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C O N F E R E N C E

Rethinking Mental Illness: The View from 2022

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Rethinking Mental Illness: The View from 2012

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Disclosures: None

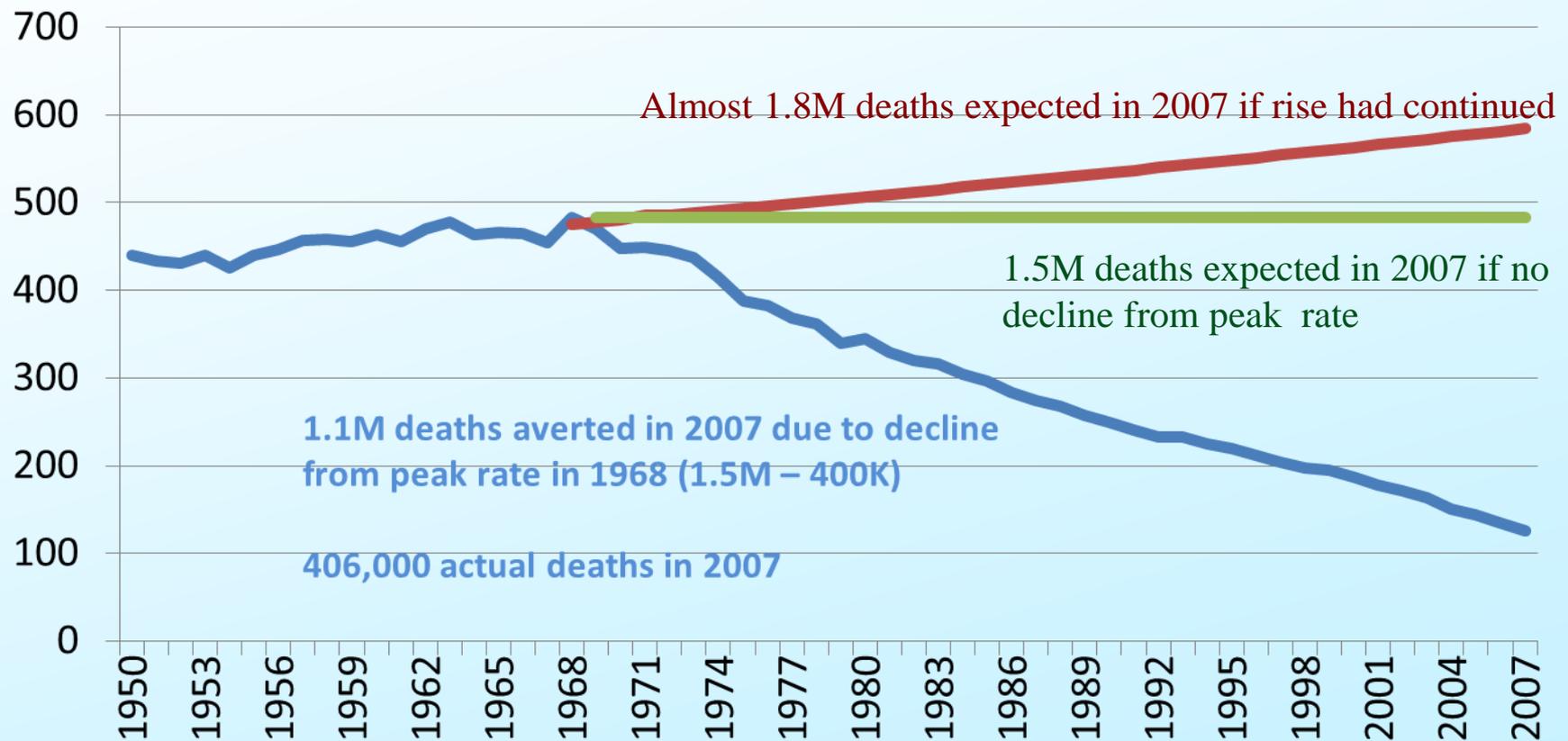
Federal employee: Public filing of all financial interests

Key Message: Research = Hope

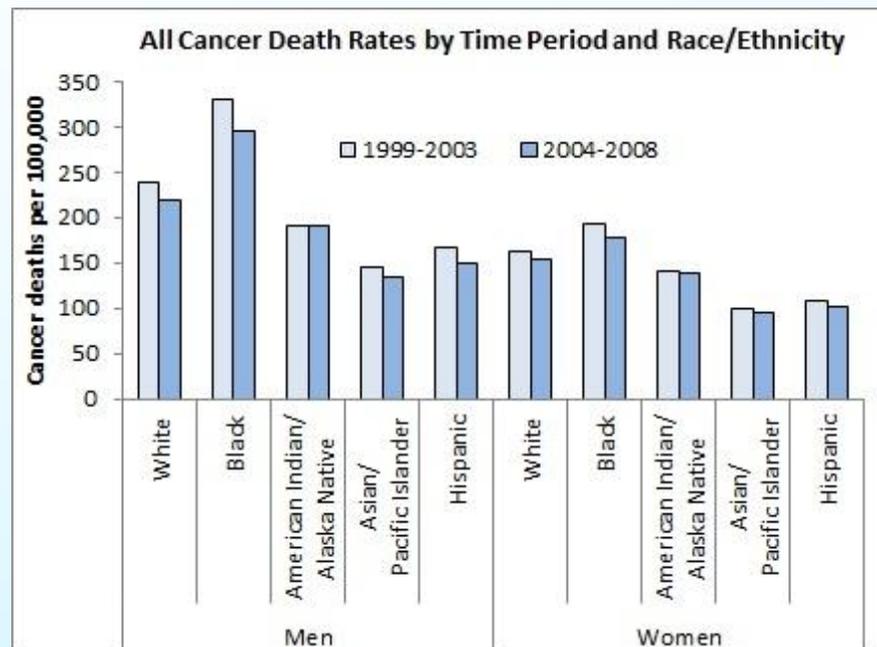
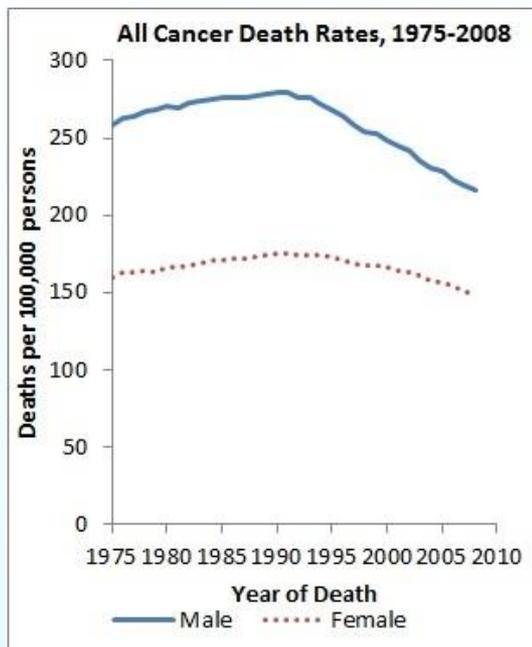
Impact of Research on Heart Disease

