John Gabrieli 9.00

What stresses you?

```
What stresses you?
```

exams, grades

deadlines

traffic

family relationships

life after college, etc., etc.

```
What stresses you?

exams, grades

deadlines

traffic

family relationships

life after college, etc., etc.

What does not stress you?
```

```
What stresses you?
     exams, grades
     deadlines
     traffic
     family relationships
     life after college, etc., etc.
What does not stress you?
     being eaten or eating another being
```

What stresses a zebra?
(Robert Saplosky, Why Zebras Don't Get Ulcers)

What stresses a zebra?

serious physical injury predators (lions) starvation

 psychological and physiological response to a stimulus (*stressor*) that alters the body's equilibrium

Acute

injury

Chronic

hunger, cancer

Psychological deadline

**Physical** 

chronic work

pressure

Social

humiliation

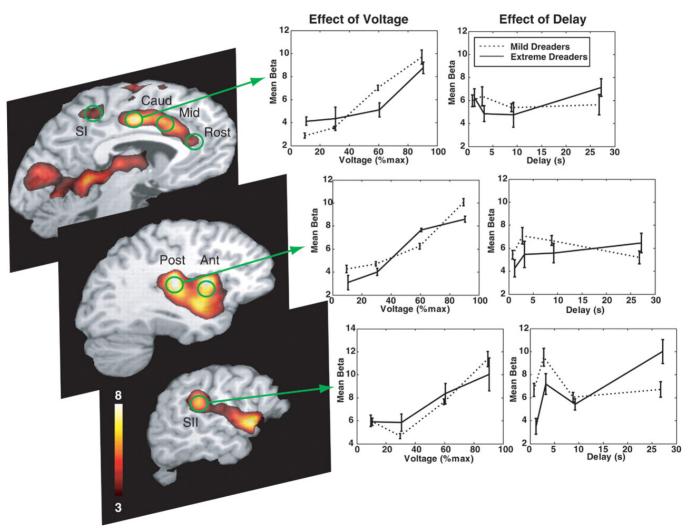
chronic isolation

- for animals, stress is often acute, physical, responsive
- for people in industrial society, stress is often chronic, psychosocial, anticipatory

### Neurobiological Substrates of Dread

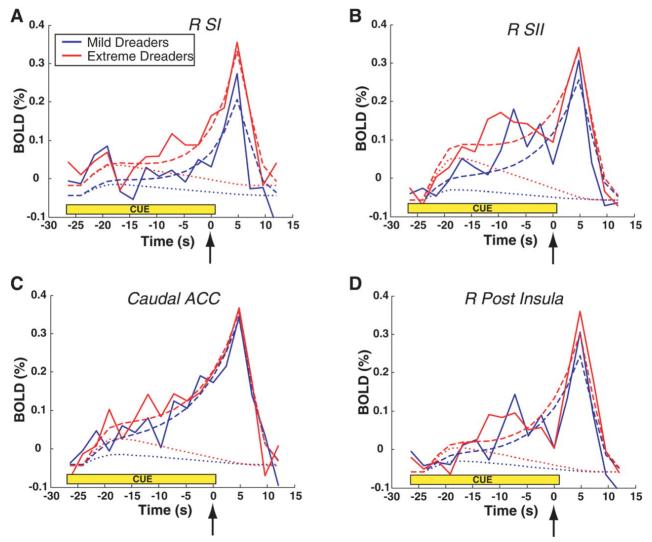
- Berns 2006, Science
- fMRI and waiting for a cutaneous electrical shock to foot
- each trial starts with information about voltage level and amount of time
- at first 100% of trials had voltage
- choice phase, e.g., 90% voltage in 3 secs or 60% voltage in 27 secs
- some people prefer more voltage now than to wait for shock (extreme dreaders)

#### More Voltage (Pain) Associated with Greater Brain Activation



Source: Berns, G. S., et al. "Neurobiological Substrates of Dread." *Science*, 312, no. 5774 (2006): 754-58. © AAAS. All rights reserved. This content is excluded from our Creative Commons license. For more information, see <a href="http://ocw.mit.edu/fairuse">http://ocw.mit.edu/fairuse</a>.

