Studying social interaction in Borderline Personality Disorder

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Mentors: Phil Corlett, John Krystal

Connecticut Mental Health Center Neuroscience Research Training Program

Thank you:

- Mary Zanarini, John Gunderson, and Lois Choi-Kain
- Emotions Matter, Families for BPD Research
- Research participants and patients
Plan for this webinar

• Quick review about BPD
  • What is BPD?
  • What is the prognosis?
  • What are the current treatments?

• What can science offer? 3 examples of BPD science.
  • Measuring social networks
  • Measuring social approach and closeness
  • Measuring social decisions
### Core BPD symptoms:

<table>
<thead>
<tr>
<th>AFFECTIVE</th>
<th>IMPULSIVE</th>
<th>COGNITIVE</th>
<th>INTERPERSONAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Changeable mood from minute to minute, hour to hour</td>
<td>- Aggression</td>
<td>- Odd ideas</td>
<td>- Difficult relationships with lots of ups and downs</td>
</tr>
<tr>
<td>- Depressed, anxious mood</td>
<td>- Driving</td>
<td>- Magical ideas</td>
<td>- Strongly conflicted relationships</td>
</tr>
<tr>
<td>- Emptiness</td>
<td>- Sex</td>
<td>- Paranoia</td>
<td>- Other symptoms come and go with interpersonal problems</td>
</tr>
<tr>
<td></td>
<td>- Alcohol/Drugs</td>
<td>- Hearing voices</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Financial</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Self-harm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
BPD epidemiology:

- Prevalence: 1-5% in the general population, 10-20% in psychiatric settings.
- Heritability 55-68% (SCZ 85%, MDD 45%).
- Not related to schizophrenia.
- **Remission** (no longer meeting criteria) is common.
- **Recovery** is less common:
  - Remission and
  - 1+ emotionally sustaining relationship
  - Full time work or school

Rates of remission and recovery after inpatient admission:

Zanarini, et al. Mclean study of adult development (recovery/remission)
Lyons & Plomin/Smoller Torgerson 2001 (genetics)
Gunderson 1983 (BPD vs. schizophrenia)
“Having BPD is like bleeding out.”

Merri Lisa Johnson
Girl in Need of a Tourniquet
Psychopharmacology for BPD:

US Prescribing patterns

- % BPD patients
- years after index admission

Psychopharmacology for BPD:

- Data is recent, inconclusive, practice guidelines still recommend no meds
- Polypharmacy is common, and inversely related to improvement
- Meds work for the expected symptom clusters:

<table>
<thead>
<tr>
<th></th>
<th>Mood stabilizer</th>
<th>Anti-depressant</th>
<th>Anti-psychotic</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affect regulation</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>++</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Psychotic-like</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

Relevant meta-analyses:
Vita et al. 2011
Mercer 2009
Binks 2006 Cochrane Review
Considerations in psychopharmacology:

Treating symptoms
• Symptoms can be debilitating
• Symptoms fluctuate as part of the disease

Maintaining safety
• Impulsivity – many medications are risky in overdose
• Suicidality and self-harm
• Co-morbidities: PTSD, panic disorder, substance use disorders...

Meaning of medications
• Adding and decreasing medications can trigger strong feelings of being judged to be sick, having help withdrawn etc...

Meaning: D Mintz, Psychiatric Times, Sept 2011
Psychotherapy for BPD:

- Good Psychiatric Management (John Gunderson, Paul Links, Lois Choi-Kain)
- Dialectical Behavioral Therapy (Marsha Linehan)
- Transference-focused Psychotherapy (Otto Kernberg and Cornell group)
- Mentalization Based Treatment (Peter Fonagy and Anthony Bateman)

Some resources for learning more about BPD-specific psychotherapy:

BPD training Institute at Mclean Hospital
https://www.appi.org/videos/gunderson-video-psychiatric-management-bpd
Workshops at the American Psychiatric Association
Family psychoeducation and Advocacy:

- Borderline Personality Disorder Resource Center
  http://www.bpdresourcecenter.org/

- Emotions Matter
  http://emotionsmatterbpd.org/

- NAMI
  https://www.nami.org/Learn-More/Mental-Health-Conditions/Borderline-Personality-Disorder

- NEA-BPD + Family Connections
  http://www.borderlinepersonalitydisorder.com/family-connections/

- TARA
  http://www.tara4bpd.org/

- Personality Disorders Awareness Network (PDAN)
  http://www.pdan.org
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Intro to Social Interaction Science:

- People with BPD are at a social disadvantage
Social networks:

• Social Network Analysis (SNA) is a way to measure this difficulty

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Ingredients for a social network analysis:

1. List people significant in your life.

2. What is the nature and quality of these relationships?

3. How are these people connected to each other?
Ingredients for a social network analysis:

1. List people significant in your life.
2. What is the nature and quality of these relationships?
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Features of a social network:
- **Ego:** The participant
- **Alter:** Person in participant’s network
- **Edges:** Connections between alters

**Centrality:** How connected a person is in a network
**Density:** How connected the network is overall

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Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social network analysis: The Egonet

