Future Directions in Mental Health Research: The View from Psychological Science

A Congressional Briefing Organized by the American Psychological Association

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American Psychological Association
Speakers

Howard Kurtzman, Ph.D., American Psychological Association
Introduction

William Hetrick, Ph.D., Indiana University
Advancing Understanding and Treatment of Schizophrenia through Basic Psychological Science

Mary Jane Rotheram-Borus, Ph.D., University of California, Los Angeles
Decreasing Adolescent Suicidal Behavior with Psychological Research

Patricia Areán, Ph.D., University of Washington
Future Directions for Behavioral Interventions Research
Future Directions in Mental Health Research: The View from Psychological Science
Advancing understanding & treatment of schizophrenia through basic psychological science

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Schizophrenia

- Fragmentation of mental processes
  - A devastating cognitive disorder:
    - Delusions & hallucinations
    - Disorganized speech & impaired cognition
    - Restricted emotional expression & avolition
    - Motor abnormalities.

- Affects ~1%; 10% suicide; shortens life by ~15 years!

- Massive societal impact
  - Annual US economic impact ~$155 billion
    - Direct health care (24% of cost)
    - Loss due to caregiving (34%)
    - Unemployment (38%)

- No objective test
  - Diagnosed based on behavioral observation & self-report.

Eugen Bleuler (1857-1939)
The take-home story

1. Using a simple Pavlovian classical condition procedure, we have identified a fundamental associative learning deficit among individuals in the psychotic disorder spectrum—schizophrenia in particular.

2. This learning deficit was also evident in individuals at risk for schizophrenia (e.g., schizotypal personality disorder & 1st-degree relatives), suggesting that we have identified a marker of risk for psychotic spectrum illness.

3. Informed by results from animal behavioral neuroscience, we used human MRI imaging to identify brain regions and circuits are responsible for the observed associative learning deficit.

4. Having pinpointed a possible brain region and mechanism for the learning deficit, we developed a novel experimental treatment for this deficit as a proof of concept.
Eye blink classical conditioning

A Pavlovian procedure
Eye blink conditioning (EBC) procedure

Skosnik et al., 2008
Cerebellar brain circuit for eye blink conditioning

Reading eye blink conditioning EMG data

HN Controls

Healthy Controls (N=62)
Eye blink conditioning acquisition deficit in 62 SZ vs. 62 matched controls

Deficits Also Observed in Schizotypal Personality Disorder

Response Acquisition Deficit

Deficits in 1st-degree relatives of individuals with schizophrenia

Acquisition Deficit

Bolbecker, Mehta, Klaunig, Forsyth, Steinmetz, O'Donnell & Hetrick (2013). *Schizophrenia Bulletin*
Bilateral cerebellar Crus II FA correlated with positive & general symptom scores

Kim et al., (2014) *Schizophrenia Bulletin*
Compared to SZ, controls show greater activation of deep cerebellar nuclei during EBC acquisition (*Acquisition – pseudoconditioning contrast*)

Crosshairs at right dentate peak maximum. (Kent et al., in prep.)

<table>
<thead>
<tr>
<th>Brain area</th>
<th>Cluster size</th>
<th>Peak T value</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right dentate nucleus</td>
<td>37</td>
<td>3.88</td>
<td>15</td>
<td>-48</td>
<td>-33</td>
</tr>
</tbody>
</table>
Can we ameliorate the associative learning deficit in SZ?

Yes!
Cerebellar brain circuit for eye blink conditioning

Effects of secretin on EBC in SZ suggest neural mechanism of dysfunction
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Ongoing basic research

1. Developing rodent model.
2. Partnering with pharma to test novel compounds.
4. Leveraging graph theory and network science methods to examine brain architecture.
Benefits of basic science

1. In 1904, no one could have predicted Pavlov’s impact on understanding and treating psychological disorders.
   - e.g., anxiety and addition disorders

2. In the 1990s, no one could have predicted that Richard Thompson’s discovery of the neural circuit for eye blink conditioning in the rabbit would be leveraged to understand and promote treatment of psychological disorders.
   - e.g., schizophrenia, alcoholism, autism

3. No one could have predicted that mere curiosity about why jelly fish glow would lead to our ability to see neurons in the living mammalian brain.