Age-Adjusted Death Rates for Coronary Heart Disease, U.S., 1950–2007

— Actual — Expected — Peak

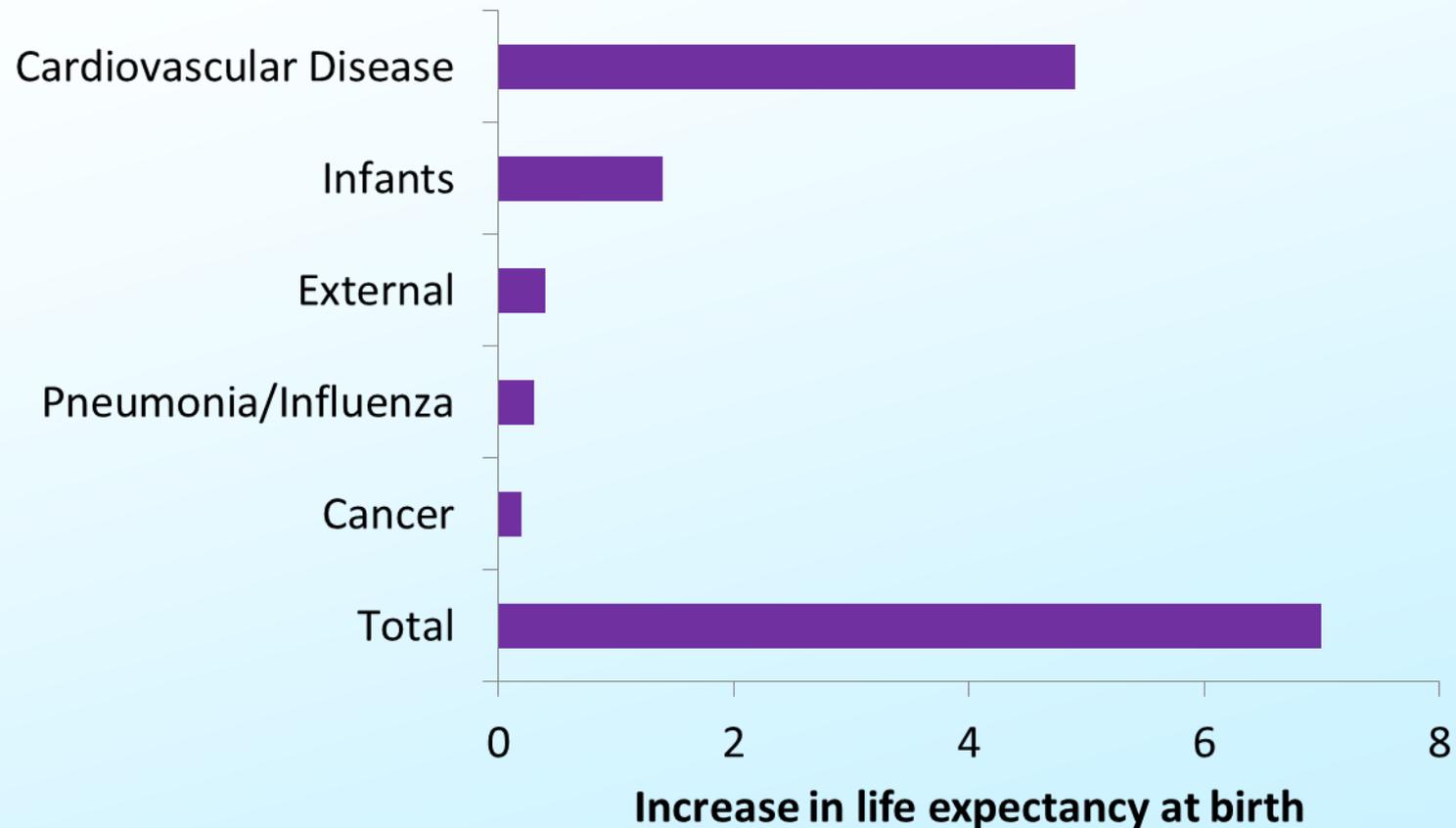


Impact of Research on Cancer



- Death rates from all cancers continued to decline in the U.S.
- Incidence rates among men decreased by 0.6% per year between 2004 and 2008
- Incidence rates among women decreased by 0.5% per year between 1998-2006, with rates leveling off from 2006 to 2008

Sources of Increased Longevity, 1960-2000



Source: Cutler, Rosen, Vijan, NEJM, 2006

Impact of Research on Mental Illness

- Diagnosis is by observation, detection is late, prediction is poor
- Etiology is unknown; prevention is not well-developed for most disorders
- Treatment is trial and error – no cures, no vaccines.

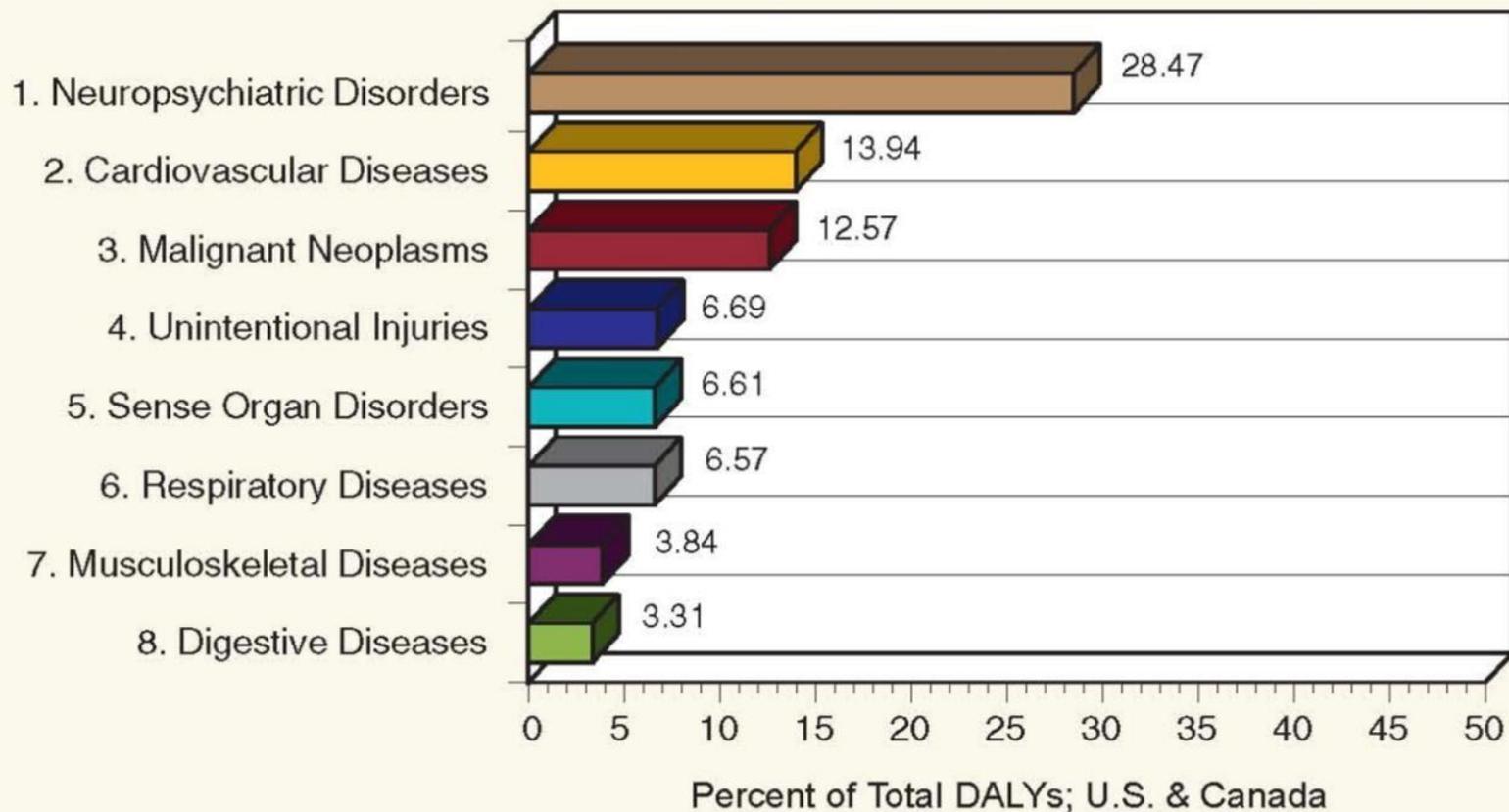
Bottom line:

Prevalence has not decreased for any illness

Mortality has not decreased for any illness

Mental Disorders are Chronic and Disabling

**Burden of Disease:
Lead Contributing Disease Categories to DALYs**



Source: WHO 2008

Mental Disorders: Mortality

- Over 36,000 suicides per year in the U.S. (2009; CDC)
 - 90% related to mental illness (Mann, 2002)
 - More suicides than combat deaths in US Army (DoD, 2011)
- For context:
 - 17,000 homicides (2009; CDC)
 - 34,000 traffic fatalities (2009; CDC)
 - < 20, 000 AIDS deaths (2009, CDC)

Life expectancy: 8 fewer years
(cardiopulmonary, metabolic, multiple conditions)
(Druss et al., Medical Care, 2011)

The Most Costly Conditions

Economic Burden of Noncommunicable Diseases, 2011-2030

(trillions of US\$ 2010)

