Using the NIH Toolbox Cognition and Emotion Batteries to Predict Neural Markers of Psychopathology

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The “Normal” to “Abnormal” Continuum

- Psychopathology as one extreme of an individual differences continuum
Part I: Electroconvulsive Therapy (ECT)
Neural Substrates of Its Beneficial Effects

1. Can ECT “normalize” the functional brain architecture relevant to visuospatial learning?
   i. Do such “corrections” predict post-ECT improvement in visuospatial learning?

2. What are the functional brain organization patterns typical of trait depression?
   i. Are they linked to rumination, a thinking pattern typical of depression?
Part II: Naturally Occurring Defenses against Depression
Neural Substrates of Vulnerability versus Resistance in Healthy Young Adults

1. Is the ECT-correctable neural profile linked to fewer depression-relevant cognitive and affective symptoms?

2. Is the trait depression neural profile linked to greater incidence of depression-relevant cognitive and affective symptoms?
Part I: Cognitive Measures

In-Scanner

Autobiographical Memory Recall

- Visuospatial reconstruction: visualize events experienced
  - Last week
  - Last month
  - Last year
  - Last 10 years

Out-of-Scanner

Brief Visuospatial Memory Test (Revised)

- Rumination/affective persistence
  - Frequency of thinking

Benedict, 1997
### Part I: ECT Sample

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Controls</th>
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<tbody>
<tr>
<td></td>
<td>(N = 15)</td>
<td>(N = 10)</td>
</tr>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>47.13 ± 13.26**</td>
<td>33.10 ± 8.02</td>
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<tr>
<td><strong>Education (yrs)</strong></td>
<td>14.97 ± 3.43</td>
<td>15.50 ± 2.99</td>
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<tr>
<td><strong>Gender (men/women)</strong></td>
<td>4/11</td>
<td>4/6</td>
</tr>
<tr>
<td><strong>Number of ECT treatments</strong></td>
<td>11.93 ± 6.23</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Number of bilateral ECT treatments</strong></td>
<td>7.57 ± 5.26</td>
<td>N/A</td>
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</tbody>
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Part I : ECT Sample

1. CONN Toolbox Functional Connectivity
   - 4 ROI-to-ROI task connectivity matrices per participant
     (autobiographical recall at time 1, number judgment at time 1, autobiographical recall at time 2, number judgment at time 2)

2. Network-Level Analyses: Brain Connectivity Toolbox
   - Louvain community detection (3 spatial resolution parameters x 100 iterations)
   - Agreement matrices

3. Brain-Behavior Associations
   - PLS: identify brain connectivity patterns that distinguish patients from controls at time 1 (pre-ECT) vs time 2 (post-ECT) on the autobiographical memory vs. the number judgment task
   - Correlational analyses: link expression of the PLS-extracted brain connectivity patterns to post-ECT improvement in visuospatial learning and rumination/affective persistence
1. ECT “normalizes” the functional brain architecture linked to visuospatial learning.
2. There are reliable functional brain organization patterns typical of trait depression.

Greater expression of the trait depression connectivity profile predicts greater rumination/affective persistence.
# Part II: Human Connectome Sample

(N = 333 healthy young adults)

## 1. CONN Toolbox Functional Connectivity

- 8 ROI-to-ROI task connectivity matrices per participant
  (working memory [zero-back, two-back], relational processing, social cognition, story processing, math processing, incentive processing, motor processing)

## 2. Network-Level Analyses: Brain Connectivity Toolbox

- Louvain community detection (3 spatial resolution parameters x 100 iterations)
- Agreement matrices
- Project the PLS-extracted LV 1 (depression-trait) and LV 2 (memory-related) from the ECT sample onto the task-related matrices from the HCP sample

## 3. Brain-Behavior Associations

- CCA: LV1 and LV2 scores (see step 2) for each of the 8 task conditions, learning, affective persistence, DSM-Depression, DSM-Anxiety, current negative emotional experience (sadness, anger, fear)
Part II: In-Scanner Tasks

**Working Memory: Two/Zero**

- Aesop's fables
  - E.g., An eagle saves a man who had done him a favor.
  - TEST: "That was about revenge or reciprocity?"

- Math
  - 14 + 18 = 32
  - 28

**Relational Processing**

- Change
- Texture

**Incentive Processing**

- 5
  - High or Low
  - Condition 1: 4 blocks
    - Reward $1.00
  - 7
  - Condition 2: 4 blocks
    - Punishment - .50 c
  - 3
  - 5
  - Condition 3: Neutral

**Social Cognition**

- Motor Processing
Part II: Cognitive Measures (out-of-scanner)

1. Affective Persistence: Reward Discounting Task

2. Visuospatial Learning: NIH Toolbox List Sorting Test

(Estle, Green, Myerson, & Holt, 2006; Green et al., 2007; Myerson, Green, & Warusawitharana, 2001)
Part II: Affective Measures (out-of-scanner)

1. Current Negative Emotion Experience (NIH Toolbox Negative Affect Survey)
   i. Sadness/Fear/Anger within the previous 7 days
      a. “I felt like a failure.”/I had a racing or pounding heart.”/“I felt bitter about things.”

2. Subclinical variations in Depression and Anxiety (Achenbach Adult Self-Report [ASR], 2009)
   i. DSM-oriented Depression vs. Anxiety Subscale (previous 6 months)
      a. "I cry a lot."/"There is very little that I enjoy."
      b. "I worry about my future", "I am too fearful or anxious."
Stronger expression of the trait depression neural profile and weaker expression of the ECT-"correctable" neural profile predict mood disturbances in healthy adults.

Connectivity Profile \[ r = .44, p = 4 \times 10^{-5} \] Cognitive Profile
Conclusions

• Successful therapeutic interventions, such as ECT, work by “normalizing” the expression of adaptive traits which are spontaneously observed in the general population.

• Need to develop assessment tools sensitive enough to detect subclinical variations in psychopathology-relevant traits.
Implications

• The NIH Cognition and Emotion toolboxes may be useful in
  ✓ the early identification of individuals who are at chronic or acute risk for developing psychopathology
  ✓ monitoring the progress of different therapeutic interventions

• Potential developments
  ✓ Assess daily transient fluctuations in cognition and affect (mobile toolboxes)
  ✓ Episodic construction: visual vs. verbal
  ✓ Somatic vs. Cognitive-Affective subscales (NIH Emotion toolbox)
Thank you!