Behavior is the Bridge Between Biology and Society. Transdisciplinary Systems Integration to Improve Health

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“My question is: Are we making an impact?”
A Brief History of OBSSR

1993: Congress establishes OBSSR within NIH OD

1995: OBSSR officially opens
Dr. Norman Anderson, Director

1997: First Strategic Plan
1. Enhance behavioral and social sciences research and training
2. Integrate a biobehavioral perspective into all NIH research areas
3. Improve communication among behavioral and social scientists and with public

2000: Dr. Raynard Kington named Director, OBSSR

2005: Dr. David Abrams named Director, OBSSR

2006: OBSSR finalizes new Strategic Prospectus
OBSSR at NIH

Office of the Director

Other Scientific and Administrative Units

OBSSR program office

Institutes and Centers

Extramural Programs

Intramural Programs

? New OPASI Division
Partnership across NIH
Given the rapidly changing scientific landscape and societal demands for accountability during tough financial times and globalization...

What has BSSR contributed
What is the current status
Where should we be headed
High Leverage opportunities
Three OPTIONS

- we are fundamentally OK but we need to communicate and market our science better

- we need some change around the edges - what ?

- we have a crisis building and need radical re-invention our sciences are being co-opted and left behind - what is our core identity ? The cheese has moved - our reaction is ?
(Mis) Perceptions of BSSR

• Behavior is hard or impossible to change, have no “laws”
• Behavior is common sense = what grandma already knew, .... so why invest in BSSR
• BSSR is soft science, immature
• Self report is unreliable - biomarkers
• Poor self- and other- image- in a natural science, engineering, big-pharma, biomedical dominant culture in health and health care
• We must be open to self criticism and change
Health as a continuum between biological, behavioral and social factors across the lifespan with sensitive periods.
Fig. 1. The society-behavior-biology nexus as depicted in multidimensional space. The large arrows represent the axes of time and nested hierarchical structures. The sphere of health-related behavior and action moves through time from infancy to old age. Behavior is influenced by structured contingencies within the social and physical environment and by biological phenomena. Structural contingencies (opportunities and constraints) are shown by paths ending with nodes, while biological phenomena (embodiment and expression) are shown by paths ending with arrows or nodes.
Human Brain Development –Synapse Formation

Sensing Pathways (vision, hearing)

Language

Higher Cognitive Function

Conception

-6 -3 0 3 6 9 1 4 8 12 16

Months

Years

AGE

Perceived and actual stress - Diathesis and coping

- Influenced by experiences, genetics, and behavior, social buffering, culture, economic adversity...

- Initiates physiologic and behavioral responses leading to allostasis, adaptation

Allostatic load can accumulate over time - wear and tear along epigenetic pathways

Overexposure to mediators of neural, endocrine, and immune stress can have adverse effects

Levels of Causation for Health

Levels of Causation

- Environmental Influences
- Social Position
- Social & Cultural Processes
- Psychological Processes
- Biological & Genetic Factors

Interventions

- Healthy Public Policy
- Organization & Community Interventions
- Primary & Secondary Prevention
- Primary & Secondary Prevention / Treatment
- Primary & Secondary Prevention / Treatment

A New Integrative Causal Model

The Biomedical Model:
Causes of disease lie in genes, molecules, proteins

The Ecological Model:
Causes of disease are behavioral and social factors

INTEGRATION OF BIOMEDICAL CAUSES & SOCIO-ECOLOGICAL “CAUSES OF CAUSES”
Emerging public health threats:

- Unsustainable cost of healthcare
- Obesity, inactivity, poor diet
- Natural & human-made disasters
- Aging population - degeneration
- Mental Illness- stress, depression

Persistent public health challenges:

- Disparities, Inequality in health
- Tobacco use, addictions, abuse
- “Toxic” built environment
- Chronic disease management
The big picture

- Genetics: 30%
- Environment: 5%
- Social: 15%
- Behavior: 40%
- Health care: 10%

McGinnis, 2003
OBSSR’s Vision at NIH

To mobilize the biomedical, behavioral, and social science research communities as partners in interdisciplinary research to solve the most pressing health challenges faced by our society.

