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

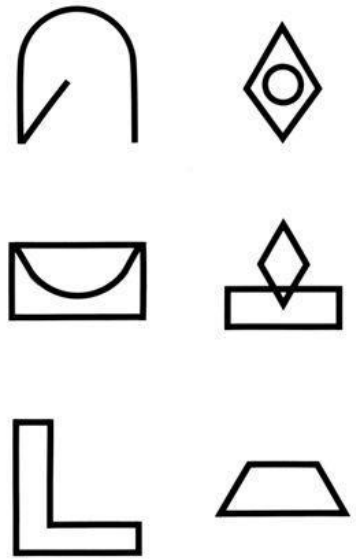
In-Scanner

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

	Patients	Controls
	(N = 15)	(N =10)
Age (yrs)	47.13 ± 13.26**	33.10 ± 8.02
Education (yrs)	14.97 ± 3.43	15.50 ± 2.99
Gender (men/women)	4/11	4/6
Number of ECT treatments	11.93 ± 6.23	N/A
Number of bilateral ECT treatments	7.57 ± 5.26	N/A

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

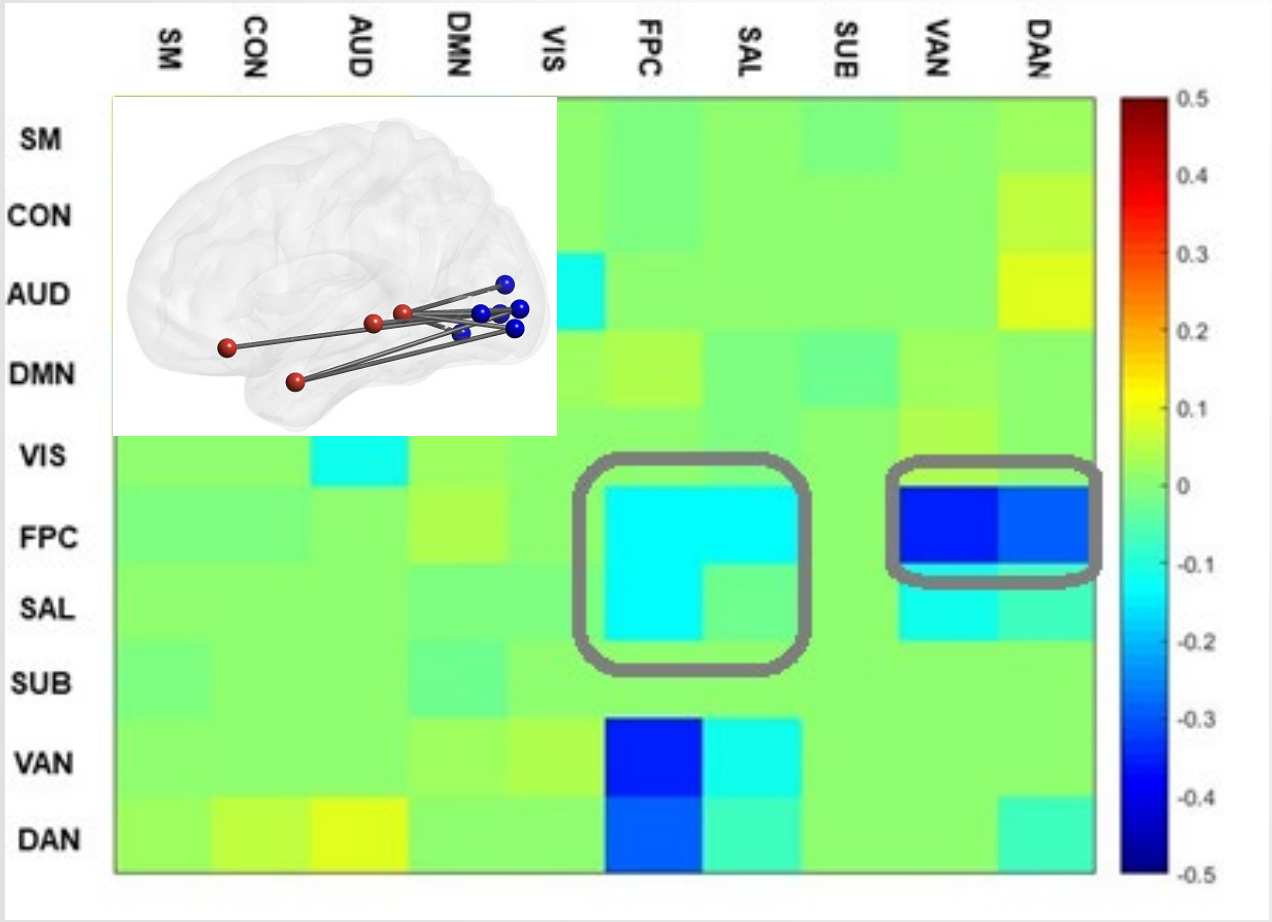
- Louvain community detection (3 spatial resolution parameters x 100 iterations)
- Agreement matrices

