Rethinking Mental Illness: The View from 2022

Thomas R. Insel, M.D.
Director, NIMH
Rethinking Mental Illness: The View from 2012

Thomas R. Insel, MD
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Key Message: Research = Hope
Impact of Research on Heart Disease

Age-Adjusted Death Rates for Coronary Heart Disease,

- Almost 1.8M deaths expected in 2007 if rise had continued
- 1.5M deaths expected in 2007 if no decline from peak rate
- 1.1M deaths averted in 2007 due to decline from peak rate in 1968 (1.5M – 400K)
- 406,000 actual deaths in 2007

Source: NHLBI Factbook, 2010
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

- Cardiovascular Disease
- Infants
- External
- Pneumonia/Influenza
- Cancer
- Total

Increase in life expectancy at birth

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

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)

<table>
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<tr>
<th>Country income group</th>
<th>Diabetes</th>
<th>Cardiovascular diseases</th>
<th>Chronic Respiratory diseases</th>
<th>Cancer</th>
<th>Mental Illness</th>
<th>Total</th>
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</tr>
</tbody>
</table>


US Annual Costs > $300B for SMI (Insel, AJP, 2008)
• 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
Mental Disorders as Neural Circuit Disorders

Mapping the Human Connectome

Wedeen et al, Science, 2012
Mental Disorders as Neural Circuit Disorders

**Depression**

**PTSD**

**OCD**
Depression as a Brain Circuit Disorder

Cognition (attention-appraisal-action)

Self-awareness insight

Mood state

Interoception (drive-autonomic-circadian)

CBT

MEDS

Arch Gen Psych 61:34-41-2004
Mental Disorders as Complex Genetic Disorders

What have we learned from genetics?

• Genetic ≠ Inherited (spontaneous mutations are common)

• Genetic ≠ Causal (genes confer risk and resilience)

• Genetics ≠ 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

P. Shaw\textsuperscript{1}, K. Ekstrand\textsuperscript{1}, W. Sharp\textsuperscript{4}, J. Blumenthal\textsuperscript{1}, J. P. Lerch\textsuperscript{5}, D. Greenstein\textsuperscript{1}, L. Clasen\textsuperscript{1}, A. Evans\textsuperscript{5}, J. Giedd\textsuperscript{4}, and J. L. Rapoport\textsuperscript{1}

AGE: 5

ADHD

TYPICALLY DEVELOPING CONTROLS
ADHD: a neurodevelopmental disorder

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

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

PNAS, 2007
Schizophrenia - A Neurodevelopmental Disorder

Stage I: Risk < 12 years
Stage II: Prodome 12 – 18 years
Stage III: Psychosis 18 – 24 years
Stage IV: Chronic Disability > 24 years

Deficient myelination
Reduced inhibitory activity
Excessive excitatory pruning

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:
Pathophysicsology
Predictive and Preemptive
Person-Centered
Public health impact
Transforming Diagnosis Research Domain Criteria (RDoC)

Schizophrenia

Anhedonia

Depression

Cognitive Systems Domain
- Attention
- Working Memory
- Cognitive Control

Perception

Units of Analysis
- Behavior
- Physiology
- Circuits
- Cells
- Molecules
- Genes

Insel et al, AJP, 2010
"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 Psycho-education
- 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

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

Orange color states = RAISE sites

RAISE 3P’s: Pre-emptive Person-centered Public health impact
Pre-emptive Interventions for Schizophrenia

Diagram showing the stages of schizophrenia:
- Premorbid
- Prodromal
- Progressive
- Residual

Key elements:
- Behavioral Adaptation
- Psychotic Symptoms
- First Episode Treatment

The diagram highlights the importance of early intervention through a RAISE approach.
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.

Source: Vinogradov et al, UCSF
Cognitive Training: Using Brain Plasticity to Alter Circuits

Changing Brain Activation with Cognitive Training

Healthy Controls
(N=15)

Schizophrenia
(N=31)

SZ Post- TCT
(N=14)

Source: Vinogradov et al, UCSF
Army STARRS Study to Assess Risk and Resilience in Servicemembers

Suicide Rate (per 100,000)

Year


Operation Desert Storm Somalia Bosnia Kosovo Force Operation Enduring Freedom Operation Iraqi Freedom

Army STARRS Study to Assess Risk and Resilience in Servicemembers

- 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
“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

Dissemination  Access  Coordination  Translation  Research to Practice

Strategic prevention  Recovery and Cure

Biodiagnostics  Treatment of core pathology
Pathophysiology
Genes  Cells  Systems  Individual  Social
Diagnosis by symptoms  Treatment of episode

Next-Gen Clin Trials  Exptl Medicine  RDoC

Personalized care