## **Extreme Dreaders Had Earlier & More Sustained Activation Between Cue and Shock**



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## Mortality

• 1900 ?

## Mortality

```
    1900 - infectious diseases & childbirth
pneumonia
tuberculosis
influenza (1918 - more than WWI)
childbirth (young women)
```

• 2007?

## Mortality

1900

```
pneumonia
tuberculosis
influenza (1918 - more than WWI)
childbirth (young women)
```

 2007 - cumulative damage heart disease cancer
 cerebrovascular disorders

 Hans Selye - 1930s - insightful scientists, not so good at handling rats

Colleague extracted ovarian chemical - what does it do? - Selye injected rats daily - dropped them, ran around - several months later - peptic ulcers, enlarged adrenal glands, shrunken immune tissue - also in control rats - exposed rats to many stressors, all had the same result

 The Stress Response is similar to a broad array of stressors

if stressors go on for too long, they make you sick

## STRESS & AUTONOMIC NERVOUS SYSTEM

- Sympathetic nervous system
  - brain to spine, organs, blood vessels, sweat glands, muscles and hairs (goosebumps)
  - emergency, arousal, activation
  - four Fs flight, fright, fight, and sex
  - releases epinephrine/norepinephrine (adrenaline/noradrenaline)
- Parasympathetic nervous system sleep, eating, relaxation

### **STRESS & AUTONOMIC NERVOUS SYSTEM**

<u>Sympathetic</u>

**Parasympathetic** 

speeds up

slows down

Heart

**Blood** 

to muscles from muscles

#### **STRESS & HORMONES**

- hypothalamus releases CRH (corticotropin releasing hormone) to anterior pituitary
- anterior pituitary (15 sec)
   releases adrenocorticotropic hormone
   (ACTH) into blood
- adrenal glands (kidney) (few minutes)
   release glucocorticoids (steroids) (cortisol)

#### Adaptive Stress-Response

- Mobilization of energy
- Increased cardiovascular tone
- Suppression of digestion
- Suppression of growth
- Suppression of reproduction
- Suppression of immune system
- Sharpening of cognition

#### **Stress-Related Disorder**

- Myopathy, fatigue, diabetes
- Stress-induced hypertension
- Ulceration, colitis
- Psychogenic dwarfism
- Amenorrhea, impotency, loss of libido
- Increased disease risk
- Neuron death

#### Adaptive Stress-Response

- Increased cardiovascular tone
- Increase heart rate
- Increase blood pressure to muscle (and brain) away from digestive system
- Decrease kidney function to keep water
- Void the bladder

#### **Stress-Related Disorder**

- Stress-induced hypertension
- Ventricular hypertrophy
  - (top predictor of cardiac arrest controlling for age)
- Damage to arteries
  - Plaque formation
  - Damaged inflamed blood vessels



This image is in the public domain.

#### Adaptive Stress-Response

Suppression of digestion

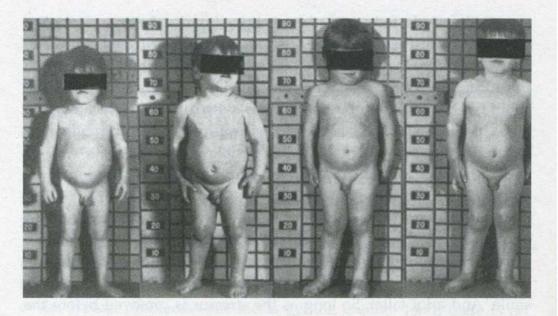
#### **Stress-Related Disorder**

- Ulceration, colitis
- Ulcer hole in the wall of an organ
- Peptic (gastric, esophageal,duodenal)
  - Robert Warren/Barry Marshall/2005 Nobel
- 1983
  - Bacterium heliobacter pylori swallowed/gastritis
  - Antibiotic treatment
  - But 15% of cases unrelated
  - And only 10% with bacterium get ulcers