Country income group	Diabetes	Cardiovascular diseases	Chronic Respiratory diseases	Cancer	Mental Illness	Total
High	0.9	8.5	1.6	5.4	9.0	25.5
Upper-middle	0.6	4.8	2.2	2.3	5.1	14.9
Lower-middle	0.2	2.0	0.9	0.5	1.9	5.5
Low	0.0	0.3	0.1	0.1	0.3	0.9
LMIC	0.8	7.1	3.2	2.9	7.3	21.3
World	1.7	15.6	4.8	8.3	16.3	46.7

Source: *The Global Economic Burden of Noncommunicable Diseases*. WEF, 2011

US Annual Costs > \$300B for SMI (Insel, AJP, 2008)

Unmet Medical Need - Summary

- Neuropsychiatric disorders are the largest source of disability for all medical causes
- These disorders are serious and deadly
- These disorders are major global economic burden

Research = Hope



Disruptive Innovations In Mental Health

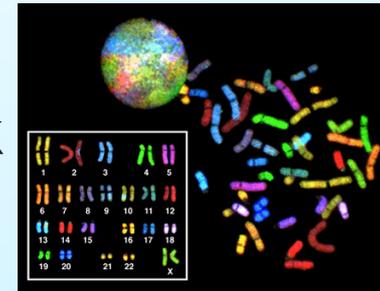
- Mental disorders are brain disorders

Circuits not lesions, not chemicals, not simple



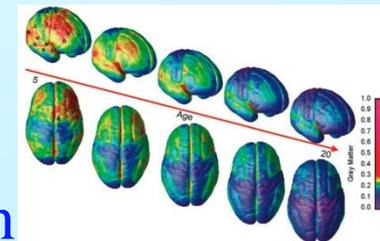
- Mental disorders result from complex genetic risk

Experience matters, so does family history



- Mental disorders are developmental disorders

Early experience + genes → circuit formation





Mapping the Human Connectome

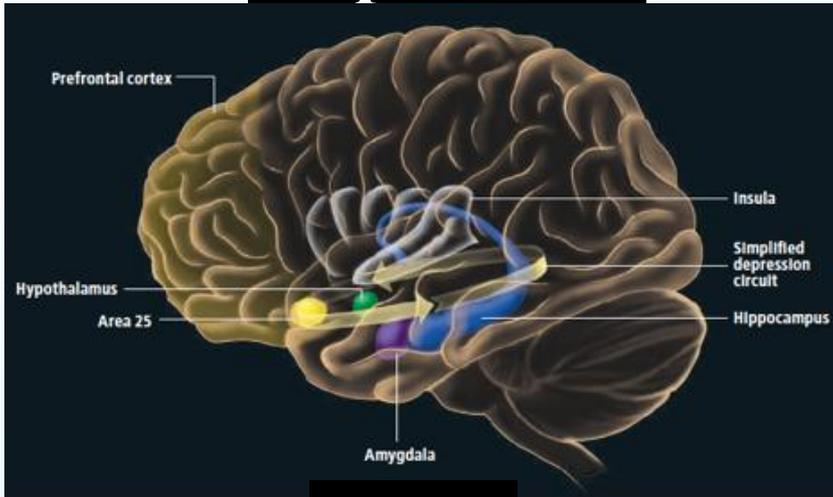


Wedge et al, Science, 2012

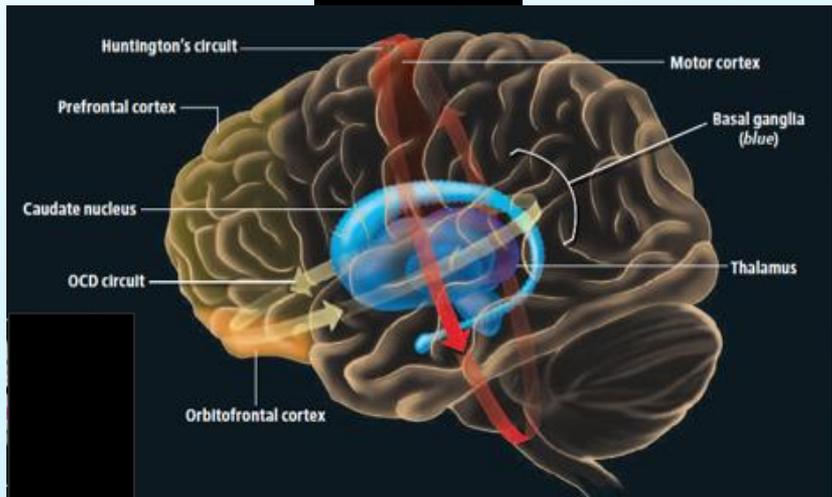
Mental Disorders as Neural Circuit Disorders



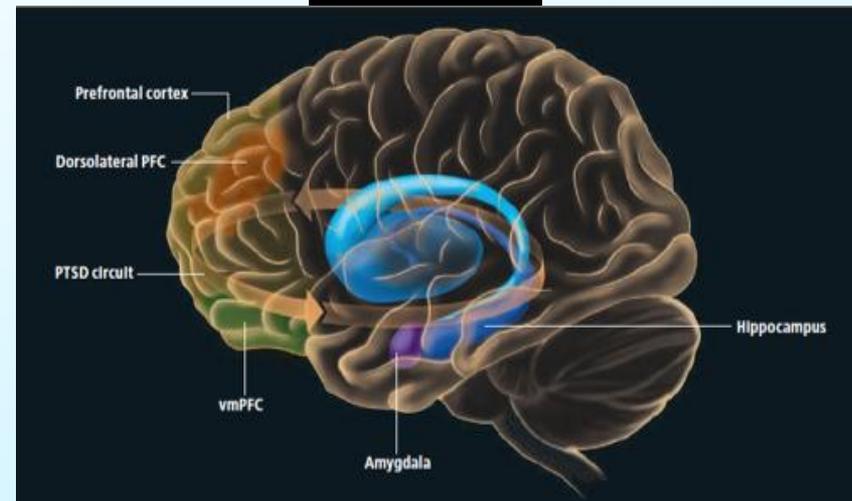
Depression



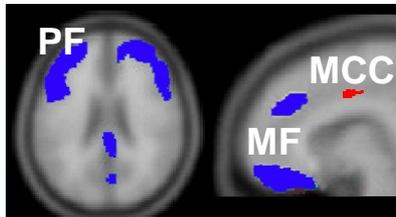
OCD



PTSD

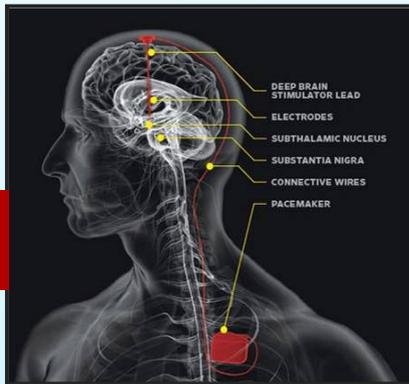


Depression as a Brain Circuit Disorder



CBT

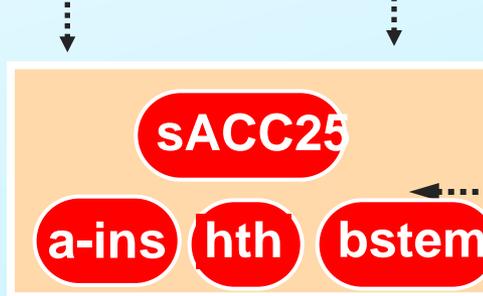
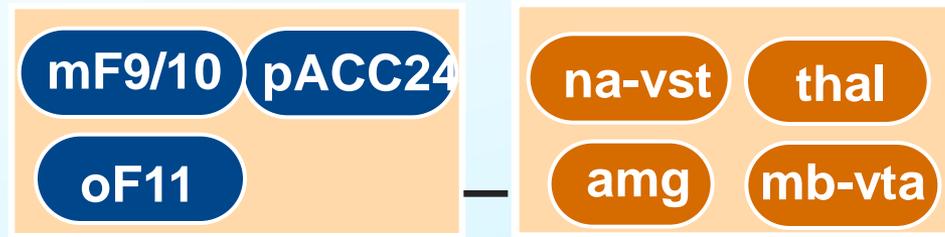
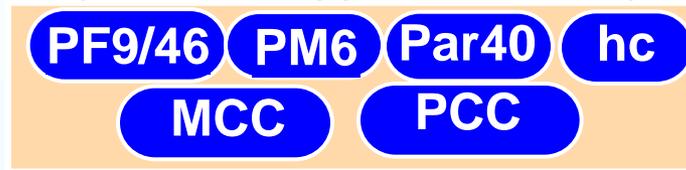
Self-awareness
insight



