



Philosophical Issues in Psychiatry V:
The Problems of Multiple Levels, Explanatory Pluralism,
Reduction and Emergence

**Challenges in the Relationships between Psychological
and Biological Phenomena in Psychopathology**

Gregory A. Miller
Department of Psychology,
Department of Psychiatry and Biobehavioral Sciences,
and Brain Research Institute, UCLA
Copenhagen, May 29, 2018

“Major Conference Themes”

“1. The importance of reduction - under what circumstances are lower levels of explanation to be preferred? **Is wholesale reduction possible** or is it more realistic to pursue “small” or “patchy” reductive approaches?”

- Elimination reduction is not an option, though now widely embraced in basic and clinical neuroscience re: the relationship between psychology and biology

“2. How is it best to conceive of the multiple ‘levels’ at which psychiatric illness can be understood? **Is ‘levels’ even a useful term here?**”

- The “levels” metaphor is underspecified and encourages naïve reductionism

“4. Given that levels of explanation in psychiatry cross **the mind-body divide - the subjective and objective worlds** - how can we best span these widely divergent perspectives on reality?”

- Is the new mechanist approach an antidote to decades of naïve reductionism?

A Premise in the Decade(s) of the Brain

Psychological phenomena should (and can) be reduced to biological phenomena

- Document the rise (and faltering decline) of NIMH's embrace of this assumption
- Touch on some policy implications of that embrace
- Raise questions for the new mechanists – and pleas for help

Disclosures:

US National Advisory Mental Health Council (“NIMH Council”)

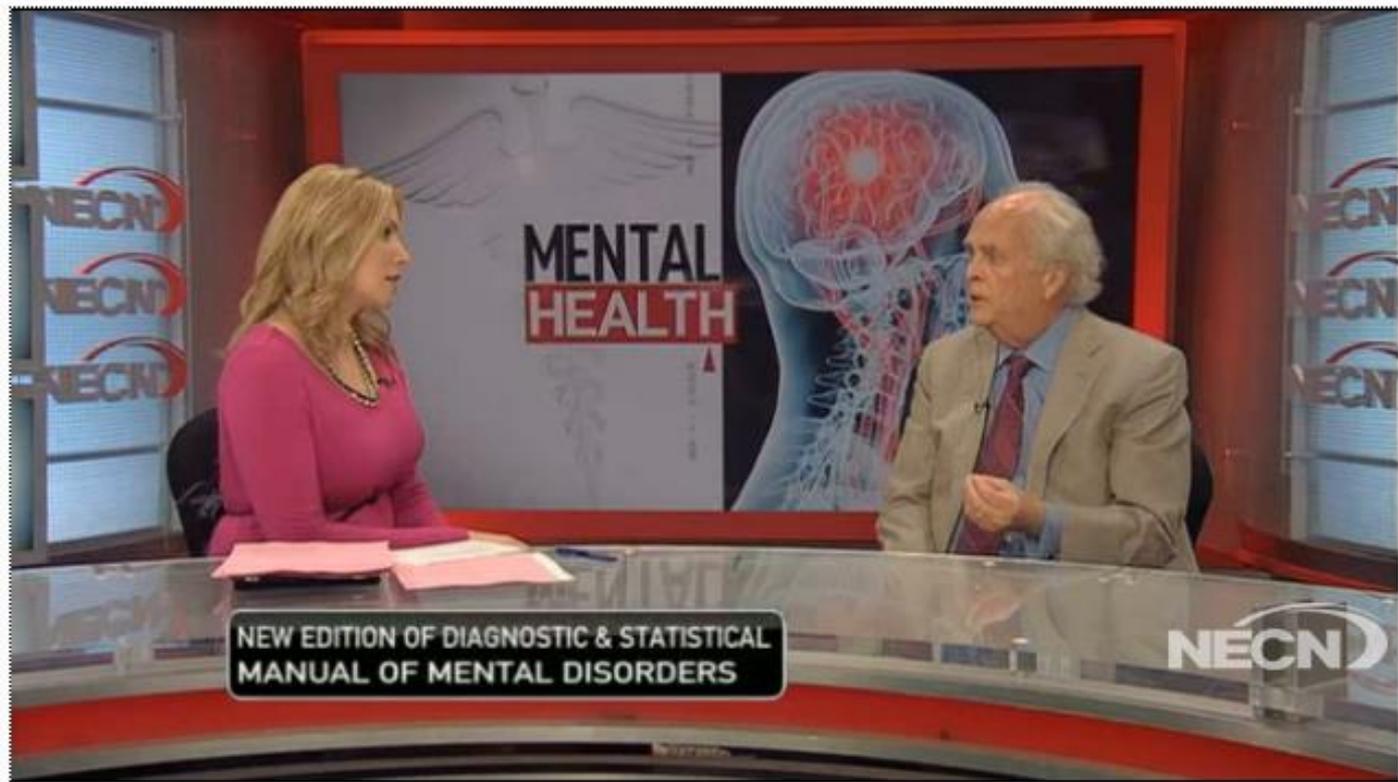
NIMH Council's Changes to the RDoC Matrix workgroup