Adaptive Stress-Response Stress-related Disorder

Suppression of growth

- Psychogenic dwarfism
- British Victorian family
- favorite son killed at 13
- Bereaved mother takes to bed
  - ignores 6 year-old son
- "David is that you? Oh, it is only you."
- David was perfect
- 5ft as an adult
- J.M. Barrie writes Peter Pan



A child suffering from stress dwarfism: changes in appearance during hospitalization (left to right).

#### A Demonstration of the Sensitivity of Growth to Emotional State

Condition	Growth hormone	Growth	Food intake
A. Entry into hospital	5.9	0.5	1663
B. 100 days later	13.0	1.7	1514
C. Favorite nurse on vacation	6.9	0.6	1504
D. Nurse returns	15.0	1.5	1521

Source: From Saenger and colleagues, 1977. Growth hormone is measured in nanograms of the hormone per milliliter of blood following insulin stimulation; growth is expressed as centimeters per 20 days. Food intake is expressed in calories consumed per day.

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mid 1950s Meyer Friedman Ray Rosenman cardiology practice

4/5 years later

TYPE A
PERSONALITY

Type-A Personality

Friedman & Rosenman, 1960s immensely competitive, over-achieving, time-pressured, impatient, hostile increased risk of cardiovascular disease like smoking, or high cholesterol

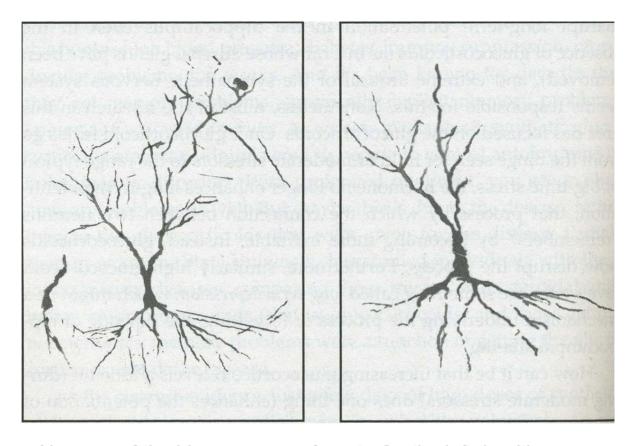
Type-A Personality
failures to replicate
applies to early age
key - hostility - many replications
suppressed expression

#### Adaptive Stress-Response

- Mobilization of energy
- Increased cardiovascular tone
- Suppression of digestion
- Suppression of growth
- Suppression of reproduction
- Suppression of immune system
- Sharpening of cognition

#### **Stress-related Disorder**

- Myopathy, fatigue, diabetes
- Stress-induced hypertension
- Ulceration, colitis
- Psychogenic dwarfism
- Amenorrhea, impotency, loss of libido
- Increased disease risk
- Neuron death



Neurons of the hippocampus of a rat. On the left: healthy neurons; on the right: neurons with their projections atrophied by sustained stress.

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- a severe anxiety disorder that can develop after exposure to any event which results in psychological trauma
- re-experience original trauma through flashbacks and dreams, increased arousal, hypervigilance
- assault/rape, combat
- sustained in about 20% of people

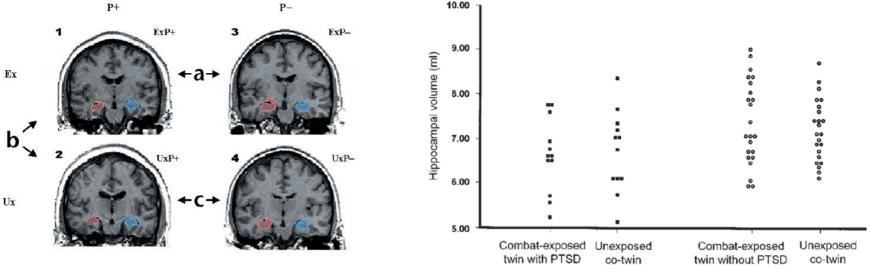
 smaller hippocampal volumes in PTSD (some variability in results)

 smaller hippocampal volumes in PTSD (some variability in results)

cause or consequence?