DBS

Br Med Bul 65:193-207, 2003
Arch Gen Psych 61:34-41-2004

Cognition
(attention-appraisal-action)

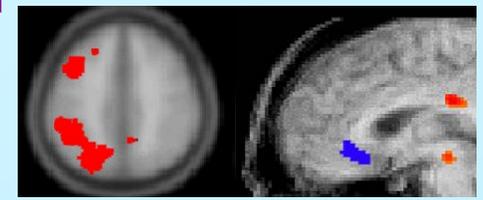


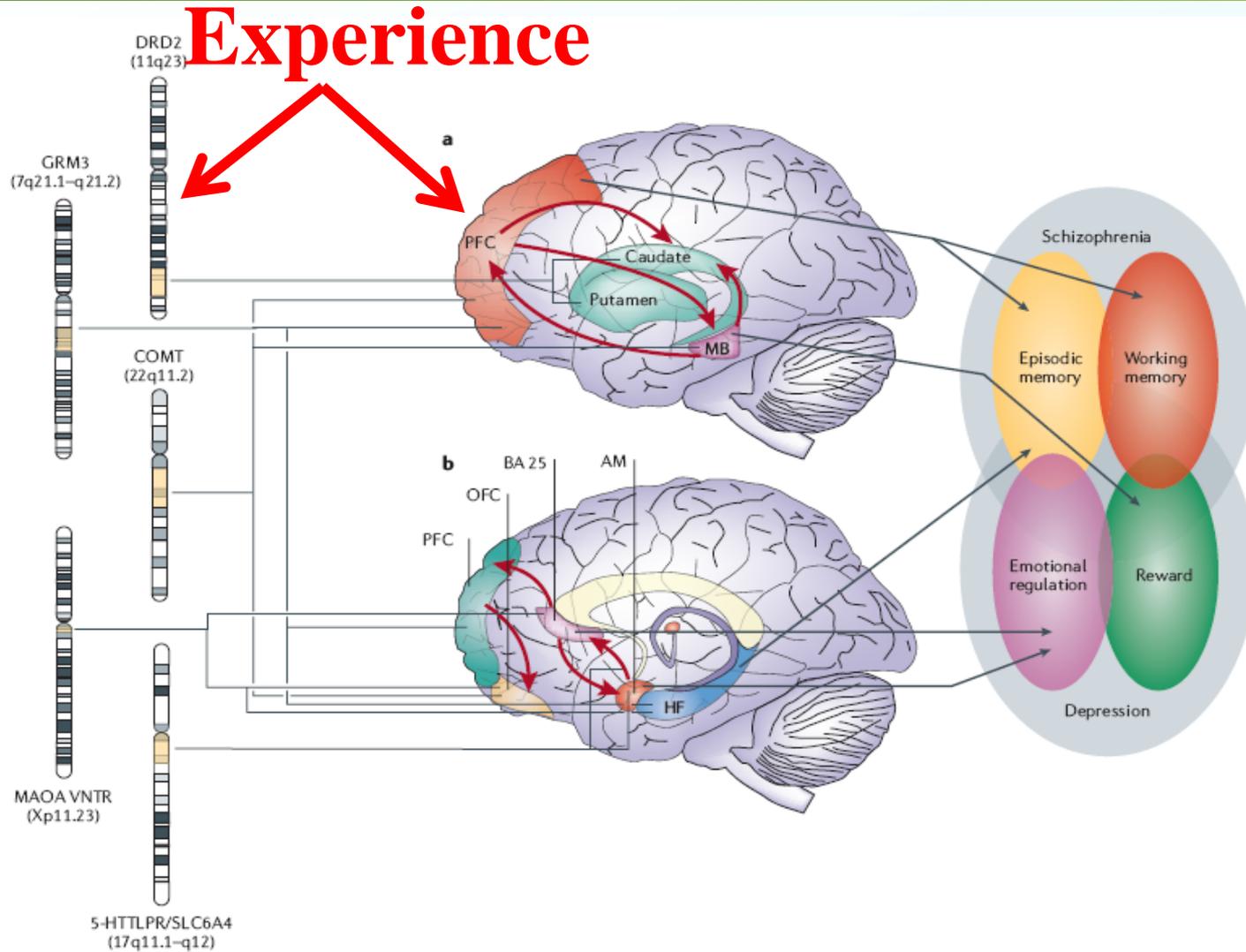
Interoception
(drive-autonomic-circadian)

**Saliency
Motivation**

**Mood
state**

MEDS





What have we learned from genetics?

- Genetic \neq Inherited (spontaneous mutations are common)
- Genetic \neq Causal (genes confer risk and resilience)
- Genetics \neq Experience is unimportant (epigenomics!)
- Genetics (genomics) is our most powerful tool for understanding individual variation

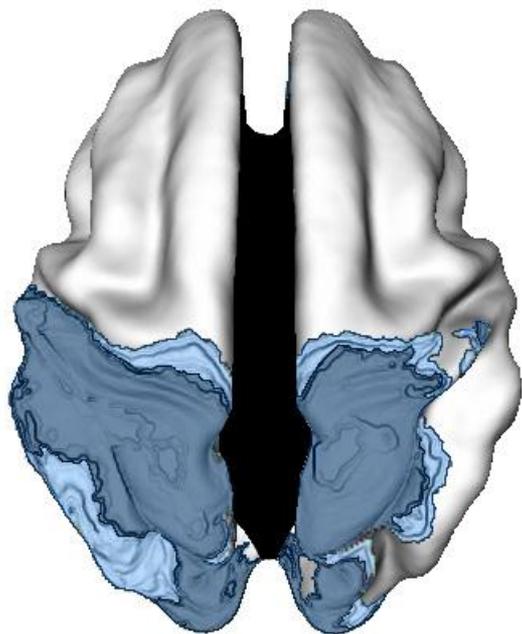
ADHD: a neurodevelopmental disorder

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation

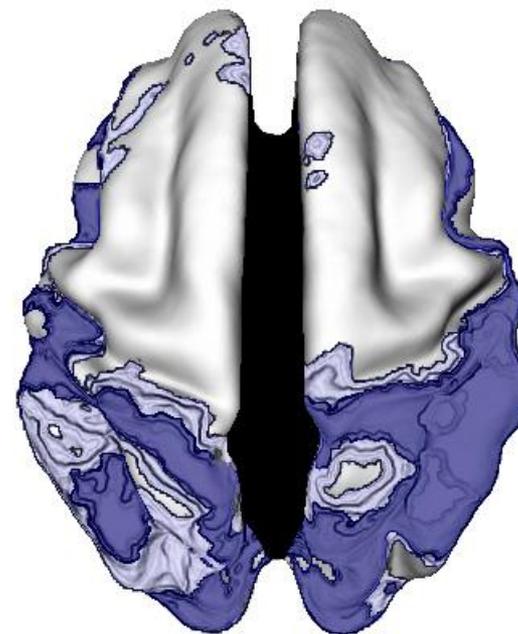
PNAS, 2007

P. Shaw^{†‡}, K. Eckstrand[†], W. Sharp[†], J. Blumenthal[†], J. P. Lerch[§], D. Greenstein[†], L. Clasen[†], A. Evans[§], J. Giedd[†], and J. L. Rapoport[†]

