
</tr>
<tr>
<td>Attentional Control</td>
<td>-0.46**</td>
<td>Derryberry &amp; Reed, 2002</td>
</tr>
</tbody>
</table>

with Oliver John @ UC Berkeley
Stress Reactivity: Dispositional

 Rodrigues et al. (2009)
 Proceedings of the National Academy of Sciences
How does the same genetic variation influence prosociality?
Davis: Interpersonal Reactivity Index (IRI)

A well-validated self-report scale that reflects the core facets of other-oriented empathic behavior
Dimensions (subscales) of the IRI

EMPATHIC CONCERN

• I often have tender, concerned feelings for people less fortunate than me.
Dimensions (subscales) of the IRI

**PERSPECTIVE TAKING**

- I sometimes try to understand my friends better by imagining how things would look from their perspective.
Dispositional empathy

Rodrigues et al. (2009)
PNAS
Reading the Mind in the Eyes

- Simon Baron-Cohen
- Performance enhanced in non-clinical populations after oxytocin administration (Domes et al., 2007)
- Performance negatively associated with autism
jealous

panicked

arrogant

hateful
alarmed  shy

hostile  anxious
Reading the Mind in the Eyes

Empathic accuracy

Percentage correct

AA/AG   GG   AA/AG   GG

male    female

Rodrigues et al. (2009)
Proceedings of the National Academy of Sciences
“14 Inevitable Scientific Breakthroughs the World Will Regret”
Listening Compassionately

• Strangers viewed 20-sec video clips of someone listening to their romantic partner talk about a time of suffering

• Evaluated nonverbal prosocial cues
  ▪ Eye contact
  ▪ Leaning
  ▪ Nodding
  ▪ Smiles
  ▪ Arm posture

Kogan et al. (2011)
Proceedings of the National Academy of Sciences (PNAS)
GGs rated more prosocial by strangers (>AAs/AGs)

Fig. 1. Differences in prosociality ratings of targets by genotype. Targets homozygous for the G allele (M = 4.21, SD = 1.40) were judged to be more prosocial than targets carrying an A allele (M = 3.80, SD = 1.41) (b = 0.42, P < 0.001). Error bars reflect standard deviations.

Kogan et al. (2011)
*Proceedings of the National Academy of Sciences (PNAS)*
Others have found that this same oxytocin receptor polymorphism relates to:

- Differential structure and function of emotional brain regions
- More sensitive parenting
- Lower risk for autism spectrum disorders
- .....more! 😊

Tost et al., 2010; Bakermans-Kranenburg & van Ijzendoorn, 2008; Tops et al., 2011; Norman et al., 2012; Wu et al., 2005; Wertmer, et al., 2009
Implications

• Genetic variability in the neurochemical systems may contribute to individual differences in complex human social and emotional behaviors.
Implications
Genes are not our destiny

Well, if your DNA made you do it, I'm sentencing your DNA to thirty years in prison.
Implications

- It is important to understand that everyone has unique obstacles to achieving inner-peace and prosociality.
What Determines Happiness

- Genetics: 50%
- Actions and Thoughts: 40%
- External Circumstances: 10%

Source: Sonja Lyubomirsky, Ph.D. University of California, Riverside
Build **resilience** with *meditation*

- increase coping skills and resiliency
- enhance and foster empathy and compassion thereby reducing and preventing burnout
- address the isolation within the healthcare community by providing opportunities for collaboration and cooperation

Mindful Medicine
*Physicians Retreat*
Mindfulmedicinepdx.org
Build **resilience** with *meditation*

- Increased in hippocampal and prefrontal gray matter volume
- Enhanced white matter connectivity
- Less age-related brain atrophy
- Decreased default mode network activation
Build **resilience** with **self-compassion**

relates to:

- *resilience*
- *stress regulation*
- *better health*
- *better sleep*
- *more prosocial traits*
- *post-traumatic growth*
Build **resiliency** with *movement*

- running
- hiking
- biking
- yoga
- dance

......*whatever moves you!* 😊
Build *resilience* by *compassion*

- Practicing
- Witnessing
MORAL ELEVATION

*Moral elevation, or elevation,* is a specific emotional state triggered by witnessing displays of virtue.