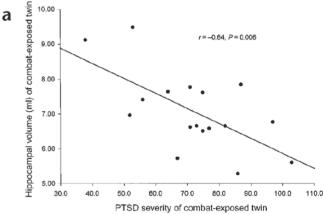
 smaller hippocampal volumes in PTSD (some variability in results)

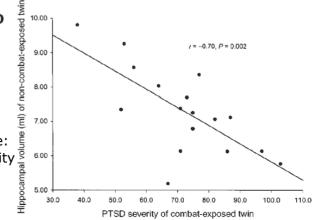
- cause or consequence?
- twin study correlation among monozygotic twins with and without combat exposure in hippocampal volume



Association between greater PTSD severity in combat-exposed twin and smaller hippocampal volume in both combat-exposed and non-combat exposed twin

Reprinted by permission from Macmillan Publishers Ltd: Nature Neuroscience. Source: Gilbertson, M. W., et al. "Smaller Hippocampal Volume Predicts Pathologic Vulnerability to Psychological Trauma." *Nature Neuroscience* 5, no. 11 (2002): 1242-47. © 2002.

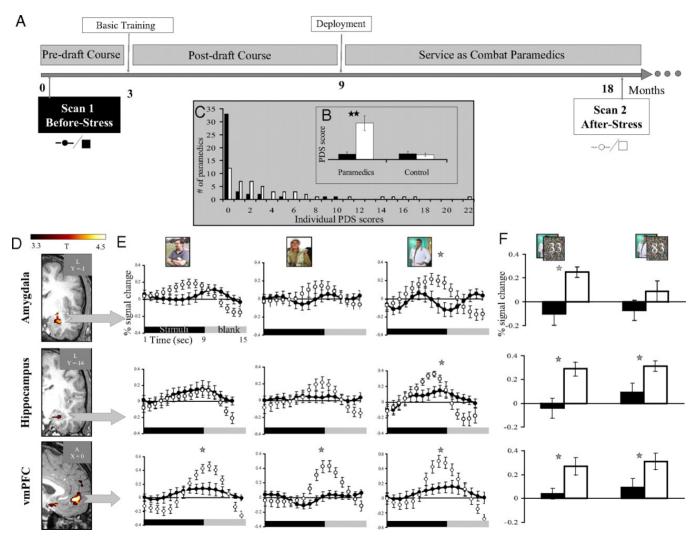




# POST-TRAUMATIC STRESS DISORDER (PTSD)

- prospective study
- Israeli military, 50 recruits before and after military service and stressful events
- increase in stress associated with greater amygdala and hippocampus response to stress-relate content
- amygdala reactivity before stress predicted increase in stress symptoms
- hippocampus change over time correlated with stress symptoms; contentspecific

#### (A) Timeline (months) of the prospective imaging study.



Admon R et al. PNAS 2009;106:14120-14125

Courtesy of Talma Hendler. Used with permission.



- Outlets for frustration
- Sense of predictability and of control
- A perception of life improving
- Social support

- Sense of predictability and of control
- rats hear warning bell before shock fewer ulcers predictability (vs. unknown)
- food delivered to rat at intermittent intervals vs. random delivery of equal food - glucocorticoid levels go up
- rat given lever to avoid shocks even if lever is disconnected to shocks, stress response is reduced
- people noxious noises one person has button to press to stop noise - less hypertensive whether button is pressed or not
- occupational stress high demand & low control

- Sense of predictability and of control
   Rodin & Langer, 1977
- nursing home

group A – make decisions for yourself
where to receive visitors
when to watch movie
what houseplant to take care of
group B – no instructions to make decisions
got plant, but staff took care of plant

1.5 years later - group A more cheerful, active, and alert, healthier, half as many had died

Sense of predictability and of control

**Cultural Influences** 

Individualist - US/Europe

Collectivist - East Asian (and rest of the world?)

