



Robert Wood Johnson Foundation

**Forum on the Future Impact of Neuroscience and
Behavior Change**

November 10-12, 2009



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- Sample innovations and research content from:
 - Emerging Neurotechnologies
 - Neurodevelopment
 - Behavior Change

Forum Host & Introduction

Who is Pioneer?

- Pioneer, a program area of the Robert Wood Johnson Foundation, invests in innovative ideas that may lead to significant breakthroughs in health and health care
- Projects in the Pioneer Portfolio are future-oriented and look beyond conventional thinking to explore solutions at the cutting edge of health and health care
- Recent Pioneer initiatives include:
 - **Games for Health** connects health and health care problems with innovative solutions emerging from the game industry
 - **Positive Health** approach that emphasizes “health strengths” rather than disease diagnosis and management
 - **U.S. Biobank**, large and diverse repository of genetic, environmental and health data

www.rwjf.org/pioneer



Robert Wood Johnson Foundation

Introduction to the Forum

- Pioneer is exploring new ways of finding and promoting innovation across health and health care.
- This project is not intended to produce a grantmaking strategy; rather, it is an effort to understand and discuss near and long-term opportunities with other stakeholders. For this prototype effort, we chose to focus on the latest developments in neuroscience and brain development, and their impact on healthy behavior.
- Thus far, the project has included secondary research and over 50 conversations with neuroscience researchers, engineers, entrepreneurs, health care providers, marketers and leading practitioners of behavior change to understand the state of innovation today, the challenges faced and the future of healthy brain development.
- The November 11th -12th forum is a cross-sector convening that will focus on identifying and advancing the next generation of innovations in this space.

Forum Objectives

- The objective of the forum is to bring together practitioners and thought leaders from neurotechnology, neurodevelopment and behavior change in order to...
 - **Identify key, related areas of innovation** in and among the three fields
 - **Explore potential futures for the fields**, what actions could lead in each direction, and the implications for American health care;
 - **Highlight the opportunities for key players** to create value in new ways and accelerate innovation in and among these fields; and
 - **Foster connectivity among participants and thought-leaders** to facilitate ongoing idea-sharing and collaboration.

Sample Organizations Attending





Introduction

Forum Agenda

The forum will feature wide-ranging discussions, interactive break-out work and co-created content. We will provide a more detailed agenda at the opening of the forum.

November 11th

(8:30am – 4:30pm)

Neurotechnology Overview

- Introductory conversation about the technologies that will influence and advance our understanding of neurology, development and, ultimately, behavior

Neurodevelopment Overview and Breakout Sessions

- Introduction to neurodevelopment with a focus on recent ideas and areas that have the potential for widespread, transformative impact on health and health care.
- Hands-on breakout sessions, group discussions and co-creation of content:
 - Key innovation areas
 - Potential futures
 - Accelerators and opportunities

Looking Beyond Tomorrow's Innovations

- Plenary discussion on how this group – and our broader respective fields – might bring about next-generation, cross-sector innovations

November 12th

(8:30am – 2:30pm)

Behavior Change Overview and Breakout Sessions

- Introduction to behavior change with a focus on recent ideas and areas that have the potential for widespread, transformative impact on health and health care
- Breakout sessions, group discussions of co-created content: key innovation areas, potential futures, accelerators and opportunities

Looking towards the Future

- Plenary discussion on designing for impact: How do we advance what we know? How do we apply what we're learning? How can health care organizations and the health care system use this and how can we help them?

Note: A reception will be held November 10th, 6:00 – 8:00pm at the Westin Hotel

Connecting Neurotechnology, Neurodevelopment, & Behavior Change



Our research into these three fields has shown us that they not only hold great promise individually but that they are also the three major components of a potentially profound revolution in neuroscience. We believe that exploring the three together presents the greatest opportunity to bring forth insights into what advances in neuroscience could mean for the future of health and health care over the next 20 years.

The most forward-leaning thinkers in neuroscience call for interdisciplinary, international, long-term research collaborations that will tap the efforts and insights of every relevant field. Each of these three fields is an important component of building the systemic understanding of the mind that they envision.

1. Advances in neurotechnology provide researchers with better tools to study the brain and understand how it functions and develops

Neurotechnology

- Technology and techniques that allow researchers to explore, understand, influence, and change the brain and how it functions

2. Based on a deeper understanding of the brain, researchers can improve or refine their approach to behavior change and better promote healthy brain development

Neurodevelopment

- Insight into brain development and function in each life stage
- Improved methods to prevent the cognitive decline associated with aging
- Better management of illnesses and declines in cognitive abilities

3. With better behavior change tools and techniques, individuals can further improve their own development over their lives through better choices

Behavior Change

- Tools and techniques to successfully influence individuals' health behavior and decision-making

As You Read...

This pre-reading packet contains a brief sampling of new innovations, interview quotes, innovation drivers & barriers and other new ideas from our research into the fields of neurotechnology, neurodevelopment, and behavior change.

These selected highlights are meant to engage the reader in what is newly possible, in preparation for the forum's focus on how to more quickly bring forward our most innovative ideas from across all three fields.

As you review our research highlights, please keep these key questions in mind:

- **What are the key next-generation innovations** in and among these fields?
- **How are these innovations likely to come about?** Who will be involved, what will need to be in place and what will need to be overcome?
- **What impact might these next-generation innovations have** on health and health care?
- **How could their impact be enhanced and their development accelerated?** What would it take?



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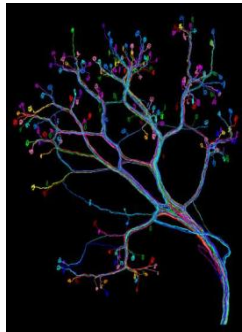
Five Key Innovation Areas

Our research and interviews identified five key innovation areas in neurotechnology