Elicitors of elevation are actions of others that are perceived as having moral beauty and great integrity.

These include moments of unexpected benevolence, kindheartedness, altruistic deeds, and displays of gratitude among strangers.
Moral Elevation

People are often profoundly moved by the virtue (moral excellence), yet neuroscience and psychology have little to say about the ‘other-praising’ family of emotions.
Moral Elevation

• Schnall, Roper, & Fessler (2010)
  o Found altruism to increase after elevation induction
  o Degree of altruism correlated with experiential self-reports of wanting to help others, feeling moved, warmth in chest, etc.
Moral Elevation

• Silvers & Haidt, 2008
  o Studied nursing mothers with infant children
  o After elevation induction (amusement as a control):
    o Mothers experienced more milk letdown
    o More likely to hug their children
  o Authors speculated that oxytocin, a hormone and neurotransmitter, may be involved

• We set out to characterize the biology underlying elevation...
The Vagus Nerve

- The social engagement system is intimately related to stress reactivity and oxytocin.
- The parasympathetic nervous system calms down the heart via the vagus nerve.
The Vagus Nerve

- One of the greatest mind-body connections
- The “love nerve”
  - connected to oxytocin system and caretaking
- Eyes, neck, heart, digestive organs

- Low “vagal tone” relates to:
  - Heart disease, obesity, diabetes
  - Psychiatric disorders

- High “vagal tone” associated with:
  - increased positive emotion
  - appearing more trustworthy to strangers
  - better social support networks
  - more prosocial children
**Parasympathetic**
- Constricts pupil
- Stimulates salivation
- Inhibits heart
- Constricts bronchi
- Stimulates digestive activity
- Stimulates gallbladder
- Contracts bladder
- Relaxes rectum

**Sympathetic ganglia**

**Sympathetic**
- Dilates pupil
- Inhibits salivation
- Relaxes bronchi
- Accelerates heart
- Inhibits digestive activity
- Stimulates glucose release by liver
- Secretion of epinephrine and norepinephrine from kidney
- Relaxes bladder
- Contracts rectum

**Spinal cord segments**
- Cervical
- Thoracic
- Lumbar
Elevation induction

Neutral baseline

Baseline

Emotion induction

Elevation

Amusement
Amusement
Rank-order Elevation Ratings

Walter, Saslow, & Saturn (2015)

Biological Psychology
Elevation boosts vagal tone (RSA) parasympathetic activity

B

Respiratory Sinus Arrhythmia (RSA)

RSA change (ms²)

1st Elev Peak  2nd Elev Peak  Amusement

Walter, Saslow, & Saturn (2015)

Biological Psychology
Elevation increases heart rate sympathetic activity

Heart Rate (HR)

HR change (bpm)

1st Elev Peak  2nd Elev Peak  Amusement

Walter, Saslow, & Saturn (2015)
Biological Psychology
Dual Activation of the Autonomic Nervous System

- During some situations that involve both arousal and social sensitivity, dual activation of the SNS and PNS may occur.

  ❖ Such situations include:
    - caring for infants (Kenkel et al., 2013)
    - crying (Trimble, 2012)
    - sexual activity (Carter, 1992)
Medial Prefrontal Cortex

- Medial prefrontal cortex (mPFC) is relevant to regulation of the autonomic nervous system and social-cognitive processing.
- Previous work has illustrated that vagus nerve activity is related to mPFC activity.

(Amodio & Frith, 2006; Thayer et al., 2012)
Functional Near-Infrared Spectroscopy (fNIR)

Figure 2 Absorption factors of 3 main chromophores in tissue

Fig. 1. fNIR sensor with 4 light sources and 10 detectors (left, top) and 16 optode (channel) measurement locations registered on sensor (left, middle) and on brain surface image (right). fNIR sensor positioned on participants’ head (left, bottom) and the fNIR Device model 1000 (bottom, middle). Brain surface image is from University of Washington, Digital Anatomist Project.
Elevation alters mPFC activity in a context-dependent manner