Elementary school 7-9 year olds, Asian-American or Anglo-American – Ms. Smith – six markers (6 colors) – six piles of anagrams (family, animal, etc. RIBD)

Random assignment to 3 groups

- you choose, teacher chooses, mother chooses
- Anglo-Americans self = 4X Ms Smith, 2.5X mother
- Asian-Americans 30% more for mother than self,
   2X than Ms Smith

Sense of predictability and of control

life and death struggle

Richter, 1957
Water temperature and endurance
Rats in a jar – how long does rat swim before drowning?
15 minutes-60 hours before giving up, much variation

Picked up rats, let them wriggle free, in and out of water,

Average of 60 hours of effort

- Social support
- Primates after stress response, among strangers worse; among friends - better (measured by glucocorticoids)
- People stressor (public speaking, math task, argument with strangers) - less cardio-vascular response with a supportive friend present
- Observations people with spouses/close friends live longer; when spouse dies, risk of dying increases; parents of children killed in war have higher risk of disease/mortality only if divorced/widowed; patients with severe coronary disease had 3x death rate over 5 years if lacking social support

- A perception of life improving (worsening)
- rats/shocks rat #1 10/hr; rat #2 50/hr;

Day 2 - all rats get 25/hr; 10-25 becomes hypertensive

### Risk of Ulcer

Shock alone + another rat + wood bar + warning signal + lever  $50 \rightarrow 25$  shocks + friends

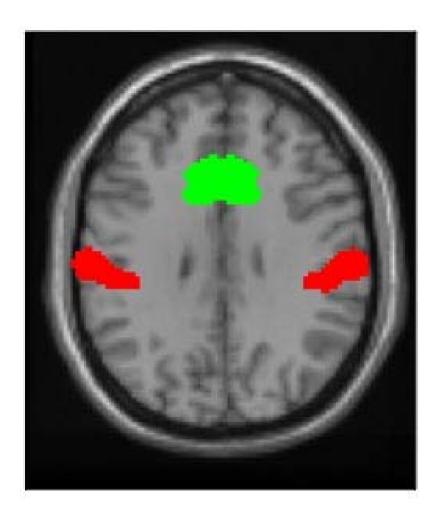
## **Embodied Cognition**

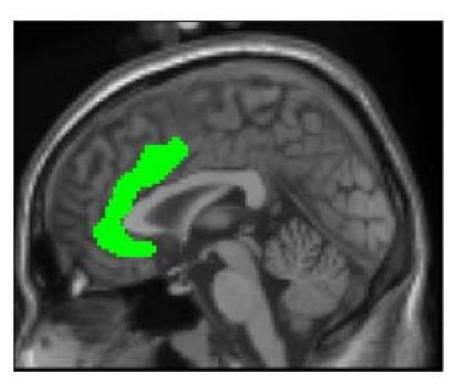
- the nature of the human *mind* largely determined by the *form* of the human body
- ideas, thoughts, concepts, categories shaped by aspects of the body
- is emotional pain (social, romantic rejection) built out of physical pain?

#### Pain

sensory - objective affective - subjective (suffering, unpleasantness)