AGE: 5



ADHD



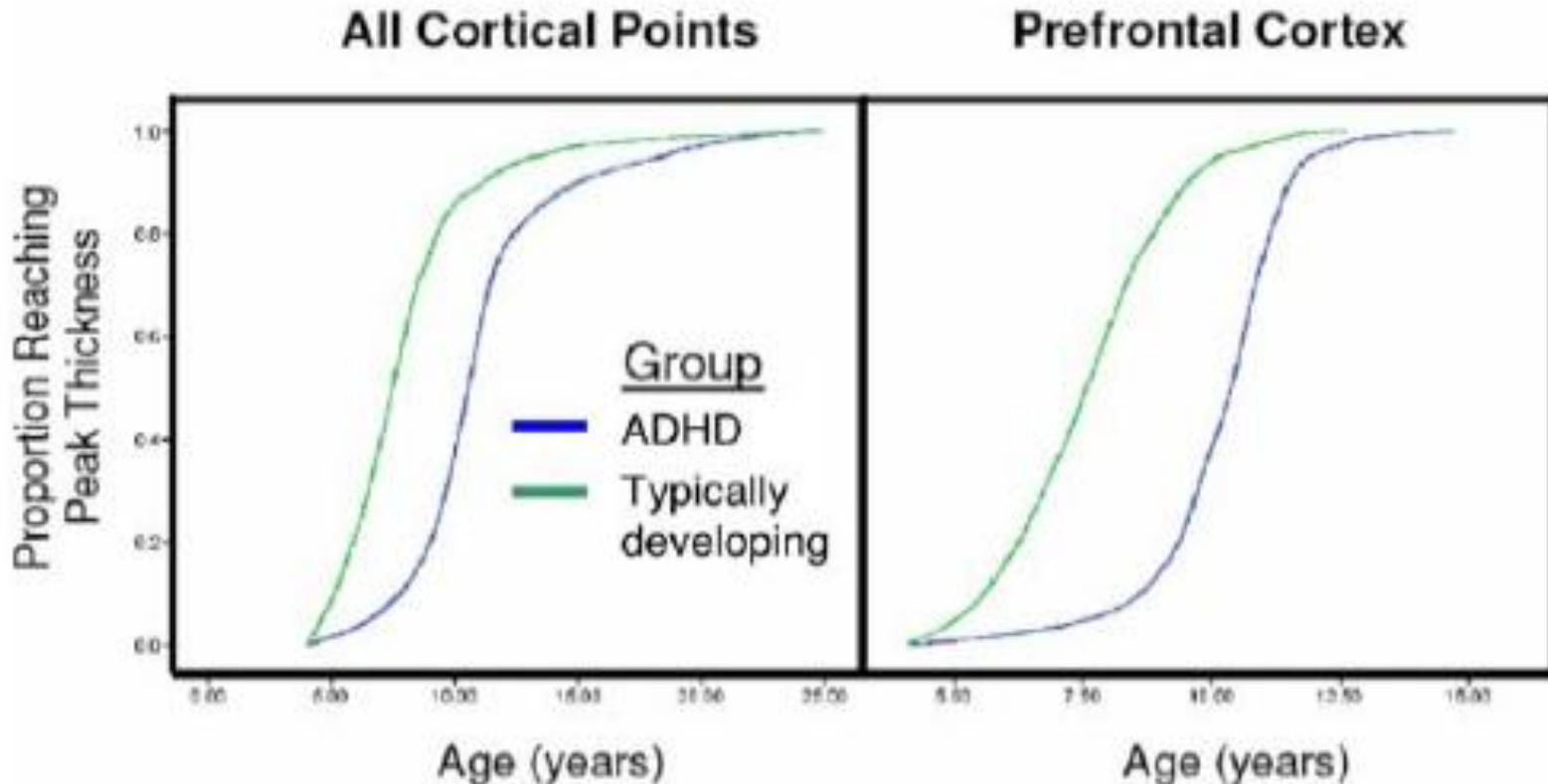
**TYPICALLY DEVELOPING
CONTROLS**

ADHD: a neurodevelopmental disorder

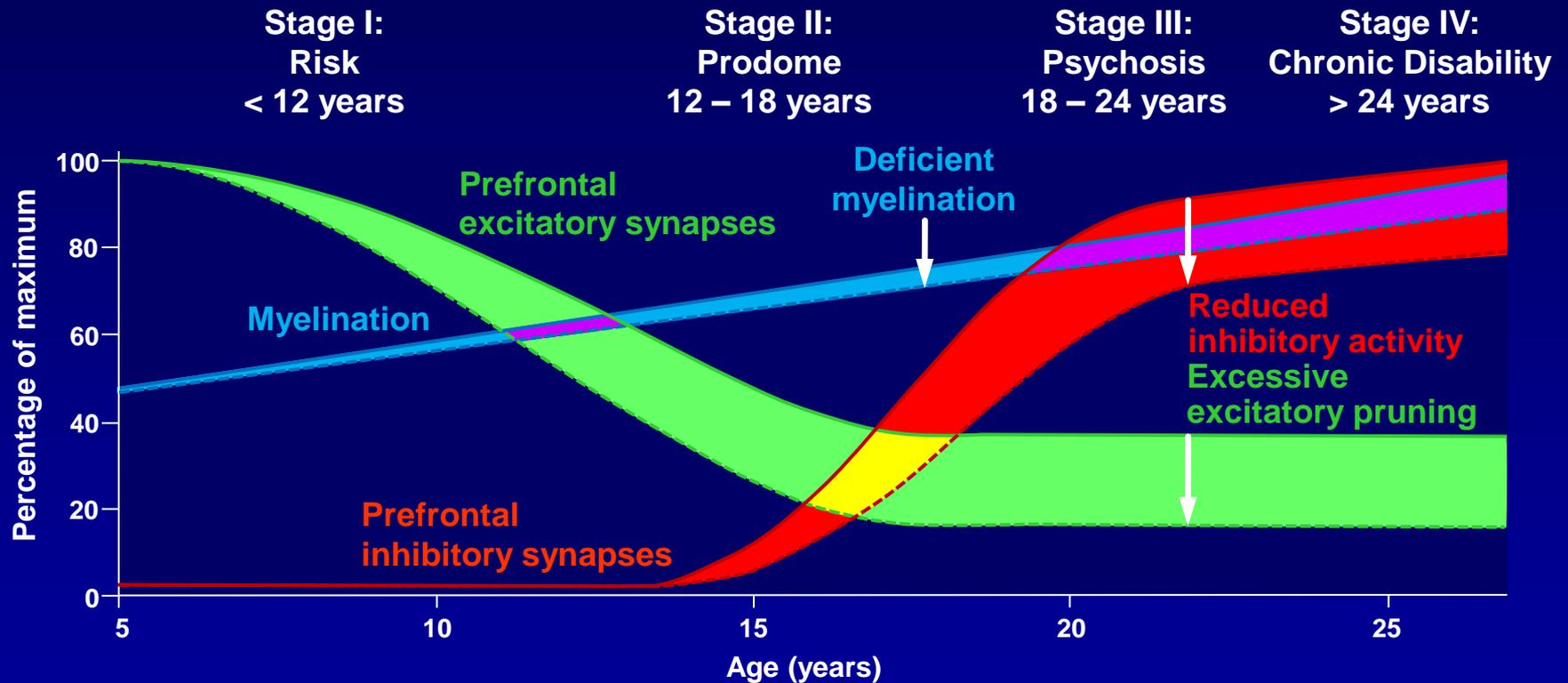
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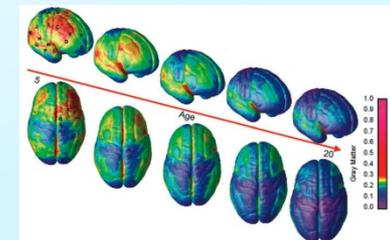
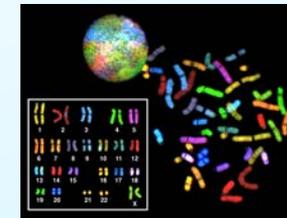
Schizophrenia - A Neurodevelopmental Disorder



Adapted from
Insel, *Nature*, 2010

Disruptive Innovations In Mental Health

- Mental disorders are brain disorders
- Mental disorders = experience + genetics
- Mental disorders are developmental disorders

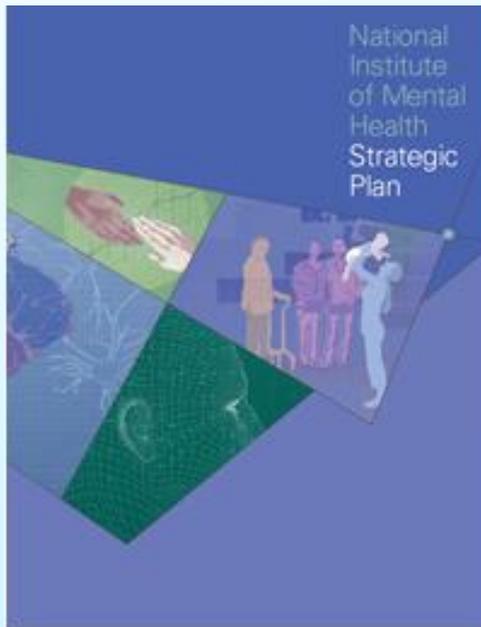


What about diagnosis?