Not speaking for NIMH

Current funding from NIMH, NSF, NARSAD



New version of 'diagnostic bible' adds emotional disorders

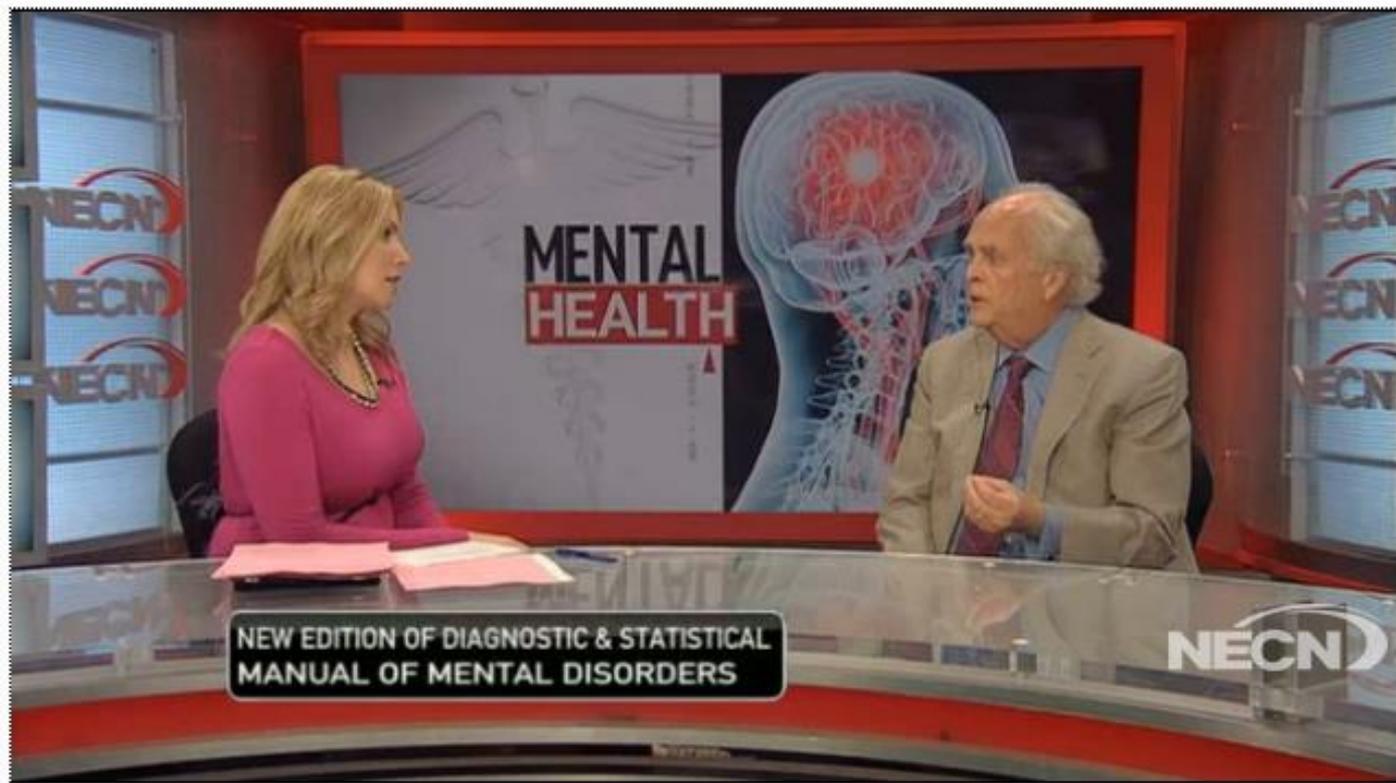


What's wrong with this picture?