4. No one could have predicted that the discovery of light sensitive bacteria growing in shockingly salty bodies of water would lead to implanting brain cells with a protein to allow light control of neurons in the living brain (optogenetics).
The BIG take-home message

1. Investments in basic psychological research (e.g., perception, attention, *learning*, cognition) yield basic knowledge and experimental procedures that are leveraged to
   - understand psychopathology;
   - identify targets for intervention.

2. Eric Lander (MIT): Basic science is “The miracle machine”
Thank you for your attention.

Questions?
Future Directions in Mental Health Research: The View from Psychological Science
Decreasing Adolescent Suicidal Behavior with Psychological Research

Mary Jane Rotheram-Borus, PhD
University of California, Los Angeles
Suicide Rate
2000–2006, United States
Age-adjusted Death Rates per 100,000 Population

Note: Reports for All Ages include those of unknown age.

Data courtesy of CDC
Suicide prevention has multiple determinants

- Structural factors
- Organizational factors
- Parent/network influences
- Person’s physical & mental health
Homeless youth attempt suicide often

80% are at high statistical risk of suicide; 9 attempts in 4 shelters in 3 months in NYC
Screening for imminent danger, by acting incompatible with suicidal behaviors

- Identify strengths
- Be aware of feelings
- 3 people to call when suicidal
- Card with risky situations – alternative actions
- Written commitment to no suicide
Yet, the organization also has to change

- Screening & referral criteria – imminent danger
- Staff training
- Made hospital beds available
- Staff met hospital personnel
Suicide attempts in shelters decrease dramatically over 21 months.
50% of suicide attempters go to follow-up outpatient care-organizations can reach 95%

- Log intakes of suicide attempters
- Improve ED organization & training
- Motivate the family with a video
- Implement a standardized TxPlan
Standarized 6 session family Tx improves outcomes for attempters over 18 months

- < depression
- < suicidal ideation
- > outpatient treatment
- > attend more treatment sessions
Adolescent evidence-based (EB) treatments extended over 20 years

4/16 EB Tx for suicide attempters
10/24 EB Tx for depression

Major extensions into primary health care
Next steps in research on suicidal behaviors

- Screening expanded into a health systems, especially in PHC
- Stepped care model broadly diffused
- Controlling access to the means of suicide are critical
Investments in mental health research & services make significant differences in the current burden of disease.
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Future Directions for Behavioral Interventions Research

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Challenges in Treatment

Deconstructed, parsed, and diagnosed.
A hypothetical example illustrates how precision medicine might deconstruct traditional symptom-based categories. Patients with a range of mood disorders are studied across several analytical platforms to parse current heterogeneous syndromes into homogeneous clusters.

Symptom-based categories
- Major depressive disorder
- Mild depression (dysthymia)
- Bipolar depression

Integrated data
- Genetic risk
  - polygenic risk score
- Brain activity
  - insula cortex
- Physiology
  - inflammatory markers
- Behavioral process
  - affective bias
- Life experience
  - social, cultural, and environmental factors

Data-driven categories
- Cluster 1
- Cluster 2
- Cluster 3
- Cluster 4

Prospective replication and stratified clinical trials
Executive Dysfunction in LLD

- 50% of older adults with depression have executive dysfunction;
- Patients with LLD+ED have a poor/unstable response to SSRIs;
- Distinct clinical presentation that is easy to assess in standard clinical interview.
Step 1 (week 1-3)

- Social re-engagement

Step 2 (week 4-6)

- Assess and select next step
- Continue with social re-engagement

Step 3 (week 7-9)

- Assess and select next step
- Continue with step 2
- Continue with social re-engagement
Ethnicity of participants

BRIGHTEN

- Non-hispanic White: 61%
- Hispanic: 17%
- African-American/Black: 13%
- Asian: 5%
- American Indian/Alaskan Native: 2%
- More than one: 0.2%
- Native Hawaiian/Other Pacific Islander: 1%

U.S. Census (2013)

- Non-hispanic White: 61%
- Hispanic: 17%
- African-American/Black: 13%
- Asian: 5%
- American Indian/Alaskan Native: 2%
- More than one: 0.2%
- Native Hawaiian/Other Pacific Islander: 1%
Study Total = 2000+
Triaging Care

- Self guided treatment
- Telemedicine
- Expert level treatment
Research needs

• Incentivize researchers to pursue development of novel behavioral interventions
• Create a Mental Health Cohort to advise and rapidly test new interventions
• Best practices for ensuring the care is matched to patient presentation
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