What about treatment?

NIMH Mission

Transforming the understanding and treatment of mental illnesses through basic and clinical research, paving the way for prevention, recovery, and cure.



4P's:

Pathophysiology

Predictive and Preemptive

Person-Centered

Public health impact

Transforming Diagnosis Research Domain Criteria (RDoC)

Schizophrenia

Anhedonia

Depression

Attention

Working Memory

Cognitive Control

**Cognitive
Systems
Domain**

Language
Behavior

Declarative
Memory

Perception

Behavior

Physiology

Circuits

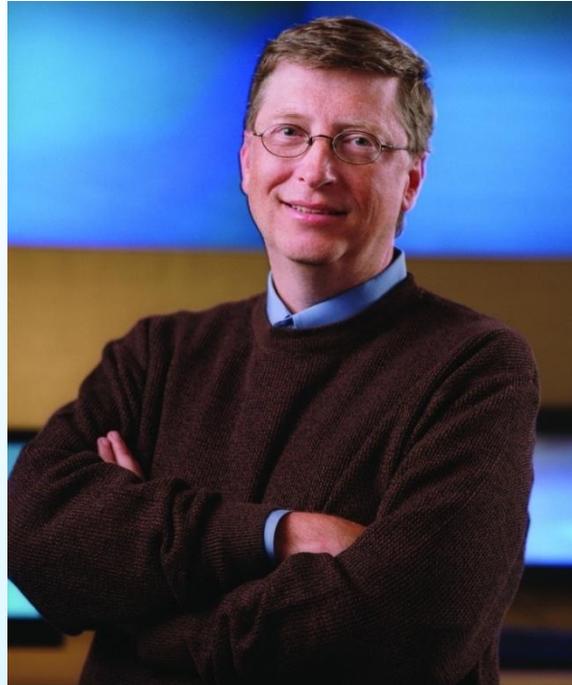
Cells

Molecules

Genes

**Units of
Analysis**

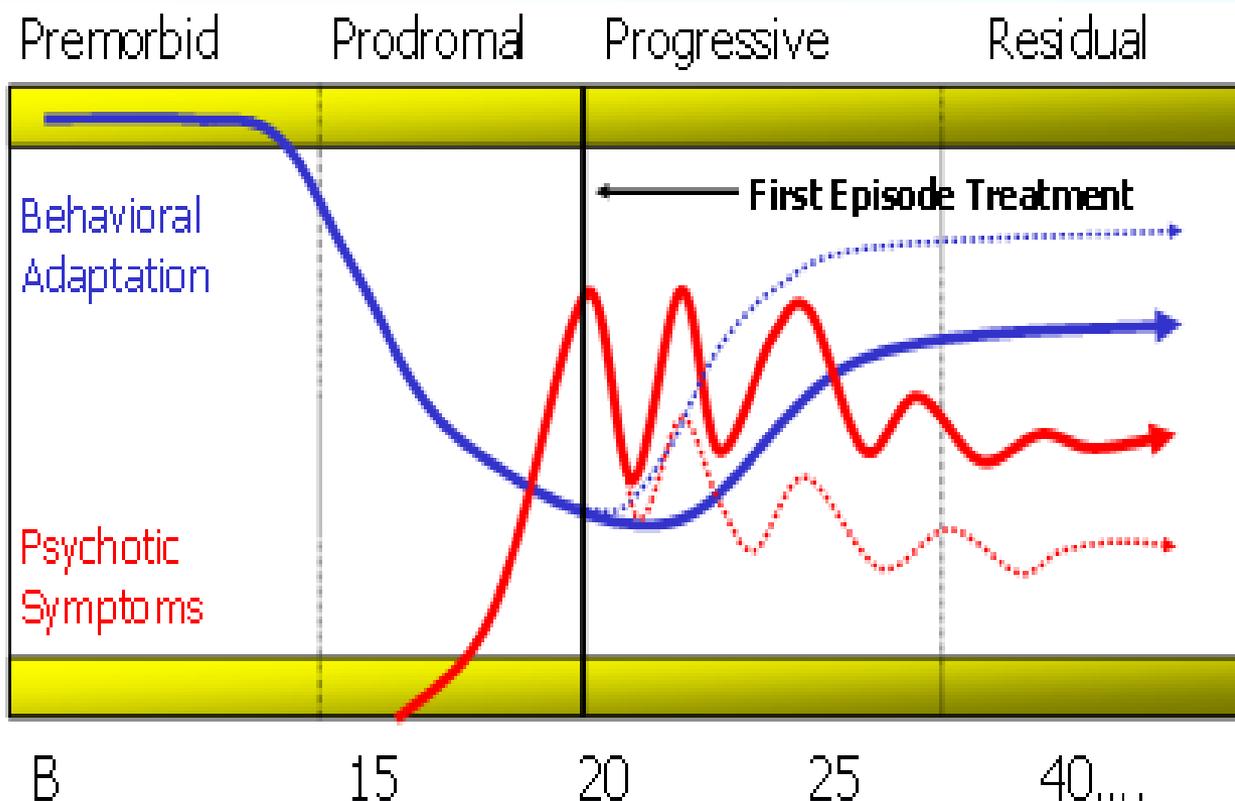
What about 2012?



“We always overestimate the change that will occur in the next two years and underestimate the change that will occur in the next ten.”

--Bill Gates Jr.

RAISE: Recovery After Initial Schizophrenia Episode



RAISE Toolbox:

- Individual Resilience Training
- Family Psychoeducation
- Supported Education/Employment
- Phase-Specific Psychopharm Rx
- Liaison w Primary Care

Person Centered Rx:
Specialized Teams
Shared decision making
Tailored to individual and family

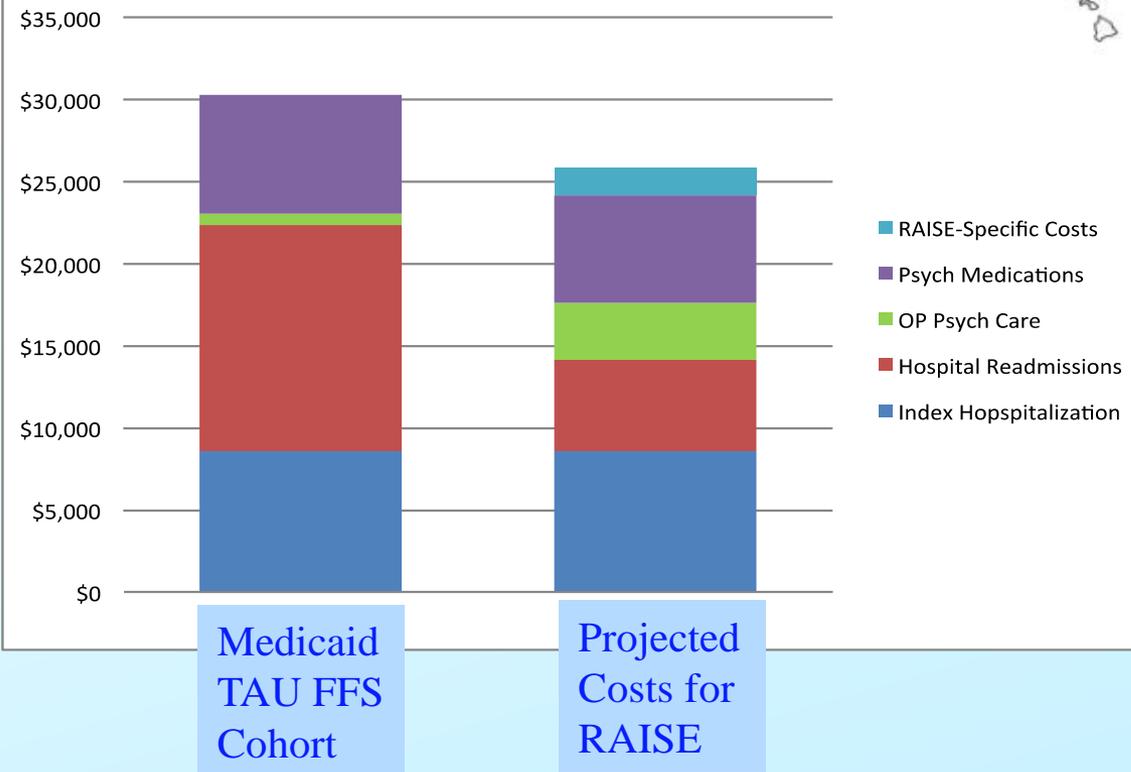
RAISE: Recovery After Initial Schizophrenia Episode