	Definition	Notes of Interest
1 Neurodiagnostics	<ul style="list-style-type: none"> Neurodiagnostics involves detection and study of electrical activity in the central nervous system (CNS) and specific bio-molecules in the body, for the diagnosis and monitoring of neurological disorders Neurodiagnostics can be broadly classified into Neuroimaging, <i>In Vitro</i> Diagnostics & Neuroinformatics 	<ul style="list-style-type: none"> VCs consider diagnostics unattractive because of limited availability of treatment therapies for the neurological diseases
2 Stem Cell Technology	<ul style="list-style-type: none"> Stem cell therapy aims to surgically transplant the stem cells in the human nervous system to achieve the following: <ul style="list-style-type: none"> – Regenerate / restore some lost part or function of the CNS – Prevent / reduce the degenerative process of neurons / injury 	<ul style="list-style-type: none"> Global cell-based markets estimated at \$60 Bn in 2010*
3 Neuromodulation Devices	<ul style="list-style-type: none"> Neuromodulation refers to therapeutic activation of nerve activity by means of implanted devices, and can be classified into two categories: <ul style="list-style-type: none"> – Neurostimulation: implanted device delivers electrical current to nerve site – Implantable Drug Infusion System: implanted pump delivers drugs through a catheter directly to the nerve site 	<ul style="list-style-type: none"> The worldwide market for neuromodulation devices was estimated to be USD 1.7 Bn in 2008, expected to increase at a CAGR of 28.3% to USD 4.6 Bn in 2012¹
4 Neuroprosthetics	<ul style="list-style-type: none"> Neuroprosthetics are devices that can substitute for sensory (e.g. cochlear implants) or motor functionality (e.g. robotic arms) that may have been lost due to disease or injury 	<ul style="list-style-type: none"> <i>“The “Walk Again” project is targeting the restoration of partial locomotion to patients by 2013– 2014”</i>
5 Targeted Neuropharmaceuticals	<ul style="list-style-type: none"> Novel therapeutics / drugs designed to treat specific symptoms , types or sub-types of neurological disorders, such as Alzheimer’s disease, Parkinson’s disease, etc. Neuropharmaceuticals includes the application of bio-molecules such as recombinant proteins, enzymes, monoclonal antibodies, etc., as possible drug candidates to treat neurological disorders 	<ul style="list-style-type: none"> Pharmaceuticals continues to be the most active area of neurotechnology in terms of VC activities

Sample Innovations in Neurotechnology (1 of 2)

1



The Mouse
Interscutularis
Muscle Connectome

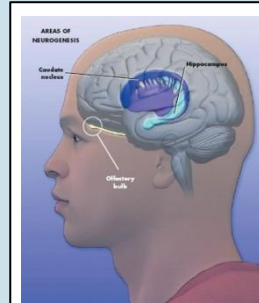
Neurodiagnostics

- Work on **Connectomes** seek to map, store, analyze and visualize the actual neural circuitry of the brain

“Similar to the human genome, the mapping of brain circuitry will revolutionize our understanding of how the brain functions and evolves through time.”

- **Lead Investigators:** Hanspeter Pfister, Jeff Lichtman and Clay Reid at Harvard University
- **Recent work:** “Reconstruction of the complete set of motor axons innervating a muscle reveals extensive wiring variability” (10 February 2009, CellNEWS)
- **Implications:** A detailed map of the connections within the human brain might allow for :
 - Understanding of “proper” wiring and “mis-wiring” associated with disease and disorder
 - Blueprint for future, targeted treatments

2



Neurogenesis

Stem Cells

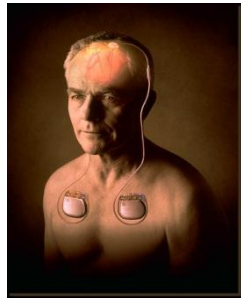
- **Neurogenesis** is the process of forming new brain cells, and unlike what was previously thought, this process continues throughout life.

“If your parents ever told you that you were wasting brain cells you could never get back, they were wrong, you can get some of them back.”

- **Leading Development:** Brain Cells Inc.
- **Recent work:** Phase 2a clinical trial for Brain Cells lead product candidate, BCI-540, for the treatment of depression with anxiety. BCI-540 directly impacts neurogenesis without affecting serotonin levels.
- **Impact:** “The fact that you might be able to take small molecules to stimulate specific cells to regenerate in the brain is paradigm-shifting,”
 - Researcher

Sample Innovations in Neurotechnology (2 of 2)

3



Deep Brain Stimulation

Neuromodulation

- **Deep Brain Stimulation (DBS)** is a surgical process placing a thin wire electrode deep in the brain, which produces electric stimulations to target nerve areas which control movements

"[A]s patients get older then the drug treatments tend to have less effect. But with deep brain stimulation you can prolong quality of life quite significantly."

- **Field Leaders:** Medtronic, St. Jude, Cyberonics
- **Recent work:** Vagus Nerve Stimulation (VNS) Therapy™ System, which is FDA-approved for the treatments of refractory epilepsy and treatment-resistant depression (Cyberonics)
- **Implications:** "I feel a newfound freedom from frustration, and my confidence is back. My life has been restored and I'll do anything to educate others about this pacemaker for the brain." (VNS patient commenting on treatment)

4



Brain Computer Interface Product:
BrainGate™ System

Neuroprosthetics

- **Brain Computer Interface (BCI)** is a direct communication pathway between the brain and an external device. It works on the principle of using electrical activity generated by cortical neurons to interact with external devices

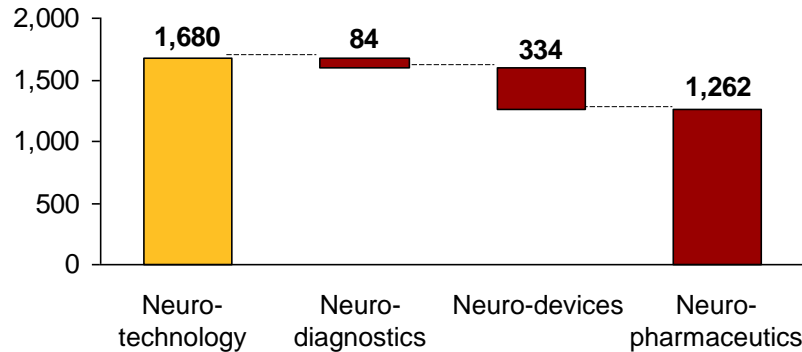
"We envision this as a system that could someday enable paralyzed people to use their own muscles again to feed themselves and more."

- **Lead Investigators:** John Donoghue, Cyberkinetics & Brown University; Dr. Miquel Nicolelis, Duke
- **Recent work:** Sung-Phil Kim, John Simeral, Leigh Hochberg, John P Donoghue and Michael J Black (2008). **Neural control of computer cursor velocity by decoding motor cortical spiking activity in humans with tetraplegia.** J. Neural Eng., vol. 5, pp. 455-476, 2008.
- **Implications:** Technology has potential to return independence and lost motor functionality to persons with injury and/or paralysis