Interview with David Barlow about DSM 5

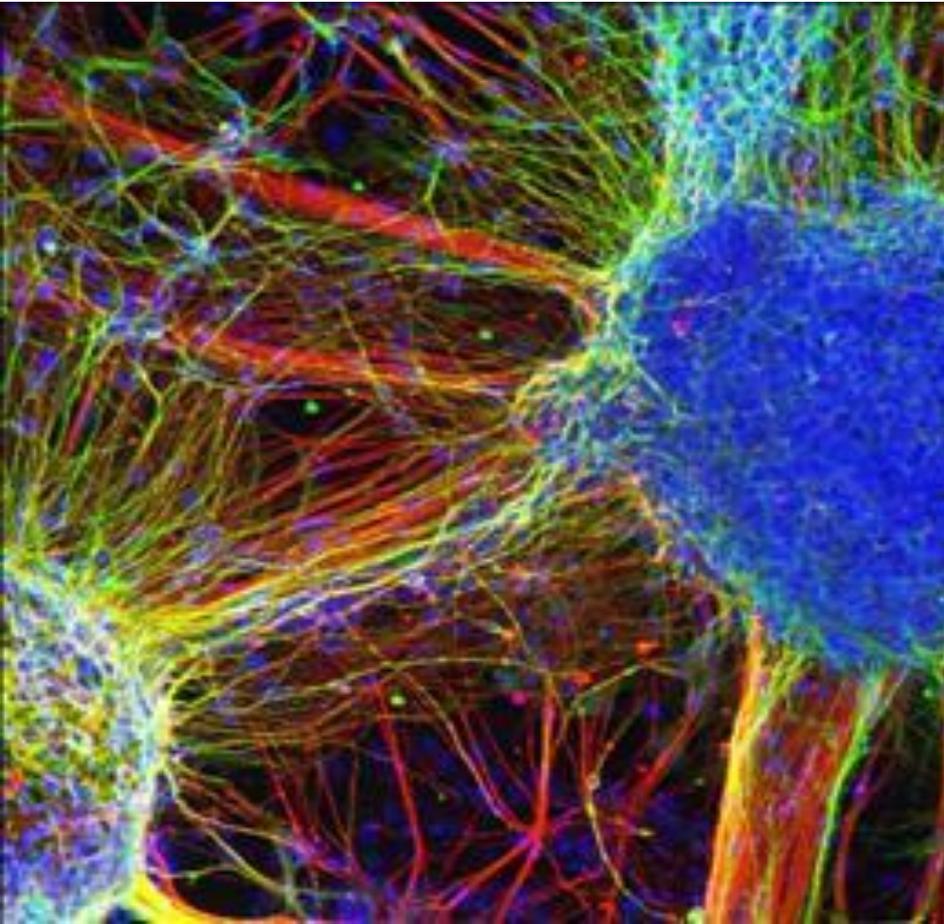
New version of 'diagnostic bible' adds emotional disorders



Why a *brain* picture to illustrate *mental* health?

What Role for Biology in Mental Illness Research?

“Schizophrenia...is a debilitating **neurological** disorder...”