RAISE Outcomes: Function, Costs, Implementation



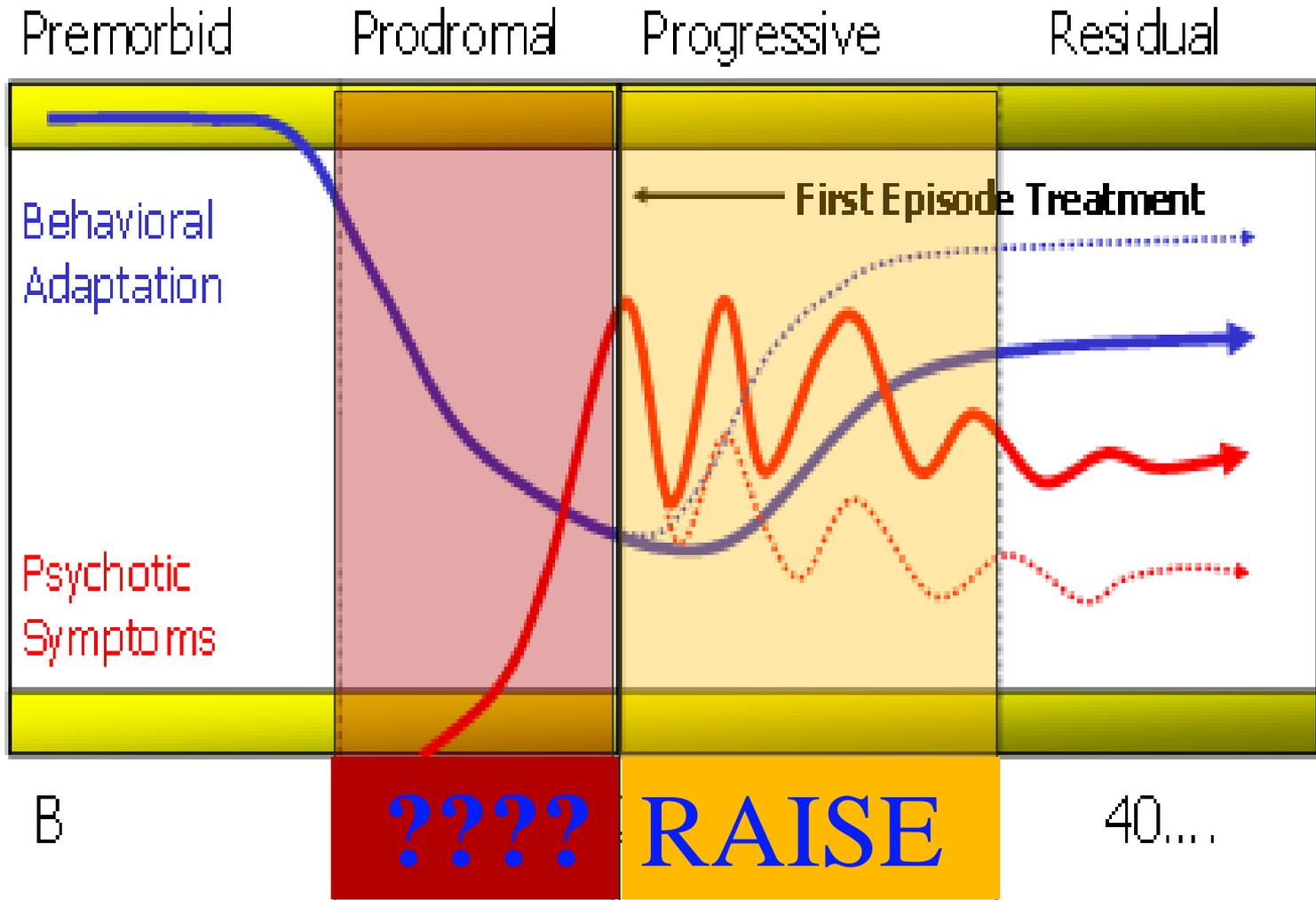
Orange color states = RAISE sites

Annual Per Patient Health Care Costs: Initial 12-Months of FEP Treatment

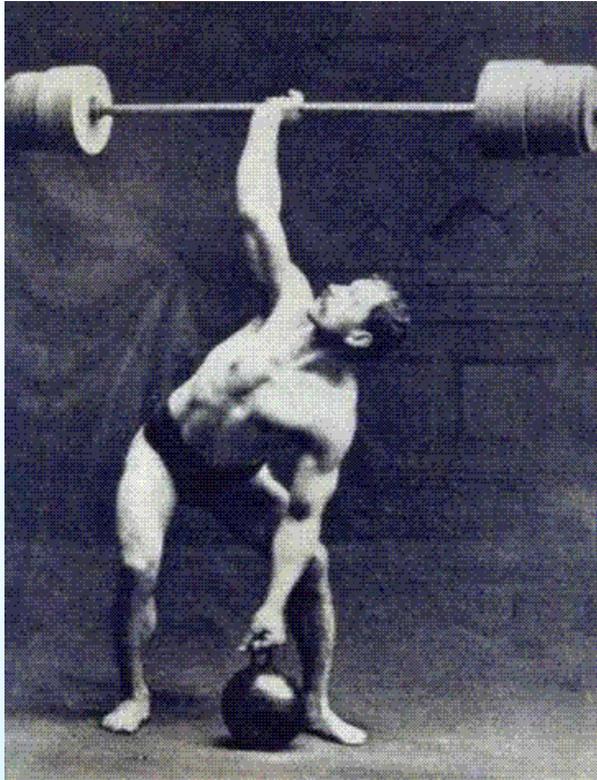


RAISE 3P's:
Pre-emptive
Person-centered
Public health impact

Pre-emptive Interventions for Schizophrenia



Cognitive Training: Using Brain Plasticity to Alter Circuits



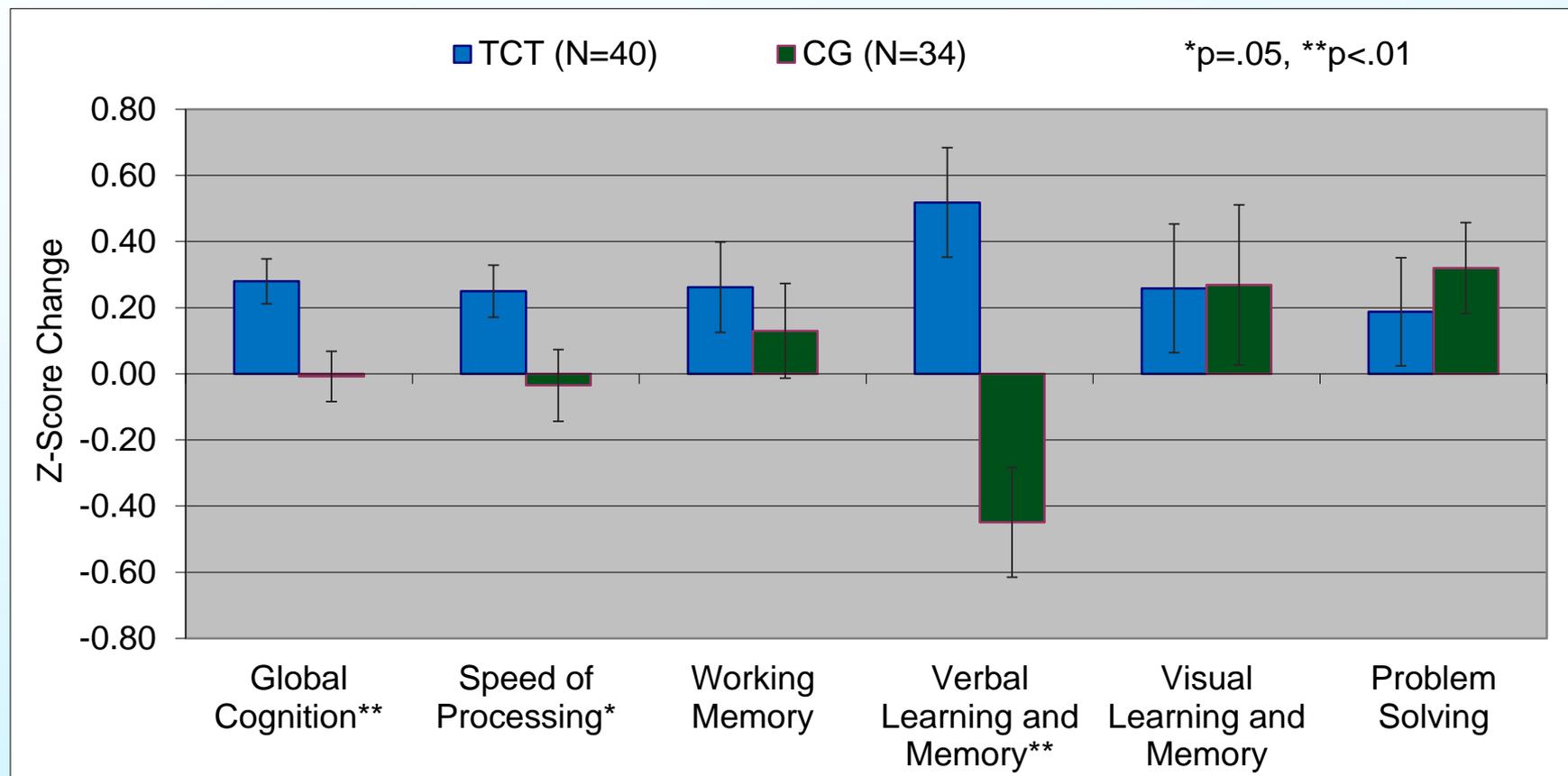
Attention (ADHD)
Appraisal (anxiety)
Social skills (autism)
Memory (MCI)
Exec Fcn (psychosis)