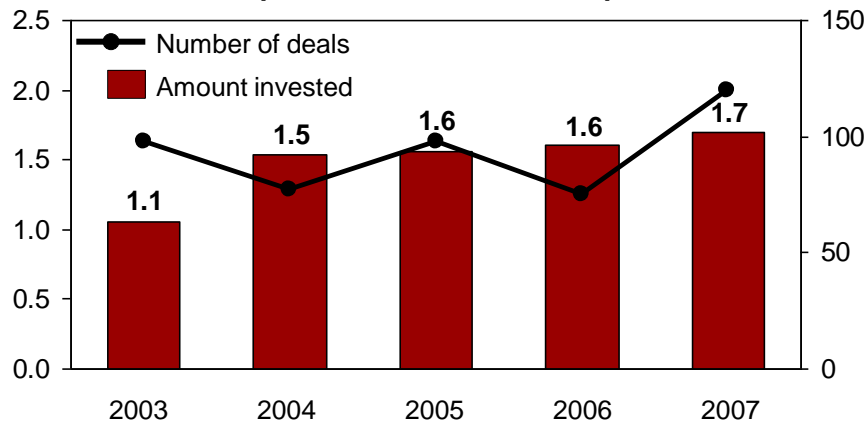
Current Funding for Neurotechnology

Neuropharmaceuticals continues to represent the majority of VC funding within neurotechnology

VC Investments in Neurotechnology (USD MM, 2007)



VC Investments in Neurotechnology (USD Bn, 2003-2007)



Barriers to VC funding in Neurotechnology

- Recent venture failures in the CNS space has discouraged investment
 - Neuropharmaceuticals cost ~ \$1.6B over 12-14 years to bring to market
 - Failure rate higher in neurotechnology space than other startups
- VCs consider diagnostics unattractive because of limited availability of treatment therapies for the diseases,
 - “Any company that comes to me as a diagnostic company, I often advise [the management team] to think of something different”*
 - Mark Cochran, GM, NeuroVentures (VC Investor in Neurotechnology)
 - “Panelists (at Neurotech Industry Conference (2007) focused on investing in neurotechnology) were hesitant to encourage investment in certain types of neurotechnology manufacturers, including neurodiagnostics, software, and complex equipment”*
 - The Venture Capital Outlook for Neurotechnology, Neurotechreports, 2007

Select Drivers and Barriers

Interviewees identified a number of drivers and barriers to advancing neurotechnology

Drivers

- **Neurological diseases/disorders represent a substantial annual economic burden**
 - Brain and nervous system disorders may cost the United States as much as \$1.2 trillion annually¹
 - Two billion people with brain disorders globally, almost 100 million in the U.S. alone¹
- **Technological advancements in diagnostic tools and therapies (e.g., neuroimaging, biochips, optogenetics)**
- **Growing interest from government actors and policy makers**
 - National Neurotechnology Initiative (NNTI) is legislation currently under consideration that has the potential to accelerate the development of neurotechnology treatments
- **Other commercial applications (e.g., emotional sensing in video game industry)**

Barriers

- **Lack of coordinated research activities across government institutes**
- **Low level of funding relative to other disease states**
- **Lengthy approval process & complex regulatory environment**
- **Ethics of certain research practices are debated and questioned**
- **Unproven track record of translating top neuroscience research into commercially viable products/services**
 - Large number of recent failures
 - Additional complexity results in higher costs and longer time to market for many neurotechnology products

Pre-Read: Emerging Neurotechnologies

Selected Insights from Interviews

● Current research and work

- “India and China will lead the brain research effort ,currently 1/3 of research is done overseas, an increase of 90% in the past 5 years.” (Association Representative)
- “Cracking the neural code is essential for the progress of neuroscience. New projects like Brainbow and techniques like Optogenetics are shedding additional light on brain signals.” (Researcher)
- “We are at the point where we can track neurosignals and know if you were thinking about yourself or not and whether you relate to what you are thinking about to you.” (Researcher)

● Complexity, Drivers and Barriers

- “The typical experimental process, in which a scientist sets out to test a specific hypothesis, is simply incapable of deciphering something as complex as the human mind.” (Researcher)
- “The difficult environment for early stage neuro companies to obtain funding will continue for the next couple years.” (Investor)
- “Cross sector contribution of actors will take action and thinking forward.” (Investor)

● Funding

- “It has been hard to receive funding given the lack of hypothesis of our project. There is enormous antipathy for tools which show you things and do not test a hypothesis. Thus, the best strategy to receive funding is by showing preliminary data.” (Researcher)
- “A new hybrid model needs to be in place to ensure the funding and success of CNS companies. This model will be based on a combination of investments from philanthropy, VC, pharma and biotech.” (Investor)

● Benefits, impacts and implications

- “200,000 quadriplegic patients in US alone can see impact with the new prosthetic devices that are being developed.” (Investor)
- Cells-related research could bring new treatments to market within the next 10 years and could transform how we treat debilitating diseases.” (Association Rep)

January 5, 2020

The New York Times

Alzheimer's Cured

Brain Cells, Inc. reports that its new neurogenesis treatment dramatically reduced the effects of Alzheimer's Disease in 87% of clinical trial patients.

Device Reduces Depression

A minimally invasive brain stimulation device, manufactured by Cyberonics, has opened up new avenues for treatment for Parkinson's Disease.

Eli Lilly to acquire Medtronic

Eli Lilly announced today that is in negotiations to acquire medical device manufacturer Medtronic, Inc. Eli Lilly is believed to be offering a cash and stock deal worth \$30 Bn, a 15% percent premium over Medtronic's current market capitalization

Spinal Cord Injury Patient Walks Again

In a landmark experiment, a quadriplegic patient was able to move prosthetic legs through a chip implanted in to patients brain stem. A global team of researchers ...

Mouse Connectome Unveiled

Researchers yesterday unveiled a detailed circuit map of a mouse's brain. This effort is considered to be a major milestone for the eventual mapping of the human "connectome."

Is Cognition Genetically Determined?

You can't jump like Michael Jordan. And you can't sing like Justin Timberlake. So why should you expect to integrate complex equations in advanced calculus? Researchers at Stanford today presented data to suggest that most cognitive ability is genetically determined.



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Overview: Four-Stage Framework for Brain & Behavior Development