Programmatic Directions to Achieve the Vision:

- Transdisciplinary science
- “Next generation”, vertically integrated, basic science
- Problem-based, outcomes oriented research - strengthen the science of dissemination and dissemination of the science
- Systems - thinking for population health improvement (impact)
Exciting Opportunities for BSSR

- Macro-Social Behavior (e.g., migration)
- Social & Interpersonal Behavior (e.g., ethnic bias)
- Perception, Learning, Emotion & Cognition (e.g., vigilance)
- Early Development (e.g., temperament early life events)
- Gene-Environment Interactions (e.g., bio-social stress)
- Technology, measures, methods (e.g., sensors, EMA, biomarkers)
- Cross-cutting research (e.g., health disparities, obesity, health services)


From Basic Science to Policy

With a Focus on Population Impact

- A large number of people at small risk may give rise to more cases of disease than a small number of people at high risk.
- A preventive measure that brings large benefits to the community affords little to each participating individual.

~ Rose, 1992

"My question is: Are we making an impact?"
OBSSR will support and facilitate the next generation of basic behavioral and social science research informed by breakthroughs in complementary areas such as genetics, informatics, and multilevel analyses.

SCIENCE RECS IN NEW HORIZONS AND Basic Science at NIH, ACD REPORT, 2004
Decade of Discovery: 1995 - 2005

Human Genome Map - Completed 4/14/03

Total: 3 billion bases across 46 chromosomes
Genes: approx 23,000
Genes in the brain: 16,000
Brain specific genes: 6,000

Genes with known function: less than 1%
A gene-environment interaction occurs

When the effect of exposure to an environmental factor on health and behavior is conditional upon a person's genotype

Or conversely, when the genotype's effect is moderated by the environment.
1057 consecutive births in Dunedin, New Zealand followed for 26 years with evaluation every 2-3 years beginning in first year.

At age 26, 17% met criteria for major depressive disorder. Neither life stress alone nor serotonin transporter genotype predicted depression.
Serotonin Gene, Experience, & Depression Age 26


Depression Risk

S = Short Allele
L = Long Allele

Early Childhood

No Abuse  Moderate Abuse  Severe Abuse
STRATEGIES FOR PROGRAMMATIC RESEARCH INTO MEASURED G × E

Testing for an Interaction

Study Sampling Designs

Most informative design for testing G × E begins with cohort sample

- Represents population variation in genotype, exposure to environmental pathogens, and variety of health outcomes

- Ideal if cohort enlisted prospectively in early life and followed longitudinally

Repeated assessments obtain unbiased measures of cumulative exposure to environmental pathogens, and ascertain history relative to timing of exposure (Collins, 2004; Hunter, 2005)

In simple case of dichotomous genotype and environment variables, four cells of participants can be compared:

<table>
<thead>
<tr>
<th>Genetic Risk</th>
<th>Environmental Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Low</td>
<td>Baseline outcomes associated with factors apart from G x E</td>
</tr>
<tr>
<td>High</td>
<td>Effect of gene</td>
</tr>
<tr>
<td>High</td>
<td>Is joint association of risk factors with outcomes additive of multiplicative?</td>
</tr>
</tbody>
</table>

The FDA acknowledges a large variation in response rates to treatments for a variety of conditions.

The Promise of Personalized Medicine

NIH Director Elias A. Zerhouni, M.D., leads the NIH’s 27 Institutes and Centers, with more than 18,000 employees and a 2006 budget of $33.6 billion. A well-respected leader in the field of radiology and medicine, he has spent his career providing clinical, scientific, and administrative leadership. Recently, Dr. Zerhouni sat down with magazine coordinator Christopher Klose to discuss some of his own experiences and hopes for the future of medicine.

Klose: What motivated you to become a doctor?

Dr. Zerhouni: I just like people: the interaction and sense of being relevant. At first, I wanted to be a mathematician or a physicist. I was more interested in robotics and some of the careers typical of the 1950s. Years later when I was in undergraduate, I volunteered in the poor areas. I saw what was going on with the poor and that shocked me. That was when I realized that it’s great to send rockets to the moon, but perhaps the most important thing is people. That’s why I went into medicine.

Klose: What did you decide to specialize in radiology?

Dr. Zerhouni: Sometimes, life is just a matter of encountering people who show you something interesting. I had a radiologist who showed me my first CAT [computed axial tomography] scan.

Right away, I realized this was important; this was something I could do. Radiology has a direct impact on understanding the biology of disease. Here is the core of my research. I’m not a biologist but I work in biology. I’m not a mathematician, yet, I use mathematics: every piece of work I’ve done has been to increase our ability to quantify. To use quantitative methods, to extract biological information. For example, I first discovered CAT scans could be used to measure calcium density within tissues, which led to getting a patent. That opened the way for doing the same with cancer and then osteoporosis. And I discovered a technique, MRI [magnetic resonance imaging] that allows you to measure cardiac function very precisely.