Improved Function

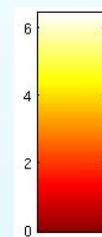
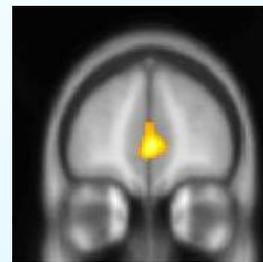
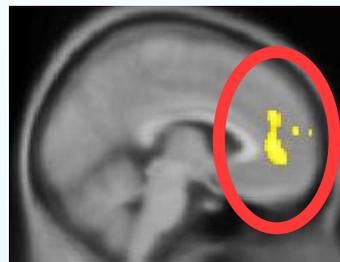
Source: Vinogradov et al, UCSF

Cognitive improvement after 10 weeks of targeted cognitive training (TCT) but not after video game control (CG) condition



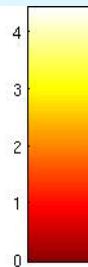
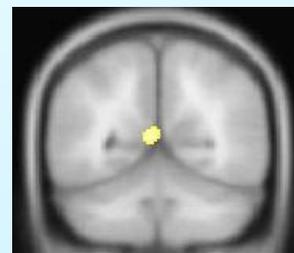
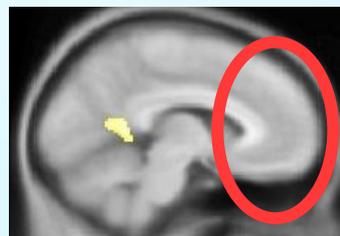
Changing Brain Activation with Cognitive Training

Healthy Controls
(N=15)



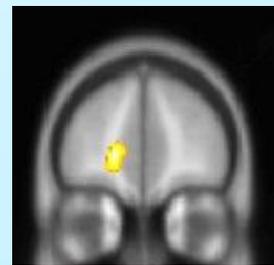
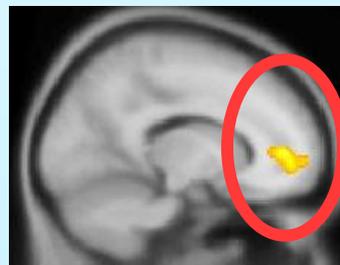
$t = 3.79, p < .001$
 $v = 678$

Schizophrenia
(N=31)



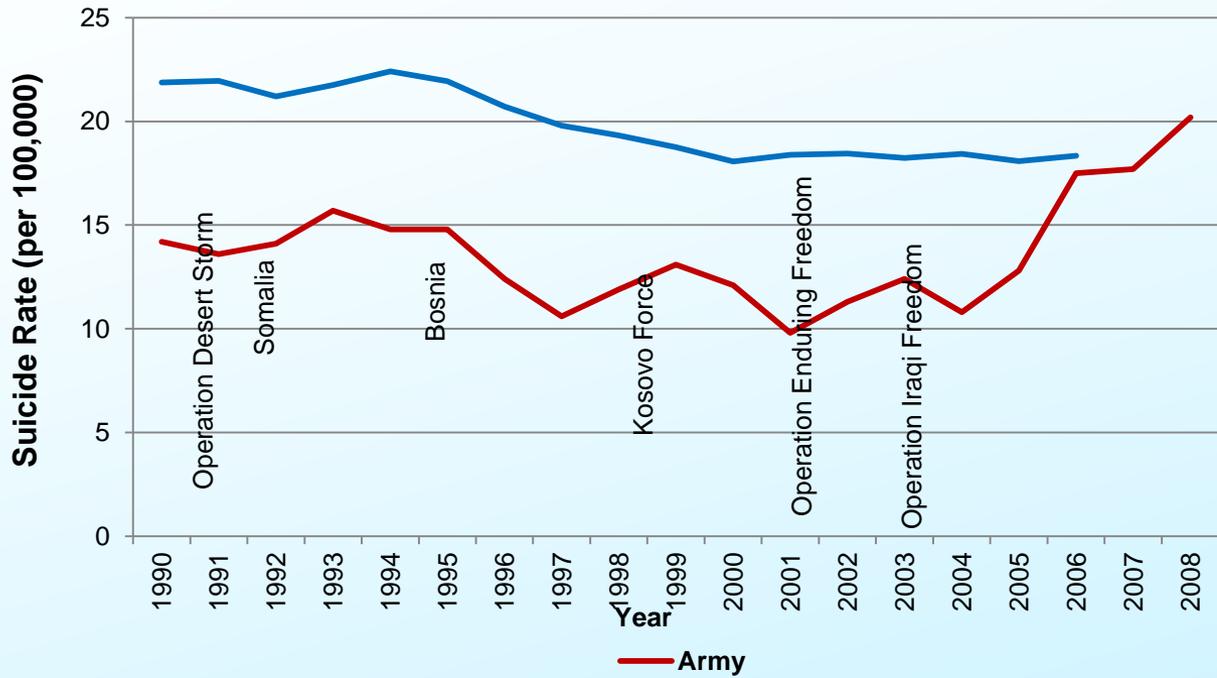
$t = 3.83, p < .001$
 $v = 201$

SZ Post- TCT
(N=14)



$t = 7.93, p < .002$
 $v = 240$

Army STARRS Study to Assess Risk and Resilience in Servicemembers



SOURCE: CDC/NCHS, National Vital Statistics System (civilian data). G1 (Army data)



- Over 50,000 soldiers enrolled in prospective study
- Retrospective study concentrates risk (1.6 million soldiers)
- Extensive repository of psychological and biological data
- Actionable data for reducing risk and saving lives

Serving as a model: leadership for increasing awareness, reducing risk, and eliminating stigma



And finally....

“One of the chief causes of poverty in science is imaginary wealth. The purpose of science is not to open the door to an infinitude of wisdom but to set some limit to the infinitude of error.”

Brecht, Life of Galileo



Paving the Way for Prevention, Recovery, and Cure

www.nimh.nih.gov

Research = Hope

From Neuroscience to Mental Health: A Vision for 2022

Discovery Technologies

Preventive interventions

Molecular diagnostics

Proteomics

Neuroimaging

Clinical genomics

Next-Gen Clin Trials
Exptl Medicine
RDoC

Strategic prevention
Recovery and Cure

Personalized care

Biodiagnostics

Treatment of core pathology

Pathophysiology



Genes



Cells



Systems



Individual



Social

Diagnosis by symptoms

Treatment of episode

Dissemination Access Coordination
Translating Research to Practice