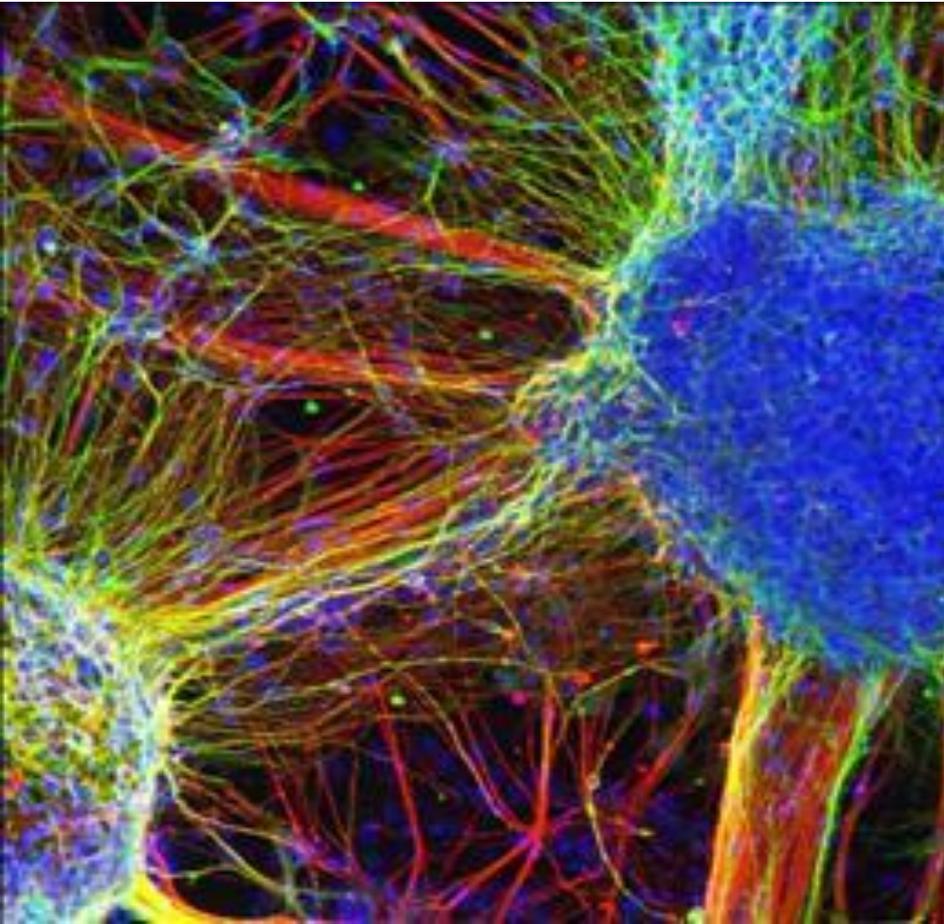


What does it mean to call something
a “neurological disorder”?

Portion of Figure 1 and opening words of Abstract,
Brennand et al. (2011), *Nature*, e-pub p. 1

What Role for Biology in Mental Illness Research?

“Neurons grown from the cells of people with schizophrenia could help pin down the **genetic basis** of the disease.”



What does it mean to say that a disease has a “genetic basis”?

Portion of Figure 1 & caption,
Brennand et al. (2011), *Nature*, e-pub p. 1



Meet the Scientist **Webinar**

A Free Monthly Q&A Series



What's New with TMS for Depression and Other Brain Diseases

TUESDAY, APRIL 10, 2018

2:00pm – 3:00pm EST.

[Register Now](#)

Premise: depression is a “brain disease”

Even from an Academic Psychology Group...

Press release* for Bates, Lewis, & Weiss (2013), *Psychological Science*

“Childhood Socioeconomic Status Amplifies Genetic Effects on Adult Intelligence”

“...the authors found that childhood SES amplified the effects of genes involved in adult intelligence.

This finding supports a biological model of intelligence in which supportive environments lead to maximal genetic effects.”

Even from an Academic Psychology Group...

Press release* for Bates, Lewis, & Weiss (2013), *Psychological Science*

“Childhood Socioeconomic Status Amplifies Genetic Effects on Adult Intelligence”

“...the authors found that childhood SES amplified the effects of genes involved in adult intelligence.

This finding supports a **biological** model of intelligence in which supportive **environments** lead to maximal genetic effects.”

Why is this just a “**biological**” model?

How is a gene x environment model just **biological**, not **environmental**?

A pervasive bias to frame psychological phenomena as biological

~2018?

“...an entire generation of researchers

tended to reduce psychiatry to neuropathology

and to reinterpret it as a natural science rather than a clinical one.

However, this wave of brain research never lived up to its promises, and, increasingly, as the expected breakthroughs from neuropathological research failed to materialize, critics began searching for alternative approaches.”

~1888

“...an entire generation of researchers [Griesinger’s students in the mid/late 1880s]

tended to reduce psychiatry to neuropathology

and to reinterpret it as a natural science rather than a clinical one.

However, this wave of brain research never lived up to its promises, and, increasingly, as the expected breakthroughs from neuropathological research failed to materialize, critics began searching for alternative approaches.

Kraepelin [>100 years ago] was one such critic.”

Engstrom & Kendler (2015), *Am J Psychiatry*, p. 1190

Kraepelin “insisted vehemently that the notion of psychiatry as nothing more than a special branch of neuropathology or neurophysiology...would never be able to deliver on its promise of a comprehensive understanding of mental disorders.

No understanding of ‘brain mechanisms’ could entirely incorporate mental processes.”

Engstrom & Kendler (2015), *Am J Psychiatry*, p. 1192

“Now That We Have the Genome...”

But environment controls gene expression,
on multiple time scales – even minutes

Your breakfast coffee, the early Danish sunrise, the behavior of the person next to you
...are plucking the strings of your DNA right now

...altering your gene expression, and even altering your genes

Be careful where you sit

“Now That We Have the Genome...”

“The impact of individual genes on risk for psychiatric illness is small, often nonspecific, and embedded in **causal pathways of stunning complexity...**

Although we may wish it to be true, we do not have and are not likely to **ever** discover ‘genes for’ psychiatric illness.”