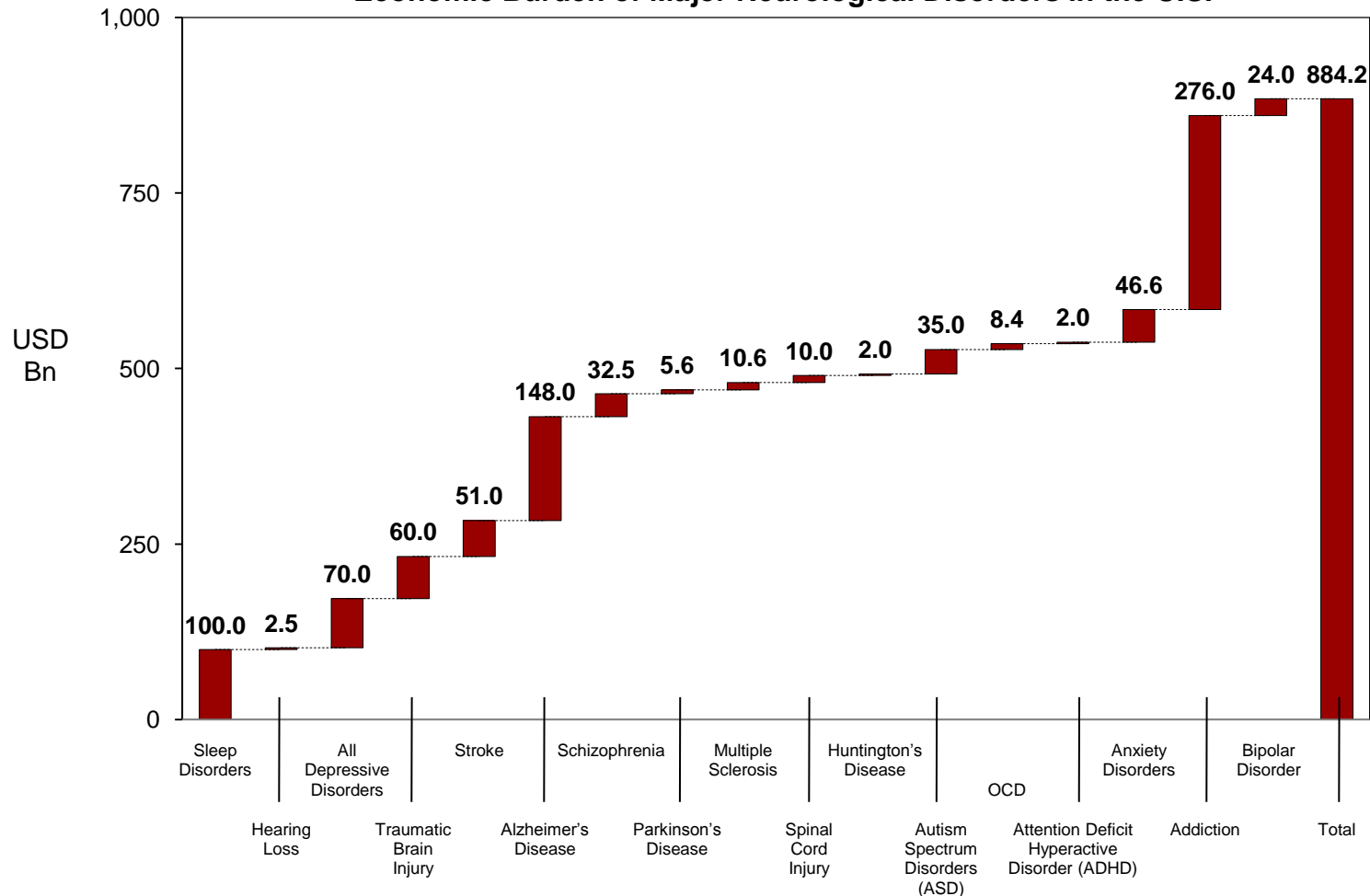
Study of how brain develops and behavior changes across each age group

Brain & Behavior Development	Children (0-5 Years)	Adolescents (6-19 Years)	Adults (20-65 Years)	Elderly (>65 Years)
Impact Potential	<ul style="list-style-type: none"> • Improve prevention, early diagnosis and management of diseases 	<ul style="list-style-type: none"> • Promote brain development while brain is malleable 	<ul style="list-style-type: none"> • Help adults manage disorders and remain productive 	<ul style="list-style-type: none"> • Increase the quality of life for elderly people
Innovation Areas Identified in the Research	<ul style="list-style-type: none"> • Development of brain process in early years • Effects of genetic, environmental and socio-cultural factors on developing brains • Neuronal basis of early age brain disorders (e.g., autism, ADHD, etc.) • Techniques for early diagnosis 	<ul style="list-style-type: none"> • Techniques for early diagnosis • Effectiveness of pharmacological and non-pharmacological therapies for disease management • Disease areas and causes 	<ul style="list-style-type: none"> • Techniques for early diagnosis • Effectiveness of pharmacological and non-pharmacological therapies for disease management • Relationship between disease areas and other mental disorders 	<ul style="list-style-type: none"> • Cellular or molecular changes occurring in the brain due to aging • Mechanisms behind loss of cognition with growing age • Tools and techniques for early diagnosis and treatment of disorders
Sample Diseases	<ul style="list-style-type: none"> • Autistic Spectrum Disorders • ADHD • Reactive Attachment Disorders 	<ul style="list-style-type: none"> • Self-injury Behavior • Eating Disorders • OCD 	<ul style="list-style-type: none"> • PTSD • Postpartum Depression • Narcissistic Personality • Social Anxiety • Addiction 	<ul style="list-style-type: none"> • Dementia • Postoperative cognitive dysfunction • Parkinson's Disease

Economic Burden of Neurological Disorders

The U.S. economic burden of neurological disorders is estimated to be between \$884B & \$1.3T

Economic Burden of Major Neurological Disorders in the U.S.



“If you can prevent an adolescent from developing a personality disorder, you would save \$1.3M per kid.”

– Researcher

“The economic cost of treating older adults who lose their independence will encourage research funding.”

– Researcher

Note: Economic burden is expenditure in health systems and lost economic output

Source: “Brain Facts – 2008”, Society for Neuroscience (SFN); World Health Organization (WHO); Center for Disease Control and Prevention (CDC); The Agency for health care Research and Quality (AHRQ); American Psychiatric Association (APA), Neurotechnology Industry Organization (NIO), Society for Neuroscience (SFN)

Sample Insights from Research

Adolescent Brain & Behavior Development

- There are numerous barriers to advancing understanding of adolescent brain and behavior development.
 - Funding of longitudinal studies
 - Research populations are hard to find, recruit, and track
- As a result, researchers are using alternative methods for researching the adolescent brain, such as sampling adolescent brains at different ages and then extrapolating the data to create models.

“The development of adolescent brains is a complete black box in our research; we need a better understanding on why there a wide variation in their development.”

–Researcher

“Creating an infrastructure, so people do not have to keep going after the money would be helpful. It’s draining to re-apply every time we need funding. Usually, non-lab work is not funded as well as lab work by the NIH.”

–Researcher

Personality Disorders

- Personality disorders typically form in adolescents (and children).
- The brain undergoes significant specification during the adolescent development stage.
- Development precursors (e.g., symptoms, genetic factors) are important for identifying and treating personality disorders.
- Precursors to development disorders may look different at different stages of adolescence – making detection more difficult

“People don’t wake at 18 and have a personality disorder, there are some precursors at the neurobiological level, but due to development these precursors look different at each developmental stage. Potentially we will be able to check the development of the reward system in the brain... and say this behavior looks different.”