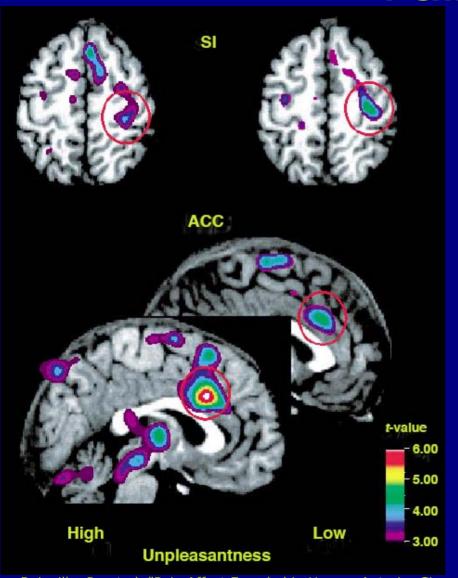
## **Pain Processing**

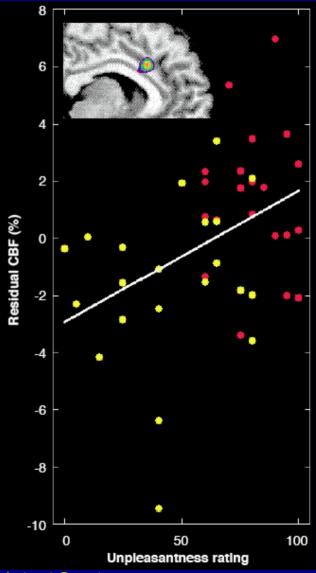




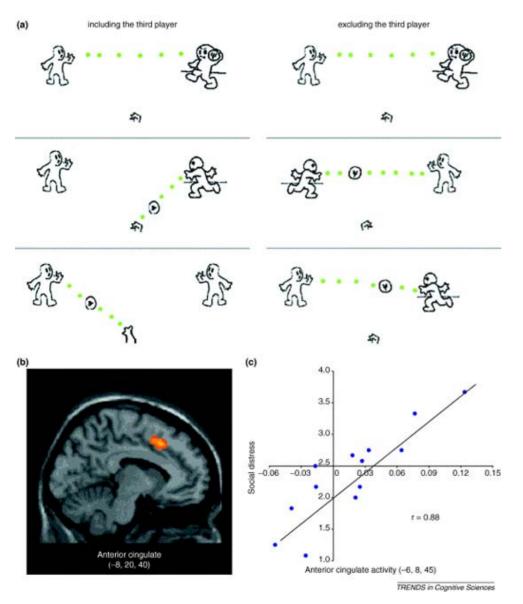
- cingulate
- somatosensory cortext

## Hypnotic Suggestion of High or Low Pain





Source: Rainville, P., et al. "Pain Affect Encoded in Human Anterior Cingulate but not Somatosensory Cortex." *Science* 277, no. 5328 (1997): 968-71. © AAAS. All rights reserved. This content is excluded from our Creative Commons license. For more information, see http://ocw.mit.edu/fairuse.



### **Social Pain**

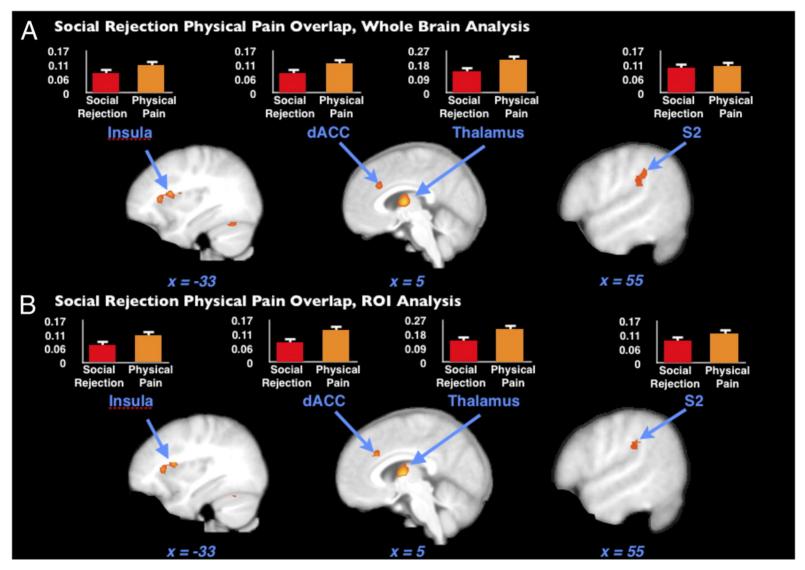
Methodology and results from an fMRI study of social exclusion. (a) Example of what participants viewed while in the scanner. Participants were included in the ball-tossing game during one round and excluded during another. (b) Participants showed increased dorsal anterior cingulate cortex (dACC) activity during the exclusion compared with the inclusion episode. (c) Participants' levels of self-reported distress correlated highly with dACC activity during the exclusion episode compared with the inclusion episode.