Kendler (2005), *Am J Psychiatry*, p. 1250

Seeking the “genetic *basis*” of mental illness is a misunderstanding of the crucial role genes play

What Role for Biology in Mental Illness Research?

Premise: a psychological construct has meaning independent of any biological implementation

Not just Fodor's (1968) contingent vs. necessary identity, or the general notion of multiple realizability...

Memory, depression, delusion (like unicorn) are meaningful constructs even if not implemented anywhere

Psychological construct \neq biological implementation

What Role for Biology in Mental Illness Research?

“Depression is a chemical imbalance.”

It's not. Even in the DSM, it's a (psychological) mood disorder

There may BE a chemical imbalance

Maybe a consistent one, maybe one worth altering

But depression isn't chemistry

The “dopamine theory of schizophrenia” was never a theory of schizophrenia – it was a theory of dopamine in schizophrenia

Be wary of naïve reductionism, pervasive in popular terminology...

neural basis

neurological disorder

genetic basis

underlying neural activity

chemical imbalance

[Ψ] is a brain disease

What Role for Biology in Mental Illness Research?

Premise: psychopathology is fundamentally a psychological phenomenon, not a biological phenomenon

Symptoms such as anhedonia or delusions refer to psychological concepts and phenomena

But biological things go awry in psychopathology

What to do with biological abnormalities in psychopathology

- Causal?
- Informative?
- Epiphenomenal?

What Role for Biology in Mental Illness Research?

Premise: psychopathology is fundamentally a psychological phenomenon, not a biological phenomenon

Not clear whether biology “underlies” psychology, or psychology “underlies” biology ... or whether “underlies” is even an appropriate way to characterize their relationship

But along came the “Decade of the Brain”...

The Decade of the Brain: 1992

“Cognitive neuroscience...begins with localization within the brain of various cognitive abilities....

It has now become possible to localize mental functions to particular sets of regions....”

Kandel & Squire (1992), *Current Opinion in Neurobiology*, p. 143

But psychological functions don't have locations in space...

Neuroimaging localizes neural activity, not psychological function

The Decade of the Brain: 1992

“The development of realistic models of cognitive processes **requires** the ability to **locate cognitive function to particular regions** of the brain.”

Kandel & Squire (1992),
Current Opinion in Neurobiology, p. 144

We must rely on localization in order to develop “realistic” cognitive models?

(Sorry, cognitive scientists)

The Decade of the Brain: 1997

“A relatively sophisticated picture is emerging that conceptualizes **mental illnesses as disorders of mind arising in the brain.**”

Andreasen (1997), *Science*, p. 1586

→ What direction(s) are the causal arrows between mind and brain?

“Convergent data using multiple neuroscience techniques indicate that **the neural mechanisms of mental illnesses** can be understood as **dysfunctions in specific neural circuits**”

Andreasen (1997), *Science*, p. 1586

→ What sorts of mechanisms could those be?

“...their functions and dysfunctions can be influenced or **altered by a variety of cognitive and pharmacological factors.**”

Andreasen (1997), *Science*, p. 1586

→ Both psychology and chemistry can cause brain events? By what mechanisms?

“Focal regions have been replaced by circuits and static changes by plasticity and molecular mechanisms.... These advances have created an era in which **a scientific psychopathology that links mind and brain has become a reality.**”

Andreasen (1997), *Science*, p. 1592

→ What IS the link? 21 years and \$billions later, what are the mechanisms?

The Decade of the Brain: NIDA 1997

“That addiction is tied to changes in brain structure and function is what makes it, fundamentally, a brain disease.”

NIDA Director Alan Leshner (1997), *Science*, p. 46

Merely being "tied to" brain phenomena entails addiction *being* a "brain disease"?

What does "tied to" mean?

Just about anything of interest to a clinician can be tied to the brain...

What disorder is not a "brain disease"?

The Decade of the Brain: NIMH 1998

“Mental illnesses are real, diagnosable, treatable brain disorders.”

NIMH Director Steven Hyman (1998), *Am J Psychiatry*, p. 36

Why bother to think about brain \leftrightarrow behavior causation at all,
if it's all brain stuff anyway?

Why bother researching psychotherapy, or having government pay for it?

These kinds of statements have major implications for clinical science
policy and clinical practice

The Second Decade of the Brain: 2003

NIMH Clinical Neuroscience Research Branch

“The Molecular and Cellular **Basis** of Schizophrenia, Mood, and other **Brain Disorders** Program

The Integrative Neuroscience of Schizophrenia, Mood and other **Brain Disorders** Program

The Developmental Neuroscience of Schizophrenia, Mood and other **Brain Disorders** Program”

www.nimh.nih.gov/diva/index.htm#cnrb, accessed 4/26/03

Those are **brain** disorders, not **mental** disorders?