Klose: Why did you decide to become a doctor?

Dr. Zerhouni: I am sort of a hybrid because I believe that science is key. I don’t lie to just analyze things. I’m entrepreneurial and want to make a difference. And that really requires what I call a personal attention. So I’m not really a detail-oriented person. I am a tool for reaching endpoints, to drive a particular vision.

Klose: How do you see medicine today changing?

Dr. Zerhouni: The relationship between patient and doctor is changing quickly. Before, the patient was passive and the doctor all-knowing and giving. We tried to cure people of what had evolved in them. Now we need to be much more patient-centric.

Hood (2003) Environmental Health Perspectives, 111(11) published by NIEHS, NIH
Graphical results of GWAS of nicotine dependence.

MEASURING phenotype, endophen. and intermediate

Summary: Modulation of Common ‘System’ Treatment-Specific Effects

Emotion-cognition integration

- mF9/10
- aCg24
- oF11

Attention-cognition

- PF9
- P40
- pCg
- hippocampus

Mood state

- bg
- thal

Vegetative-circadian

- Cg25
- a-ins
- am
- hth
- bs

Treatment-specific effects:
- CBT
- SRI
- Drug

Legend:
- CBT inverse
- SRI
- CBT only
- SRI only
Liability to Schizophrenia

Harmful

Protective

Reaction Surface

Schizophrenia

Schizophrenia Spectrum

Environment

Candidate Endophenotypes

Working memory

Sensory motor gating

Oculomotor function

Glial cell abnormalities

Etc.

Etc.

Quantitative Trait Loci in Genome

1q41, 1q42.1 — disrupted-in-schizophrenia 1 gene
22q11.21 — catechol-O-methyltransferase
8p21 — neuregulin
6p22.24 — dysbindin
15q14
13q14-21 — serotonin 2A receptor
1q21-22
6q21-25
10p11-15
13q32-34 — G72 protein
2q

?
Mental Health Care in the Pre-Genomic Era??
OBSSR will stimulate research that integrates multiple levels of analysis – from cells to behavior to society – required to understand the ways in which individual and contextual factors interact to determine health status.
1. Capitalize on new discoveries and new tools
   - Informatics, Computer technology
   - Gene-Environment Interaction
   - Predict, pre-empt, personalize

2. Conduct interdisciplinary science

3. Partner to solve problems whose scope overwhelms single paradigms
   - Translation, Dissemination, Policy
   - Systems integration, problem-based
   - Population Outcomes focus

“The idea of a sharp distinction between health and disease is a medical artifact for which nature, if consulted, provides no support.”

Pickering (1937)
Common Interactive Factors

STRESS, VIOLENCE
EARLY LIFE
In UTERO, CHILDREN
ADOLESCENT RISK
TOBACCO USE
UNHEALTHY DIET
PHYSICAL INACTIVITY
ALCOHOL
POVERTY, POOR ACCESS TO CARE

MENTAL ILLNESS
CVD
DIABETES
CANCER
COPD
MUSCULOSKELETAL
PREMATURE AGING
COGNITIVE DECLINE
ORAL HEALTH

………
The shape of things to come
Obesity Diabetes: Systems Integration from cells to society

Dynamic Hypothesis for the Drivers of Diabetes Incidence and Progression
Alternative Futures: Obesity in Pop (age 20-74)

Obese fraction of Adults (Ages 20-74)

Fraction of popn 20-74


Base
SchoolYouth
AllYouth
School+Parents
All Adults
All Ages
All Ages+WtLoss
www.plosmedicine.org

Figure 1. County Life Expectancies by Race

**Figure 3.** Life Expectancy at Birth in the Eight Americas (1982–2001)

Estimates for Americas 1 and 3 have been adjusted for differential underestimation of population and mortality among Asians (see Methods).