– Researcher

Schizophrenia

- Dopamine-based treatments have dominated the schizophrenia space.
- Given commercial implications, drug companies have tended to focused on improving dopamine treatments rather than discovering alternative therapies.
- Further, common pharmacological treatments for schizophrenia often result in a loss of brain tissue.
- New innovation needed around which part of the brain is being targeted.

On schizophrenia drugs:

“They block basal ganglia activity. The prefrontal cortex doesn’t get the input it needs and is being shut down by drugs. That reduces the psychotic symptoms. It also causes the prefrontal cortex to slowly atrophy. If I were developing new drugs, I’d switch targets. Till now it’s been chemically formulated targets. I believe we should be thinking more anatomically and asking, With schizophrenics, which brain regions are functioning abnormally?”

– Researcher

Vulnerable Populations

While some neurological disorders receive substantial support, several “vulnerable” populations receive insufficient support given the nature of the affected population or the disorder

Foster Children

- Children living in foster care have an unusually high prevalence of Reactive Attachment Disorder
 - A recent study found 38% of children living in foster homes suffered from RAD compared to an estimated 1% of children under 5 in the US
- Administration for Children and Families is funding research into treatments for RAD, but RAD sufferers lack a strong advocacy voice that could further additional research

Pregnant Teenagers

- One interviewee highlighted the need for funding to research therapy options for women at teenage pregnancy homes, a population at high risk of developing personality disorders
- While pregnant teenagers receive a host of supports designed to ensure that they deliver healthy babies, there seems to be little research on neurological disorders impacting this segment

Soldiers Suffering from PTSD

- Estimates of the rate of PTSD among veterans returning from Iraq range from 12% to 20%
- Several factors discourage soldiers from disclosing PTSD, including stigmatization by peers and family and risks to career advancement
- PTSD research is currently funded by NIMH, Department of Defense and the Department of Veteran Affairs, but interviewees indicate the need for significant PTSD research innovations

Schizophrenics

- Schizophrenics represent less than 1% of the US population, and constitute one third of the nation’s homeless, a difficult population to access for treatment
- Drug intake may hasten brain tissue loss, new medications with low dose options and non-medication oriented treatments are needed
- *“People with schizophrenia are losing brain tissue at a more rapid rate than healthy people of the same age. Some are losing as much as 1% per year”* -Researcher

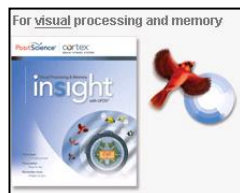
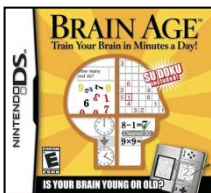
Sample Innovation: Brain Fitness Software

Brain fitness software is a recent innovation garnering interest from researchers and private industry for its potential as intervention and maintenance tool in the brain development field

Overview

- Brain fitness software, an intervention for maintaining healthy brain during early stages of brain development and as we age, is based on the premise that cognitive abilities can be improved through training
- Most of the products are aimed at general brain development, some are specific to neurological disorders
- Key user segments of brain fitness products include:
 - Consumers
 - health care and insurance providers
 - Administrators of K-12 Schools
 - Companies, military and sports teams
- According to a report by SharpBrains, the US brain fitness market was ~ USD 225 MM in 2007 (increase of over 100% since 2005)
- Lack of independent research is a barrier to the development and credibility of brain fitness industry.
- Users and buyers need to be educated to help them navigate through the complex landscape of products and claims

• E.g.,



“There is an opportunity to expand brain fitness [software] studies to other age groups in the population.”

– Researcher

“Our studies in the elderly suggest that brain fitness programs maintain and prevent the deterioration of their abilities.”

– Researcher

Sample Innovation: Addressing Post Traumatic Stress Disorder

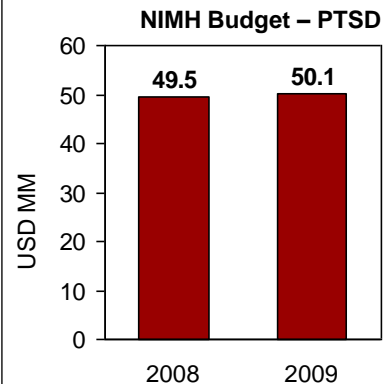
“We’re at the beginning of a really big problem in terms of dealing with all of the veterans returning from Iraq. Companies are trying to figure out how to address this.”

–Venture Capitalist

Overview

- A study of the first 100,000 [Iraq and Afghanistan] veterans seen at VA facilities showed that 25% of them received mental health diagnoses, with PTSD, substance abuse, and depression among the most common diseases
- The significant economic burden of caring for veterans with PTSD is already driving funding towards research
 - Multiple clinical trials are underway to explore various pharmacological treatment options for PTSD
- Recent non-pharmacological innovations include Virtual Iraq, a video simulation designed to treat soldiers suffering from PTSD

Funding



- NIMH provides funding for research in the field of PTSD through its Traumatic Stress Research Program (TSRP)
- In 2009, TSRP will focus on developing diagnostic tools to determine risk factors for PTSD

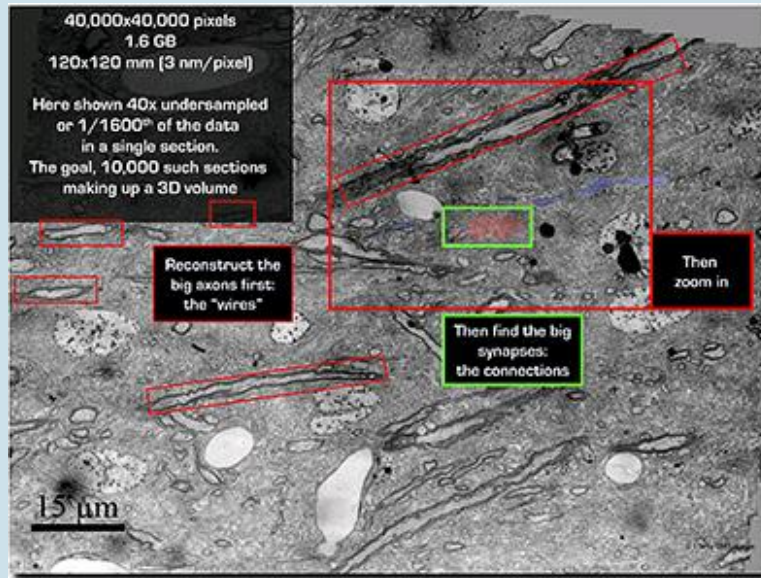
Innovation Highlight: Virtual Iraq



- Based on immersion therapy, allows soldiers to see, hear and smell original trauma
- Developed by Dr. Albert Rizzo of USC, Creative Technologies Laboratory, and Virtually Better, with funding from the U.S. Naval Research Office

Sample Innovation: The Connectome Project

While the Connectome Project is focused on long-term insights and impact, it represents an opportunity to significantly add to our understanding of brain and behavior development



“The smallest piece of brain that you can monitor with fMRI contains something along the order of 100,000 nerve cells.”