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social networks in BPD

BPD symptoms are associated with:

- reduced closeness
- more negative interactions

### Table: Mixed Effects Models for BPD Symptoms

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>F(1, 141)</th>
</tr>
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<tbody>
<tr>
<td><strong>Closeness and support</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Closeness</td>
<td>-0.04</td>
<td>0.01</td>
<td>12.15***</td>
</tr>
<tr>
<td>Trust</td>
<td>-0.04</td>
<td>0.01</td>
<td>15.14***</td>
</tr>
<tr>
<td>Advice</td>
<td>-0.03</td>
<td>0.01</td>
<td>7.83**</td>
</tr>
<tr>
<td>Support</td>
<td>-0.02</td>
<td>0.01</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Attachment strength</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximity seeking</td>
<td>0.00</td>
<td>0.02</td>
<td>ns</td>
</tr>
<tr>
<td>Separation</td>
<td>0.00</td>
<td>0.00</td>
<td>ns</td>
</tr>
<tr>
<td>Safe haven</td>
<td>0.04</td>
<td>0.02</td>
<td>ns</td>
</tr>
<tr>
<td>Secure base</td>
<td>-0.01</td>
<td>0.03</td>
<td>ns</td>
</tr>
<tr>
<td><strong>Negative interactions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argue</td>
<td>0.03</td>
<td>0.01</td>
<td>7.75**</td>
</tr>
<tr>
<td>Criticism</td>
<td>0.04</td>
<td>0.02</td>
<td>5.58*</td>
</tr>
</tbody>
</table>

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social networks in BPD

In relationships, people with high vs low BPD symptoms:

- Have partners less central to their networks

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social networks in BPD

In relationships, people with high vs low BPD symptoms:

- Have partners less central to their networks
- Spend less in person time with their partner

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social networks in BPD

In relationships, people with high vs low BPD symptoms:

- Have partners less central to their networks
- Spend less in person time with their partner
- Feel less attached to their partner

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
For control subjects, more central relationships have:

- More positive experiences
- More conflict

For BPD subjects, more central relationships have:

- The same low level of positive interactions
- More conflict
- AND all relationships have more conflict than controls

Beeney et al. *Personality Disorders: Theory Research and Treatment* (Jan 2018)
Social Networks and BPD

• Social networks can provide webs of support, closeness, and connection with people in our lives.

• People with BPD often have social worlds that provide less support and have more conflict than people without BPD symptoms.

• Future research: How do interpersonal challenges in people with BPD contribute to differences in their social networks?
  • Trust and cooperation
  • Mentalization
  • Interpersonal sensitivity
  • Ability to change social beliefs
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Personal space regulation

• Rodents prefer shelter

• Anxious rodents explore less

• Measuring anxiety: the open field test

control mouse

anxious mouse
Personal space regulation

Imagine yourself:

Living in the country in the middle of nowhere.

Standing in the middle of an empty stadium.

Standing in an elevator that has stopped between floors.

Standing at the edge of a stadium.

control

anxious person

Personal space regulation

Imagine yourself:

Preparing to throw a free throw in front of a large crowd.

Giving a speech to a big audience.

Walking through a crowded market to haggle with a merchant.

Sitting in the middle of a crowded movie theater.
Personal space regulation: social distance

Personal space regulation: social distance

Personal space regulation: social distance

Personal space regulation: social distance

Personal space regulation: social distance

Personal space regulation: social distance

Personal space regulation: social distance

Amygdala is hyper-active in BPD

- Negative attribution bias in BPD has been linked to amygdala hyper-activity
- Finding not present in BPD patients on medication

Left amygdala/HC
Post. Cingulate cortex
Left m. temporal gyrus
(less) insula
DLPFC etc

Hypothesis:

In BPD,

amygdala hyperactivity \[\leftrightarrow\] interpersonal behavior

Is preferred social distance a way to measure amygdala activity or negative attribution bias in BPD?

First step: do people with BPD choose a different distance than controls?
Subject demographics