DOI: 10.1371/journal.pmed.0030260.g003
Basic Dynamics in the Health System
and Recap Why S/E/E Drivers are So Important

Public Work
(organizing, governance, citizenship, mutual accountability)

Professional Work
(customers, products, services)

more inter-organizationally complex,
slower rate of improvement

organizationally complex,
faster rate of improvement

FOR SELF INTEREST
FOR OTHERS IN NEED

Safer, Healthier Population

Vulnerable Population

Afflicted without Complications

Afflicted with Complications

Society’s Health Response

General protection
Targeted protection
Primary prevention
Secondary prevention
Tertiary prevention

Becoming no longer vulnerable
Becoming Vulnerable
Becoming Afflicted
Developing Complications
Dying from Complications

Adverse Living Conditions

From: Milstein B, Homer J. The dynamics of upstream and downstream: why is so hard for the health system to work upstream, and what can be done about it? CDC Futures Health Systems Workgroup; Atlanta, GA; 2003.
A Rare Opportunity to Complement Downstream Health Care with Upstream Health Action

Healthy Public Policy

Medical and Public Health Policy

Safer, Healthier Population

Vulnerable Population

Afflicted without Complications

Afflicted with Complications

Society’s Health Response

Primary prevention

Secondary prevention

Tertiary prevention

Adverse Living Conditions

By Strengthening...

• Leaders
• Institutions
• The meaning of work
• Mutual accountability
• Plurality
• Democracy
• Freedom
• Etc…

World of Providing...

• Education
• Screening
• Disease management
• Pharmaceuticals
• Clinical services
• Physical and financial access
• Etc…

World of Transforming...

• Deprivation
• Dependency
• Violence
• Disconnection
• Environmental decay
• Stress
• Insecurity
• Etc…

By Strengthening...

BCBSMF Initiative
Age-adjusted mortality rates of coronary heart disease in North Karelia and the whole of Finland among males aged 35-64 years from 1969 to 2002.

- North Karelia: -82%
- All Finland: -75%

Mortality per 100,000 population

Year:
- 1969
- 1972
- 1975
- 1981
- 1984
- 1987
- 1990
- 1993
- 1996
- 1999
- 2002
Understanding the “Whole” System

Cyberinfrastructure, Sensors, Geospatial coding, bioinformatics, bioimaging, systems biology, simulation Modeling...

- Pandemic flu
- Tobacco use, obesity, diabetes, stress....
- Health inequalities
- “non health factors”
- Housing, violence
- Bioterrorism ..........
Behavioral & Social Sciences Research (BSSR) at a Crossroads

• We have made significant contributions
• Even greater contributions are possible
• Behavioral and social sciences can and MUST be an integral part of the discovery, development, and delivery process
• BSSR can partner to improve population level health and quality of life
• Can improve prediction, pre-emption and personalized intervention
• Through basic science and systems integration - transdisciplinary, cyber-informatics, strengthening the science of dissemination.
New breakthroughs in the BSS are possible due to advancements in science and technology—especially informatics.

New challenges and emerging public health threats need new approaches (e.g., obesity, terrorism, natural disasters, pandemic flu).

Old problems need new approaches (e.g., health disparities, tobacco use, health literacy).

Changes at NIH require re-evaluation of priorities.

Rising demand and unsustainable costs threaten our current healthcare system.
Call to action: take home messages

Can ANY of the lofty goals of biomedicine be achieved,

Can ANY of the pressing public health challenges be overcome

WITHOUT

Basic and applied BSSR
- the grandest challenge of all understanding individual and collective behavior and sustained behavior change,
- and without our science being used - the adoption of what we know in practice and policy?
SOCIETY CAN DO IT - BSSR CAN HELP

• BRANDING - Need more communication and education of our sciences -- more marketing, direct to consumer advertising of core messages to audiences

• Culture change and consumer health literacy

• Who are WE, what do we know, what do we do, what do we have to offer society?

• How do we want others to see us, respect us and value us?

• Why should we be a partner and where do we fit in this rapidly changing global landscape?
Take home messages (continued)

• Have our sciences taken more seriously as hard science- We have matured and come of age

• We can and deserve to take our place at the table as equal partners with the natural and biomedical sciences, engineering, big business…….

• Political will is needed to take our knowledge and evidence base more seriously and to use the laws and discoveries of BSSR to improve health and societal wellbeing, locally, nationally and - globally
Take home messages (continued)

• Need for CULTURE CHANGE to balance the overblown promises and hopes for magic bullet cures from biomedical science and big pharma…

• Other big industry self interest - food, beverage, tobacco, automobile, communications, media, games …in an Increasingly global, FLATTENING WORLD.