-Researcher

“Similar to human genome, the mapping of the brain circuitry will revolutionize our understanding of how the brain functions and evolves through time

-Researcher

- Researchers from multiple universities are collaborating for the Connectome Project, to map and analyze neuronal network of the brain
 - Create a physical map of neuronal interconnections
 - Study signal flow in the network
 - Monitor changes in the network over time
- The current focus is to develop
 - Physical map of neuronal interconnection
 - New imaging, cutting and computational tools to study brain at micro and meso levels
- The research is expected to help:
 - Understand molecular mechanisms of brain processes
 - Develop better treatment options for neurological disorders
- Harvard University, in collaboration with MIT, is leading the research
- The funding is being provided by institutes, such as NIH, Gatsby Charitable Foundation and Microsoft Research

March 26 2020

The New York Times

New Hope for Earlier Diagnosis of Schizophrenia

A biomarker-based therapy, funded by the National Institute of Mental Health, successfully identifies who is at risk for schizophrenia.

Closer to a Cure for Alzheimer's

MIT brain researchers have developed an experimental drug treatment, now in human clinical trials, that may effectively reverse the symptoms of Alzheimer's disease.

Consciousness Revealed

Researchers at the Barrow Neurological Institute yesterday presented findings on the key components of consciousness. These findings include the relationship of visual and olfactory perception to consciousness.

Educational Interventions Boost IQ of Disadvantaged Children

An eight-week long intervention program, targeting specific prefrontal processes affected by socioeconomic disparity, has been shown to enhance the IQ of economically disadvantaged children. The intervention may significantly alter the landscape of our nation's education system...

Research Holds Promise for New Epilepsy Treatments

Researchers at Stanford University yesterday presented a breakthrough in epilepsy treatment that controls the excessive synapses thought to be responsible for epilepsy attacks. The treatment is based on glial and other non-neuronal cells research

Select Drivers and Barriers

Interviewees identified a number of drivers and barriers to advancing our understanding of neurodevelopment

Drivers

- **High economic burden associated with neurological disorders should drive additional research**
- **Strong advocacy groups for several key neurological disorders**
 - e.g., Michael J. Fox Foundation for Parkinson's Disease
- **Advancements in brain development understanding**
 - Diagnostics
 - E.g., fMRI, Magnetoencephalography
 - Impact of socio-economic environment

Barriers

- **Subject recruitment and retention**
 - Most fMRI studies take place on college campuses with subjects between the ages of 18 and 22, a non-representative sample
 - Difficult to get informed consent from some research subjects, including
 - Minors
 - Institutionalized individuals
 - Schizophrenics
- **Funding**
 - NIH grants are only for 5 year periods
 - Current NIH funding environment prioritizes substantial research data over innovation
- **Private sector focuses on expanding existing treatment lines, often at the expense of new treatment / innovations**
- **Need for interdisciplinary attention**
 - Need for the integration of research across different fields, including psychology, sociology / anthropology, cellular and molecular, etc.

Sample Field-Level Innovation: Cross Sector Network

Many interviewees have called for a cross sector network to foster innovation, information exchange, and collaboration

- **Provide Impartial Knowledge on Commercial Products**
 - Serve as an impartial party to educate stakeholders on the benefits and limitations of these products
 - e.g., Much of the research on brain fitness software is sponsored by their commercial developers, and may serve to “market” to consumers and not “educate” them.
- **Transform Processes for Research Subject Recruitment & Retention**
 - Reform existing process for obtaining research subjects to better access to high-quality populations
 - e.g., Many of the researchers interviewed expressed concerns with the ability to identify and access representative samples, especially over time
- **Facilitation & Coordination**
 - Encourage cross-sector collaboration through convening neuroscience, behavior change, and brain development leaders
 - Coordinate efforts in complex multidisciplinary problems (e.g., smoking cessation)
- **Funding**
 - Organize and/or fund multi-year exploratory research campaigns



Table of Contents

- Introduction to Pioneer and the Forum
- Emerging Neurotechnologies
- Neurodevelopment
- **Behavior Change**



Pre-Read: Behavior Change

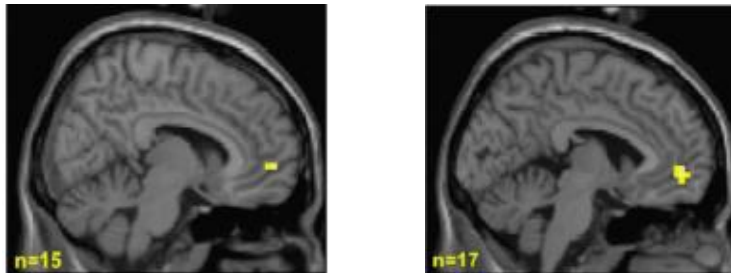
Overview: Three Key Areas in Behavior Change

	Neuroeconomics and Decision-making	Consumer Models	Tools & Techniques
Description	<ul style="list-style-type: none"> Science of analyzing how the human brain assesses choices, evaluates risks and rewards, and makes an economic decision 	<ul style="list-style-type: none"> Theories on how consumers make decisions <ul style="list-style-type: none"> E.g., Transtheoretical Model of Behavior Change (TTM), Loss Aversion Model, Simplification of Choices Model 	<ul style="list-style-type: none"> Tools and techniques to influence consumer decision making and behavior
Key Takeaways	<ul style="list-style-type: none"> Research in this field is currently in its infancy stage Additional breakthroughs will have wide ranging implications on understanding how the brain makes decisions 	<ul style="list-style-type: none"> Several consumer models exist but there is no overarching framework / theory Difficult to predict outcomes solely based on models 	<ul style="list-style-type: none"> Much of the current innovation in this area is driven by private industry & technology
Innovation Areas Identified in the Research	<ul style="list-style-type: none"> Understanding brain activity related to factors influencing decision making process: <ul style="list-style-type: none"> Preferences Utility and reward system Social factors, such as fairness, altruism & trust Dynamic concepts, such as learning, memory and knowledge Extend application of new brain imaging techniques (e.g., Single-Neuron Measurement, etc.) for understanding brain activity 	<ul style="list-style-type: none"> While there have been no recent innovations in the creation of consumer models there are innovative approaches to utilizing these models <ul style="list-style-type: none"> E.g., Pro-Change bases its interventions on TTM 	<ul style="list-style-type: none"> Groundswell based tools Mobile marketing Wireless surveys Data mining tools Portable People Meter (PPM) Others (scent marketing, sound marketing, advergames, in-game advertisements, observational techniques, personalized advertising, etc.)