Source: Eisenberger, N. I., and M. D. Lieberman. "Why Rejection Hurts: A Common Neural Alarm System for Physical and Social Pain." *Trends in Cognitive Sciences* 8, no. 7 (2004): 294-300. Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.

### **Romantic Pain**

- Physical pain (heat)
- Romantic pain/social rejection
- Participants "felt intensely rejected as a result of recently experiencing an unwanted romantic relationship breakup"
- Viewed pictures of ex-partners and thought about being rejected (vs. viewing pictures of friends and thinking about positive experiences

### Neural overlap between social rejection & physical pain



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## Pain of Social Rejection

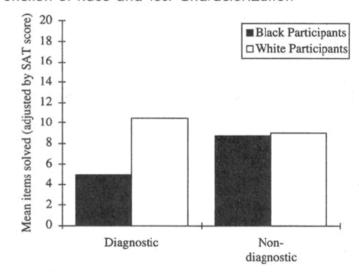
- random assignment
  - 2000 mg acetaminophen (Tylenol, Excedrin) for 3 weeks
  - placebo
- provide daily reports
- by Day 15, less painful resposne to rejection
- less brain response to social rejection

### **Stereotype Threat**

threat that others'
judgments or one's own
actions will confirm
negative stereotypes about
one's group

stress from stereotype knowledge undermines performance

Figure 2
Mean Performance on a Difficult Verbal Test as a
Function of Race and Test Characterization



Note. SAT = Scholastic Assessment Test.

Source: Steele, Claude M. "A Threat in the Air: How Stereotypes Shape Intellectual Identity and Performance." *American Psychologist* 52, no. 6 (1997): 613-29. Courtesy of American Psychological Association. Used with permission.

## **DEMO**

### <u>Unpleasant</u>

**Pleasant** 

abuse crash filth murder sickness accident death grief poison stink assault disaster

caress freedom health love peace cheer friend heaven loyal pleasure diamond gentle

### **Black Americans**

### White Americans

ALONZO JAMEL

**LERONE** 

THEO

**JEROME** 

LEROY

DARNELL

LAMAR

RASHAUN

DEION

LAMONT

MALIK

ADAM

CHIP

HARRY

ALAN

FRANK

IAN

JUSTIN

FRED

JED

TODD

HANK

WILBUR

LEFT for Unpleasant

cancer health corpse diamond truth devil assault triumph glory brutal talent agony kindness family divorce stink peace torture

RIGHT for Pleasant LEFT for BLACK

**ALONZO** JAMEL ADAM **LERONE** HARRY CHIP MALIK **TODD** LEROY DARNELL JUSTIN **FRED** LAMAR HANK DEION FRANK **JED** RASHAUN

RIGHT for WHITE LEFT for Unpleasant or BLACK

FRANK devil **ANDREW** diamond MALIK health **TYRONE** triumph BRAD brutal RASHAUN agony HARRY family JACK beauty LAMAR stink

RIGHT for Pleasant or WHITE LEFT for WHITE RASHAUN DARNELL JUSTIN **FRED** LAMAR HANK DEION FRANK JED **ALONZO** JAMEL ADAM **LERONE** HARRY CHIP MALIK **TODD** LEROY

RIGHT for BLACK LEFT for Unpleasant or WHITE

LAMAR corpse MATTHEW truth **JED** assault DEION glory **JONATHAN** talent LAMONT kindness JAMEL divorce **TERRYL** peace **JUSTIN** 

cancer

RIGHT for Pleasant or BLACK  faster for "unpleasant or black" than "unpleasant or white"?