Walter, Saslow, & Saturn (2015)
Biological Psychology
<table>
<thead>
<tr>
<th>Manipulation check item</th>
<th>Mean (SE) in elevation (N = 50)</th>
<th>Mean (SE) in amusement (N = 48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happiness/joy</td>
<td>4.08 (0.19)</td>
<td>3.94 (0.17)</td>
</tr>
<tr>
<td>Warmth**</td>
<td>4.30 (0.17)</td>
<td>3.44 (0.19)</td>
</tr>
<tr>
<td>Inspiration**</td>
<td>4.64 (0.14)</td>
<td>2.92 (0.19)</td>
</tr>
<tr>
<td>Admiration**</td>
<td>4.60 (0.16)</td>
<td>2.83 (0.20)</td>
</tr>
<tr>
<td>Hope**</td>
<td>4.38 (0.18)</td>
<td>2.94 (0.19)</td>
</tr>
<tr>
<td>Tenderness**</td>
<td>4.08 (0.20)</td>
<td>3.02 (0.18)</td>
</tr>
<tr>
<td>Uplifted**</td>
<td>4.24 (0.21)</td>
<td>3.27 (0.21)</td>
</tr>
<tr>
<td>Awe**</td>
<td>3.72 (0.19)</td>
<td>2.98 (0.21)</td>
</tr>
<tr>
<td>Amused*</td>
<td>3.36 (0.19)</td>
<td>4.27 (0.22)</td>
</tr>
<tr>
<td>Sympathy/compassion**</td>
<td>4.44 (0.21)</td>
<td>2.79 (0.19)</td>
</tr>
<tr>
<td>Optimistic about humanity**</td>
<td>4.48 (0.20)</td>
<td>3.08 (0.22)</td>
</tr>
<tr>
<td>Wanted to help others**</td>
<td>4.50 (0.20)</td>
<td>2.69 (0.17)</td>
</tr>
<tr>
<td>More open and loving towards people in general**</td>
<td>4.22 (0.22)</td>
<td>2.79 (0.19)</td>
</tr>
<tr>
<td>More curious about the world</td>
<td>3.62 (0.22)</td>
<td>3.65 (0.22)</td>
</tr>
<tr>
<td>Eyes watering/tearing up**</td>
<td>3.55 (0.21)</td>
<td>1.33 (0.12)</td>
</tr>
<tr>
<td>Lump in throat/choked up**</td>
<td>2.76 (0.21)</td>
<td>1.31 (0.12)</td>
</tr>
<tr>
<td>Warm or expansive feelings in chest**</td>
<td>3.56 (0.22)</td>
<td>2.52 (0.22)</td>
</tr>
<tr>
<td>Heart beating faster*</td>
<td>2.52 (0.18)</td>
<td>1.94 (0.17)</td>
</tr>
<tr>
<td>Change in breathing</td>
<td>2.88 (0.21)</td>
<td>2.35 (0.20)</td>
</tr>
<tr>
<td>Chills, goose bumps, tingling on skin**</td>
<td>2.80 (0.24)</td>
<td>1.38 (0.11)</td>
</tr>
<tr>
<td>Laughter**</td>
<td>2.22 (0.17)</td>
<td>3.81 (0.21)</td>
</tr>
</tbody>
</table>

significant differences between conditions, determined by Student t-tests.
Future Directions

• Measure levels of oxytocin before and after elevation in mother-infant dyads and older adults
  ❖ Combine with social, genetic, autonomic, and epigenetic profiles
Magic pills for resiliency?!?
How can we get more resilient?

• build social bonds with loved ones and strangers
• witness and perform compassion and altruistic acts
• give and receive affection freely
• nourish and center our bodies, minds, and spirits
Take-home message

• **EVERYONE** can fight the damaging effects of stress on the brain and the body by integrating **social support** into their lives
Cultivate prosociality

• Being prosocial is amazingly beneficial to both your body and your brain.

• Therefore, being good to others is also good for you!
Acknowledgements

• OHSU Department of Psychiatry
• My greatest sources of social support
• My wonderful collaborators and research assistants
• National Science Foundation:

    NSF CAREER Grant BCS-1151905

• You! 😊