No longer the National Institute of **Mental** Health?

Looking Back

“The siren call of biological fixes for biopsychosocial problems has dominated medical research for decades....”

Phillips (2014), *World Psychiatry*, p. 41

“NIMH was at the center of the neuroscience enthusiasm...
betting the house on a narrow biological agenda to replace
what had been a more balanced portfolio....”

NIMH turned itself into a ‘brain institute’ rather than an
“institute of mental health.”

“[But] it is a dangerous myth to assume that patients who meet
criteria for ‘schizophrenia’ suffer only from a brain disease.”

Frances (2014), *World Psychiatry*, p. 48

Looking Back

The track record of NIMH's swing to the hyper-reductionistic "mental illnesses are brain disorders" premise:

- 30 years of modern DSMs had failed to connect mental illness to biology...
- DSM 5 wasn't shaping up to be any more biological
- Not even one instance in our literature where we'd worked out the full causal chain from biology to a nontrivial psychological construct

Having the genome... having a brain connectivity map...
can't provide a full account of psychological phenomena
Kraepelin was right...

Eliminative reduction is not an option

Late in the Second Decade of the Brain: 2009

NIMH borrows (a little) from the new mechanists

Announces Research Domain Criteria (RDoC) framework

Insel & Cuthbert (2009), *Biological Psychiatry*

Insel & Cuthbert (2010), *American Journal of Psychiatry*

Sanislow et al. (2010), *Journal of Abnormal Psychology*

Begins to shift policy language away from hyper-biological reductionism

RDoC: NIMH's Research Domain Criteria

“...the RDoC guidelines accord no a priori theoretical precedence to any particular unit of analysis...” [biological or psychological]

“All measurement classes are potentially relevant in examining the role and functioning of the constructs.

The RDoC internal workgroup's aphorism for this idea was, ‘Behavioral science studies what the brain does, and neuroscience studies how the brain does it’; both are essential to an understanding of adaptive functioning.

This consideration constitutes a major postulate of the overall RDoC framework, consistent with the goal of promoting an integrative, rather than a reductionist, approach (Bechtel, 2007; Wright & Bechtel, 2007).”

Kozak & Cuthbert (2016), *Psychophysiology*, p. 292

RDoC: NIMH's Research Domain Criteria

“The RDoC initiative...is at once more biological and less biologically reductionistic than the DSMs.”

“The RDoC matrix is not under consideration as a replacement of the DSM in clinical practice. Instead, the RDoC premise is that clinical research should build on the best available genetic, neuroscience, and psychological science concepts, findings, and relationships.”

Yee, Javitt, & Miller (2015), *JAMA Psychiatry*, p. 1159,1160

The Third Decade of the Brain: 2011

NIMH Neuroscience and Basic Behavioral Science Branch

“...ensuring that relevant basic science knowledge is generated and then harvested to create improved diagnosis, treatment, and prevention of **mental and behavioral disorders.**”

Not “brain disorders”

The Third Decade of the Brain: 2011

NIMH Molecular, Cellular, and Genomic Neuroscience Research Branch

“...supports research aimed at developing an integrative understanding of basic brain-behavior processes that provide the foundation for understanding **mental disorders**”

Not “brain disorders”

The Third Decade of the Brain: 2014

NIA Individual Behavioral Processes Branch: Behavioral Genetics of Aging Section

“The behavioral genetics unit focuses [in part] on ... genetics and genomics of social behavior and social environments ... including examinations of **social influences on gene expression, and genetic influences on selection of environments.**”

The causal arrows go both ways, between social processes and genes

The Third Decade of the Brain: 2014

NIMH Division of Neuroscience and Basic Behavioral Science

Psychological phenomena are in every priority area

“Areas of High Priority

- Develop new and use existing physiological and computational models to understand the biological functions of genes, gene products, cells, and brain circuits in normal and abnormal **mental function**.
- Elucidate how **cognitive, affect, stress, and motivational processes** interact and their role(s) in **mental disorders** through functional studies spanning levels of analysis (genomic, molecular, cellular, circuits, behavior) during development and throughout the lifespan.
- Elucidate fundamental mechanisms (e.g., genetic, biological, behavioral, environmental) of complex **social behavior**.
- Identify in diverse populations from the US and around the world genetic variants, epigenetic mechanisms, and gene-environment interactions that influence vulnerability to **mental disorders**, endophenotypes, and pharmacologic response profiles.
- Identify biological markers (e.g., genetic, proteomic, imaging) in model systems and humans that could be further validated as methods for diagnosing and/or detecting risk/vulnerability, onset, progress, and/or severity of **mental disorders**.
- Identify and validate new molecular targets and tools for drug discovery relevant to the treatment of **mental disorders**.”