### IMPLICIT ASSOCIATION TEST IAT

 faster for white + pleasant than black + pleasant? 75% of whites; 50% of blacks

automatic sterotypes?
 attitudes vs.associations?

 many domains - aging, techies vs. fuzzies/in-group vs. outgroup

https://implicit.harvard.edu/implicit/

## IMPACT OF INTERRACIAL CONTACT ON EXECUTIVE FUNCTION

- Richeson et al., 2003
- White individuals completed IAT
- Go to a different room, interact with either black or white experimenter, videotaped comments on college fraternity system and racial profiling after 9/11
- Go back and perform Stroop task
- Measure interference (incompatible (BLUE) minus control (BLUE) trials))

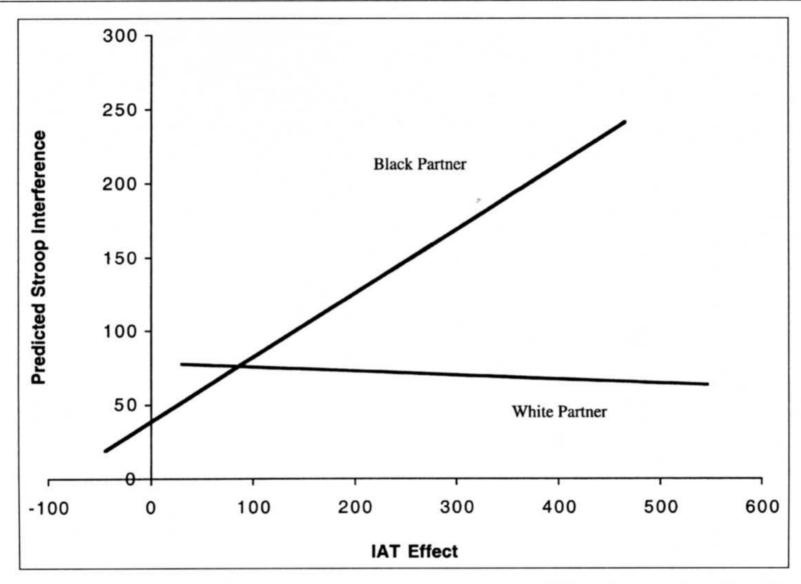


Fig. 1. Predicted Stroop interference as a function of Implicit Association Test (IAT) bias, after interaction with a White or Black partner.

Source: Richeson, J., and J. Shelton. "When Prejudice Does Not Pay: Effects of Interracial Contact on Executive Function." *Psychological Science* 14, no. 3 (2003): 287-90. © Sage publications. All rights reserved. This content is excluded from our Creative Commons license. For more information, see <a href="http://ocw.mit.edu/fairuse">http://ocw.mit.edu/fairuse</a>.

### The Yerkes-Dodson Law

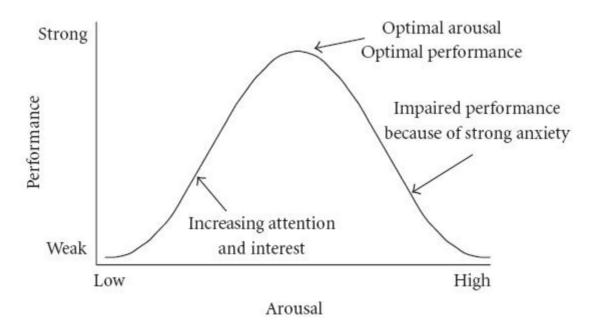


Image is Figure 3 from Diamond D. M., et al. "The Temporal Dynamics Model of Emotional Memory Processing: A Synthesis on the Neurobiological Basis of Stress-Induced Amnesia, Flashbulb and Traumatic Memories, and the Yerkes-Dodson Law." *Neural Plasticity* 33 (2007) dx.doi.org/10.1155/2007/60803.

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