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>BPD</th>
<th>statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>30</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>33.4 +/- 13.05</td>
<td>36.9 +/- 12.5</td>
<td>t = 0.10, p = 0.32</td>
</tr>
<tr>
<td><strong>Education (yrs)</strong></td>
<td>15.2 +/- 2.69</td>
<td>14.0 +/- 2.52</td>
<td>t = 1.66, p = 0.10</td>
</tr>
<tr>
<td><strong>NAART (reading test)</strong></td>
<td>21.2 +/- 9.04</td>
<td>19.77 +/- 7.55</td>
<td>t = 0.59, p = 0.55</td>
</tr>
<tr>
<td><strong>Taking psychiatric meds</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-depressant</td>
<td>0</td>
<td>52.2%</td>
<td></td>
</tr>
<tr>
<td>Mood stabilizer</td>
<td>0</td>
<td>26.1%</td>
<td></td>
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<tr>
<td>Anti-psychotic</td>
<td>0</td>
<td>13%</td>
<td></td>
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<tr>
<td>Benzodiazepine</td>
<td>0</td>
<td>21.7%</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Subject demographics</th>
<th>Control</th>
<th>BPD</th>
<th>Statistics</th>
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<tbody>
<tr>
<td><strong>borderline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSL</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>26</td>
<td>21</td>
<td>t = -6.26, p &lt; 0.001</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td>5.08 +/- 6.2</td>
<td>32.19 +/- 19.06</td>
<td></td>
</tr>
<tr>
<td><strong>depression</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>27</td>
<td>20</td>
<td>t = -6.15, p &lt; 0.001</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td>2.56 +/- 4.3</td>
<td>21.4 +/- 13.9</td>
<td></td>
</tr>
<tr>
<td><strong>anxiety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>27</td>
<td>20</td>
<td>t = -4.90, p &lt; 0.001</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td>6.52 +/- 9.2</td>
<td>23.0 +/- 12.8</td>
<td></td>
</tr>
<tr>
<td><strong>impulsivity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>25</td>
<td>21</td>
<td>t = -5.10, p &lt; 0.001</td>
</tr>
<tr>
<td>Mean +/- SD</td>
<td>51.10 +/- 9.59</td>
<td>71.0 +/- 16.5</td>
<td></td>
</tr>
</tbody>
</table>

Preferred social distance expands in BPD

Personal space regulation in BPD:

People with BPD prefer a larger social distance.

How does preferred social distance change with:
- Familiarity?
- Social difficulty?
- Treatment?
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Learning in BPD:

How are social attributions acquired and updated in BPD?

Start with looking at all learning:

- Working memory deficits (Stevens et al Psychiatry Res. 2004)
- Reversal learning not different from controls (Berlin et al. AJP 2005, Paret 2015)
- Acquisition not different from controls (Paret 2015)
What about social learning?

- predictions from the clinic → bias to extreme views, reversing from neg. is tough

- Trust game

Trust game image adapted from Cecada et al. PLoS ONE 9(9):e108733 · September 2014
Trust game data from King-Casas et al. 2008
Computational models of social behavior:

- Mathematical models can improve on initial descriptions of behavior.
- A new model of trust game data found two features that influence behavior.

| Risk Aversion (Belief) $\omega (b(\omega))$ | $\{0.4, 0.6, 0.8, 1.0, 1.2, 1.4, 1.6, 1.8\}$ | Value of money kept over (potential) money gained. |
| Irritability $\zeta$ | $\{0, 0.25, 0.5, 0.75, 1.0\}$ | Tendency to retaliate on worse than expected partner actions. |
| Irritation Belief $q(\zeta)$ | $\{0, 1, 2, 3, 4\}$ | Initial belief on likelihood of the partner being irritable. |

Computational models of social behavior:

More BPD trustees are "0" = ignorant about their partner’s irritability

More BPD trustees have low level guilt

Social exchange:

- People with BPD cooperate less
- Amygdala signal in trustees decreases with bigger investor investments in controls, but not BPD subjects
- People with BPD coax a defecting partner less.
- Computational modelling shows that BPD trustees may coax less because of:
  - Not noticing their partner’s irritability
  - Not acting “guilty”

Trust game data from King-Casas et al. 2008
**Testing a new possible treatment:**

- **Ketamine** is a medication used in anaesthesia

- It rapidly decreases depression and suicidal thinking in people with major depressive disorder

Will people with BPD get the same benefits?
- decreased depression
- decreased suicidal thinking

How will people with BPD feel as ketamine wears off?

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Zarate et al. 2012 Biol. Psych
Ketamine in BPD:

- In animal models of depression, ketamine increases **neuroplasticity**
- The increase lasts ~ 3 days

**More neuroplasticity** means:
- nerve cells make new connections
- nerve cells strengthen new circuits
  
  This can promote new learning
Ketamine in BPD:

• In animal models of depression, ketamine increases **neuroplasticity**

• The increase lasts ~ 3 days

• We hypothesize that the post-ketamine neuroplasticity may offer an opportunity to revise old social beliefs

  More neuroplasticity means:
  • nerve cells make new connections
  • nerve cells strengthen new circuits

  This can promote new learning
Ketamine in BPD:

• New randomized controlled trial of ketamine vs. placebo for adults with Borderline Personality Disorder

• Each participant gets one dose: either ketamine or placebo

• Outcomes:
  • Suicidality
  • Mood Symptoms (depression / anxiety)
  • BPD Symptoms
  • Pain
  • Social
Ketamine in BPD:

- Real-world social experiences
- Social distance
- Trust Game

$3x$
Ketamine in BPD:

- Real-world social experiences
- Social distance
- Trust Game

clinicaltrials.gov
Search “Borderline Personality Disorder”
Review of this webinar

Quick review about BPD:

• What is BPD?
  4 core symptom clusters

• What is the prognosis?
  many people remit, fewer recover

• What are the current treatments?
  PSYCHOTHERAPIES and medications
  Family interventions

Measuring social interaction:

Social networks

Social distance

Social exchange

Ketamine in BPD Study

Follow and support research organizations: BBRF with Families for BPD Research, NIMH, AFSP