The Third Decade: 2015

NIMH Molecular, Cellular, and Genomic Neuroscience Research Branch

“...studies that contribute basic knowledge of the molecular processes driving the development, structure, and function of neural circuits, with a focus on those most relevant to **mental disorders**”

Not “brain disorders”

The Third Decade: 2018

Division of Neuroscience and Basic Behavioral Science

“...ensuring that relevant basic science knowledge is generated and then harvested to create improved diagnosis, treatment, and prevention of **mental and behavioral disorders**....

- Elucidate how cognitive, affect, stress, and motivational processes interact and their role(s) in **mental disorders** through functional studies spanning **levels of analysis** (genomic, molecular, cellular, circuits, behavior) during development and throughout the lifespan.
- Elucidate **fundamental mechanisms** (e.g., genetic, biological, behavioral, environmental) **of complex social behavior**.

Disorders are “mental and behavioral” – not genetic, not neural...

The Third Decade: 2018

Adult Psychopathology and Psychosocial Interventions Research Branch

“Emphasis is placed on studies that **combine approaches from neuroscience and behavioral science** to produce **integrative models** of risk, disorder, and recovery, consistent with the RDoC framework.”

“Innovative research to understand the **psychological, behavioral, cognitive, and neural mechanisms** that **cause mental disorders**”

Not “brain disorders”

Psychology & Biology: Parity?

“...research on the **convergence of biology and behavior** can deliver on the promise of precision medicine for mental disorders...”

“**The brain** continually rewires itself and changes gene expression **as a function of learning and life events.**”

“...it is imperative to include **measures of both brain and behavior** to understand the various aspects of dysfunction associated with disorders.”

“Symptoms would be an important starting point, but the [RDoC] framework would include a focus on systems or dimensions that had **both cognitive and biological validity.**”

Insel & Cuthbert (2015), *Science*, p. 499

But All Is Not Well

“the RDoC framework conceptualizes **mental illnesses as brain disorders....**”

Insel & Cuthbert (2010), *Am J Psychiatry*, p. 749

“As these rapidly evolving sciences yield new insights into **the neural basis of normal and abnormal behavior**, syndromes once considered exclusively as “mental” are being reconsidered as “**brain**” **disorders**—or, to be more precise, as syndromes of disrupted neural, cognitive, and behavioral systems.”

Insel & Cuthbert (2015), *Science*, p. 499

“As new diagnostics will likely be **redefining ‘mental disorders’ as “brain circuit disorders,**” new therapeutics will likely focus on tuning these circuits”

Insel & Cuthbert (2015), *Science*, p. 500

The Third Decade: 2018

Behavioral Science and Integrative Neuroscience Research Branch

“This branch supports innovative basic neuroscience studies that incorporate empirical, theoretical, and computational modeling approaches **to understand neural bases** of cognitive, social, arousal, regulatory, and positive and negative valence systems, and their development and interaction across the lifespan in experimental systems.”

“neural bases” is back! ... what does that mean?

The Third Decade: 2018

Division of Translational Research

“Delineate **neurobehavioral mechanisms** responsible for the development of psychopathology...”

“neurobehavioral”

Can we solve the hard mind-body problem via concatenation?

“Utilize behavioral phenotypes reflecting dimensional processes (e.g., attention, mood regulation) to maximize discovery of **underlying neural systems and genes....**”

“underlying” is back! ... what does that mean?

And Yet...

“...one of the most powerful and precise interventions to alter such activity may be targeted **psychotherapy**, such as cognitive behavioral therapy, which uses the brain’s intrinsic plasticity to alter neural circuits and as a consequence, deleterious thoughts and behavior.”

Insel & Cuthbert (2015), p. 500

The impact of a **psychological** intervention is on **biological** mechanisms, not (or not only) on **psychological** mechanisms?

Psychology underlies biology?

Is that a viable way to think of how psychotherapy works?

Can the new mechanists sort *that* out?

Psychology Back in the Game?

NIMH Director Josh Gordon during CAPPS town hall phone conference, Nov 1, 2017:

“We endorse biomarkers at any level of analysis.” [explicitly including psychology]

“[Psychology] is one level of biology.”