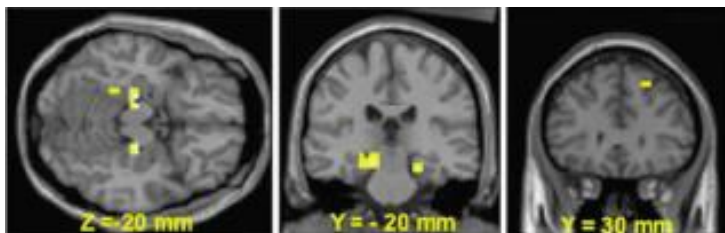
Sample Case Study: Neuroeconomics and Coke vs. Pepsi

Researchers are developing an improved understanding of where decision making happens in the brain

Pictorial Representation of Key Findings



Activation of VMPFC during Phase 1



Activation of Hippocampus and DLPFC during Phase 2

Overview

- This study focused on brain activity and behavioral preferences, based on sensory and cultural information
 - In Phase 1 of the study participants were asked to identify the tastier drink between Coke and Pepsi, solely based on their taste senses by not disclosing the brand names.
 - In Phase 2 a different group of participants were asked the same question but were told the brand names of the drinks.
 - In Phase 1 50% of people identified Pepsi as the tastier drink, but in Phase 2 only 25% selected Pepsi.
- Researchers found that In Phase I, the perception of reward was closely related to the ventromedial prefrontal cortex (VMPFC) of the brain. Whereas, in Phase II the response was governed by the activation of dorsolateral prefrontal cortex (DLPFC)

Potential Implications for Health

- This research has allowed scientists to develop hypotheses on the roles played by different parts of the brain in decision making
 - VMPFC is believed to be the part of the brain associated with behavioral senses such as fear, risk, reward and plays a central neural substrate in preference judgment
 - DLPFC is believed to employ past affective (cultural) information to execute a biasing decision/behavior
- Further research on the brain's role in decision making can provide insight on tools for promoting healthier decisions

Sample Innovation Area: Mobile Health (1 of 2)

Mobile telephones are increasingly being used to deliver health services, particularly with segments of the population that have been difficult to access

Description



- Mobile marketing is used to influence behavior by enhancing brand awareness and customer loyalty, increasing participation in events, and visits to a store, etc.
- Mobile marketing can be done by:
 - Sending text messages and mobile ads
 - Offering mobile coupons and reward programs
 - Developing location-based services, mobile applications, and mobile games, etc.

Potential Implications for Health

- Mobile marketing techniques are **low cost**, **accessible** to a significant portion of the US (particularly urban adolescents who are typically hard to reach) population and can be **deployed fairly rapidly**, creating a triumvirate of drivers
- Several constraints to large scale adoption exist
 - Low usage among the elderly and children
 - Potential confidentiality challenges
- Health professionals have already begun mining mobile marketing techniques for health specific applications
- Currently there are mobile applications designed to provide the following health services:
 - Remind patients to adhere to treatment regimes
 - Educate the public on risky behavior
 - Support healthy lifestyle changes

Sample Innovation Area: Mobile Health (2 of 2)

Several organizations are using mobile health applications to help people stay healthy through increased information, improved treatment adherence, and additional physician contact

SexInfo



- San Francisco based **text message service providing youth with sexual health information and referrals** to area health centers
- Started in 2006 to combat rising STD rate among youth of color the SexInfo program
- In the first 25 weeks of the pilot, the SexInfo line received 4,500 inquiries, with 55% of the inquiries leading to requests for more information or referrals
- In April 2009 Planned Parenthood launched a mobile application that allows teens to identify neighborhood STD testing locations

InteleCare Compliance Solutions

- InteleCare distributes **health care communications tools and notification services**
- Recent studies have found that a minimum of 24% of patients do not adhere to physician's treatment and that 84% of patients cited forgetfulness as cause of non-adherence
- InteleCare's goal is **to improve treatment adherence through a series of reminders** sent via text message, voice mail or email



BeWell Mobile Technology



- BeWell provides **patient engagement software** for the health care community
- Mobile software application allows patients to record health data and receive treatment recommendations while giving physicians access to real time health data that aids in doctor in developing care plan
- Current offerings primarily focus on supporting patients with asthma and diabetes

Sample Innovation Area: Technology Based Health Solutions (1 of 2)



Organizations are looking at new technologies, and unique uses for existing technologies, to promote behavior change

Description

- Researchers are identifying **unique ways to use new and existing technology** to spark behavior change among consumers
- New technology based behavior change tools can favor one of several strategies, including:
 - Exploit widely accepted principles of consumer behavior (i.e. compensation as a key motivator)
 - Take advantage of widely utilized technological advancements(i.e., social networking websites)
- Marketers are currently exploring new ways to utilize these tools to influence consumer buying habits:
 - Company blogs
 - Customer engagement websites
 - Video game advertising

Potential Implications for Health

- Researchers interested in motivating people to undertake healthy behavior change have begun co-opting technology based marketing tools
- The allure of these tools is that they are often widely used, and are a relatively inexpensive method for implementing behavior change
- Several challenges constrain the potential impact:
 - Targeted users might interpret these methods as marketing tactics, limiting the effectiveness of these tools in creating positive health change
 - Several key populations, including the elderly and the children, may not be widely accessed through technology based methods

Sample Innovation Area: Technology Based Health Solutions (2 of 2)



Organizations are using new technologies to solve pressing health challenges

Smart Pillbox



- Electronic **pillbox that records each time a user opens it**
- Researchers are studying whether the monitoring mechanism of this device can improve treatment adherence
- Recent studies have shown that smart pillboxes when packaged with incentive schemes may have a positive impact on treatment adherence
- A potential limitation on wide scale adherence issues is that users may open the pillbox but may not actually take pills

QuitNet



- Smoking cessation website that **utilizes principles of social networking combined with practical elements of group therapy**
- Quitnet was initially founded in 1995, but its current incarnation most closely resembles the interfaces found on MySpace, or other social networking sites
- Users can connect with other people trying to quit smoking, and gain valuable resources to aid the lifestyle change

Get Yourself Tested



- **Multi-media campaign** focused on changing sexual risk behaviors among teens
- GYT site shares characteristics with existing consumer engagement websites
 - E.g., celebrity video messages, tools to increase peer sharing of website, etc.
- GYT was launched in April of 2009 so there is no impact data - some critics contend the behavior change message may be diluted by the marketing tactics



Pre-Read: Behavior Change

Sample Innovation Area: Commitment Devices

A new marketing tool provides individuals with support for implementing desired behavior change