• The BSSR reality of human brain and behavior in context - behavioral, social, ecological causes and solutions

• Create a new world view -- What world view is realistic and “user friendly” to our genes, sustainable and stable on a global basis?
Take home messages (continued)

- Transform Biomedicine’s 4 Ps- Personalized Preemptive Predictive and Participatory from narrow biomedical frame to broad Personalized health and health care frame - put the PERSON and the social context into personalized medicine
- From systems biology to systems medicine, behavioral, social and systems population science
- Informatics and Communications Technology are transforming the BSS’s as systems biology, bio-imaging, genomics, is transforming / has transformed cell biology - from “genomics” to “populomics”
- From gene chips and high throughput individual biological signatures to cyber infrastructure and creating the societal level “gene chips” - the signatures in the nested contexts at the individual, household, neighborhood, community, national and global level over lifespan and generations
NIH Support for Transdisciplinary, Systems Strategies to address pressing challenges in health/health care

- NIH Roadmap - all NIH Institutes and Centers
- NIH Neuroscience Blueprint
- Office of Portfolio Analysis and Strategic Initiatives (OPASI)
- Other agencies, Global trends,
  - National Science Foundation, SBE, DBASSE....
  - Centers for Disease Control and Prevention
  - Homeland Security, DoD, DoE, DoJ, CMS, AHRQ....
  - Cyber-infrastructure, competitiveness in a flattening world.........
The next generation: Strengthening Behavioral and Social Science Educat., Training

- development of enhanced courses, curricula to prepare for the future
- provide curriculum and other products for dissemination to other schools
- foster health-related research and careers in behavioral and social science within medical school and public health settings
COMPLEXITY

• The world is complex, contextual and multiply determined.

• For every complex problem there is a simple solution ………and its usually wrong

• Research designs, methods and measures should take this into account and capitalize on advances in technology, informatics. Imaging, data and knowledge management and communications

• Vertical integration from cells to society is needed

• Solid basic science is needed as a firm foundation
The world is complex, multi-level, multi-determined and contextual. Biology, behavior, social and physical environment dynamically interact. These systems transform and reciprocally modify one another. Systems within systems. 

Biomedical "causes" and socio-ecological "causes of causes" are two sides of the same coin.

Complex diseases are the product of Gene-Environment interaction - some during sensitive lifespan developmental episodes in time.
Transforming Science

• Surveillance
• GIS, EMA, sensors
• Cohorts with bio & behavioral assays
• Advanced technologies
• Real-time data capture
• Risk Prediction Models
• Intervention models - policy
• Knowledge/Data mgmt

Science is determined by the questions we ask & methods for asking them. - Gordon Rugg, 2004
Transforming Health Care Delivery

"Health care today is characterized by more to know, more to manage, more to watch, more to do, and more people involved in doing it than at any time in the nation’s history."

- IOM, 2001

- Tailored and targeted tx
- Valid measures of quality care
- Performance monitoring
- EMRs
- User-centered design
- Evaluation of e-health tools
- Personalized medicine
Fig. 1. The society-behavior-biology nexus as depicted in multidimensional space. The large arrows represent the axes of time and nested hierarchical structures. The sphere of health-related behavior and action moves through time from infancy to old age. Behavior is influenced by structured contingencies within the social and physical environment and by biological phenomena. Structural contingencies (opportunities and constraints) are shown by paths ending with nodes, while biological phenomena (embodiment and expression) are shown by paths ending with arrows or nodes.
“My question is: Are we making an impact?”
Conclusion

- Behavior is the bridge between biology and society
- The vision of OBSSR is to mobilize the biomedical, behavioral, social science, and population science research communities as partners to solve the most pressing health challenges faced by our society.
Three OPTIONS

- we are fundamentally OK but we need to communicate and market our science better

- we need some change around the edges - what?

- we have a crisis building and need radical re-invention our sciences are being co-opted and left behind - what is our core identity? The cheese has moved - our reaction is?
Where are we in Kuhnian “Scientific Revolution” terms? - stage of our science and practice

• Will the BSSR paradigms that worked so well in the 20th century - basic and applied - still be useful in a rapidly and radically changing world
• Silos within BSSR communities and factions within Silos
• Silos across the Biological, Behavioral-social and Population/public health science Paradigms
• Scientific revolutions - are we seeing the dissolution of old structures, but not clear what the new structures should be

• What are the most pressing health problems facing our society and what can BSSR do to solve them -- must skate to where the puck is going to be