“Psychological and biological measures as far as we’re concerned are biology.”

“When we say biological, we include psychological.”

Is this viable?

Can the new mechanists make this inclusion of **psychology as biology** work?

Is “Underlie” How Mechanisms Fit Together?

“If psychiatry seeks to tie disorders to etiology and **underlying mechanisms**, ...mutually reinforcing networks of causal mechanisms [are promising].

Thanks to the Decades of the Brain,

“underlying” carries hyper-reductionistic baggage

Can we just delete “underlying”? Try it out today and tomorrow?

We argue that psychiatric disorders are objectively grounded features of the causal structure of the **mind/brain.**”

Kendler, Zachar, & Craver (2011), *Psychological Medicine*, p. 1143

What kinds of causal mechanisms (if any) cross the mind/brain barrier?

Counterpoint Unheard: Channeling Kraepelin 1982

“In attempts to relate psychophysical problems to physiology, too often there is confusion about the level at which problems should be addressed.

... some phenomena may be explained at only one or two [levels of analysis]...

The explication of each level involves issues that are rather independent of the other [levels]...

...trying to understand perception by studying only neurons is like trying to understand bird flight by studying only feathers...”

Marr (1982)

Though the new mechanists wouldn't buy that “independence” claim.

Counterpoint Unheard: Channeling Kraepelin 1992

Mental events are “not the same thing as neural activity; phenomenological experience cannot be described in terms of ion flows, synaptic connections, and so forth.”

Mental events “and brain events are members of *different* [logical] *categories*, and one cannot be replaced by the other.”

Kosslyn & Koenig (1992), *Wet mind: The new cognitive science*, p. 432

Counterpoint Unheard: Channeling Kraepelin 1992

“The aim is not to replace a description of mental events by a description of brain activity.

That would be like replacing a description of architecture with a description of building materials.

Although the nature of the materials restricts the kinds of buildings that can be built, it does not characterize their function or design.”

Kosslyn & Koenig (1992), *Wet mind: The new cognitive science*, p. 4

How Do Levels of Mechanisms Connect?

[According to the new mechanists] “A mechanism is defined as a dynamic system realizing a phenomenon in virtue of the orchestrated functioning of its component parts and activities (Bechtel, 2008).”

[The new mechanists provide] "a new definition of levels as different scales of organization within mechanisms, as well as how to think about reduction and autonomy across such levels....."

Sharp & Miller (in press), *J. Theoretical and Philosophical Psychology*

Does the new mechanistic approach provide
a way to fully reduce psychology to biology?

Or an alternative to that pervasive premise?

How Do Levels of Mechanisms Connect?

“...**causal relations are exclusively intralevel**....

Mechanistically mediated effects are hybrids of constitutive and causal relations in a mechanism, where the **constitutive** relations are **interlevel**, and the **causal** relations are exclusively **intralevel**.”

“...we find no metaphysical puzzle imagining that items in the proper domain of one science, however that domain is defined, **interact** with items in the proper domain of another science.”

Craver & Bechtel (2007), *Biology and Philosophy*, p. 562, 547, 550

No hint of eliminative reduction of psychology to biology

A Premise in the Decade(s) of the Brain

Psychological phenomena should (and can) be reduced to biological phenomena

➤ Not just peaceful coexistence and mutual constraint, but eliminative reduction

“Many of these authors conclude that **psychological explanations** either **reduce to** or **ought to be replaced by neuroscientific explanations....**”

Not the new mechanists:

“**Our argument...is *not* an argument for reductionism**, either as it has been classically conceived (as the derivation of one theory from another) or **as it is now commonly conceived (as the idea that lower-level mechanisms are explanatorily privileged).**”

Piccinini & Craver (2011), *Synthese*, p. 285, 284

It's that **privileging** of biology over psychology accounts that I'm arguing against

A Solution to What Craver & Bechtel Call “The shroud of mystery surrounding interlevel causation”

“...the **constitutive** relations are **interlevel**, and the **causal** relations are exclusively **intralevel**.”

Craver & Bechtel (2007), *Biology and Philosophy*, p. 562

“Craver and I dissociated our treatment of levels from many in the literature, such as the notion of levels of science that were invoked in the theory-reduction literature....”

Bechtel (2017), *Philosophy of Science*, p. 255

So psychology doesn't reduce to biology
Perhaps with some help from the new mechanists, the “mental” in mental illness
will survive recent decades' science and science policy

Thank you