Description

- Companies are exploring “commitment devices” as a way to aid employees, consumers, and even the companies themselves in engaging in positive behavior change
- Commitment devices lock people into behaviors that they would like to do but may not be strong enough to do without some enforcement
 - Recent study found that over 75% of college students opted to self impose binding deadlines for papers due at the end of the semester, a commitment against procrastination
- If properly utilized these devices can effectively induce behavior change, however they may also anger customers if not well structured

Potential Health Related Example

- Commitment devices **could be used to motivate a range of health behavior choices** (e.g., eating nutritious foods, exercising more, quitting smoking, limiting drinking, etc.)
 - Existing health related commitment devices include gastric bypass surgery to treat obesity and Antabuse to treat alcoholism
- One of the primary challenges of this tool is identifying the best structure for implementing and coordinating the commitments.
- Parties fear the resentment and potential privacy infringement that may befall the coordinator of the commitment contract



- Web based system lets **people place bets on their ability to change** their own behavior
- Users make a commitment, select a referee to decides whether the commitment has been met, and then place a bet (via credit card) on their ability to keep this commitment
- If the user fails to keep the commitment the money is kept and given to charity (or an anti-charity, one opposed to the user’s value system), and if the commitment is kept the money is returned

Sample Innovation Area: Voucher Based Incentive Therapy

Voucher Based Incentive Therapy is a contingency management treatment based on the principle that an individual repeats the behavior which is rewarded or reinforced

Treating Substance Abuse

- The National Institute of Drug Abuse is testing the use of VBRT in preventing substance abuse
- Voucher Based Incentive Therapies (VBRT) substance abuse treatment process:
 - Subject submits multiple urine specimens every week to the center conducting the program
 - In exchange for a urine specimen that tests negative for the presence of drugs or alcohol the subject receives a voucher that be used to buy retail items and services
 - The value of the vouchers improves with an increase in the abstinence period or retention to the treatment
 - Program also includes intensive counseling to help subjects improve their work skills and social relationships
- These therapies have shown increased abstinence and improved retention of treatment with various substance abusers

Other Examples



- Core components of VBRT can be found in several approaches to implementing behavior change on key health care issues
- Several programs incentivize healthy behavior change (e.g., quit smoking, undergo preventive screenings, etc.) through lowering out of pocket health care costs or providing gift cards
 - BeWell@Stanford Employee Incentive Program
 - United health care
 - Cigna Health Plan



Pre-Read: Behavior Change

Sample Insights from Research

- Behavior change is a nascent science.
- There is a need to for mid-level organization theories for decision-making research

“We need a lot more work on mapping out the response system of the brain and understanding how to effectively change behavior.”

– Researcher

- Behavior change frameworks can be applied to multiple settings
- Widespread dissemination of behavioral research can facilitate the spread of frameworks to other settings

“In behavior change we are starting to collect valuable information and recommending good decisions to people.”

– Researcher

- Technological advancements have created new opportunities for the behavior change field

“We recommend someone in weight management find social support to reinforce positive behavior in their lives. This support can sometimes be a social network”

– Industry Expert

“Electronic devices are only the tip of the iceberg of the opportunities available to digital medicine..”

– Physician

- Internet based social networks are becoming a viable alternative to in-person support groups, making this critical behavior change tool accessible to a wider group of people

*“For someone who is in preparation for weight management, we recommend they find **social support as way to reinforce positive behavior** in their lives, this support can sometimes be a social network”*

– Researcher

April 17, 2020

The New York Times

Mobile Phones Contain Key to Health

Health care professionals are using mobile phones to aid them in treating patients. Physicians currently use mobile phone applications to provide patients with test results, schedule appointments, and in some cases, provide diagnoses...

Smoking Addiction is History

Smoking cessation programs and pharmaceutical treatment options developed over the last 10 years have left the nation's public health officials poised to announce victory over an epidemic that once...

Self Diagnosis Database Ready for Use

A health care database that allows users to input their medical history, vital statistics, and symptoms into a database and receive a highly accurate diagnosis is now available to the public. Advocates of the new system say this innovation will help individuals to take control of their health and reduce the burden on the health care system.

New Program Prevents Adolescent Obesity

Researchers at Pro-Change have developed a youth targeted web-based interactive program that combines social networking with healthy living messages. The program, currently piloted in five urban areas, is experiencing high participation rates, and showing encouraging initial data getting users to change their diet and exercise more. Additional data on the program's success is expected to be released next year...

Targeted Interventions Help People Make Better Health Decisions

For the last twenty years experts in public health, medicine, and behavior change have been pooling key insights from their respective disciplines to improve decision making. This collaboration is responsible for recent interventions in obesity, substance abuse and sexually transmitted diseases.



Pre-Read: Behavior Change

Select Drivers and Barriers

Interviewees identified a number of drivers and barriers to advancing our understanding of and capability to influence behaviors

Drivers

- **Private industry's interest in marketing and consumer behavior** drive a high portion of behavior change research, which can often be applied to health issues
- General **technological advancements** (e.g., mobile phones, social networking sites, etc.) and **widespread technology adoption** have created new platforms for behavior change tools
- Public's **desire to reduce the economic burden** of diseases that could be prevented through behavior change
- **Increasing focus on the role of behavior in health** may drive additional interest in the field
 - Recent New England Journal of Medicine article attributed 40% of premature deaths to health behaviors

Barriers

- **Funding** challenges
 - health care financing system favors treatment over prevention
 - Longitudinal studies need to be funded
 - Studies involving brain imaging are costly
 - Government funding requires preliminary data and favors incremental advancement over innovation
- Lack of **collaboration** in behavior research, both amongst different academic departments and between academia and industry
- **Medical model** is more widely used than public health model in behavior change research so most studies focus on people seeking help, rather than all people in need of help
- Difficult to achieve widespread adoption of behavior change tools by medical stakeholders
- Need for improved **brain imaging technology**

Sample Field-Level Innovation: A Cross Sector Network

- Connect **disparate behavior change stakeholders** in meaningful ways
 - Support convenings and inter-disciplinary work
 - Bridge the gap between academic researchers and business professionals (e.g. build a mentoring program to encourage innovation and business development)
 - Streamline coordination costs across multiple players in neurospace (e.g., multiple stakeholders doing the same thing)
 - Create new opportunities for people who are not intimately connected to field to join the work
 - E.g., Construction company that wants to build communities by forecasting health care implications of the future
- Ensure **social / ethical implications** of behavior change are addressed
 - Host discussions and sponsor research on social /ethical implications
- **Raise awareness** of behavior change work
 - Publicize interesting areas of research and innovation
 - Contextualize popular understanding of scientific findings
 - Support public policy efforts
- **Provide funding** for new behavior change research
 - Spur innovation through sponsoring competitions