3. Brain-Behavior Associations

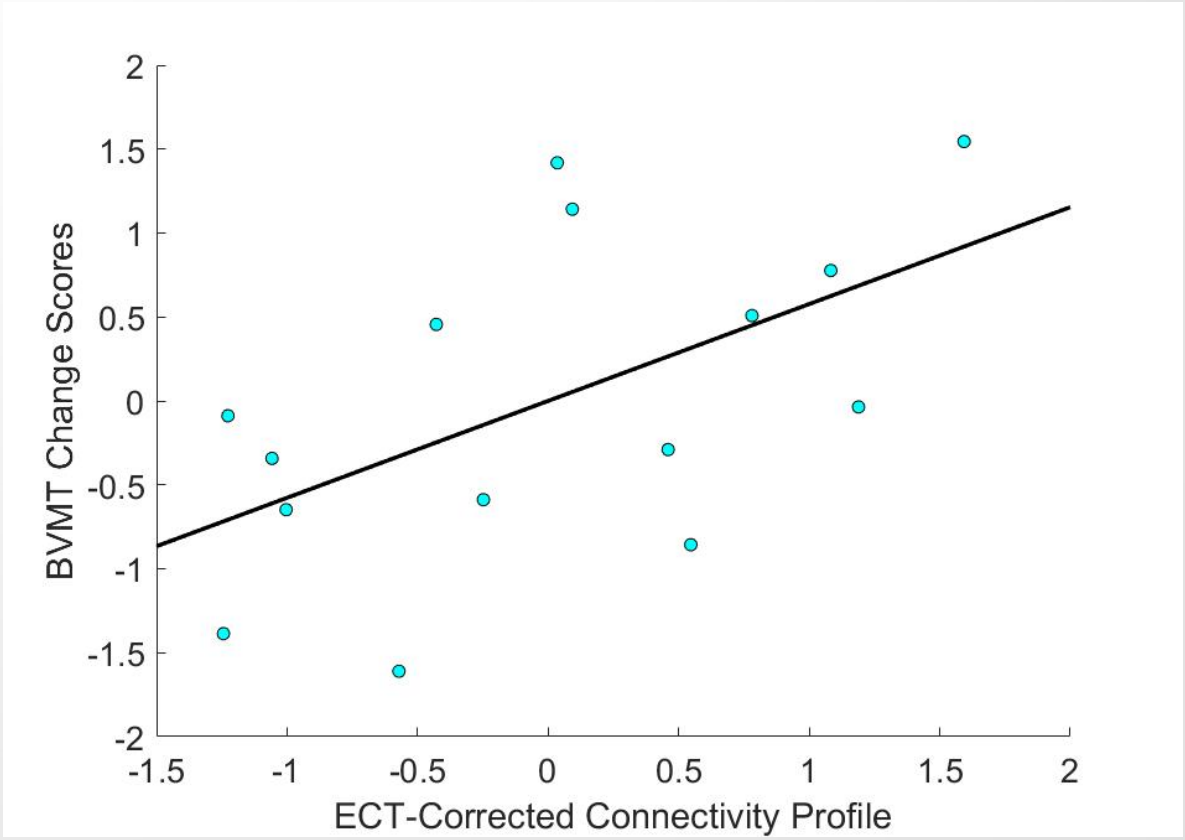
- PLS: identify brain connectivity patterns that distinguish patients from controls at time 1 (pre-ECT) vs time 2 (post-ECT) on the autobiographical memory vs. the number judgment task
- Correlational analyses: link expression of the PLS-extracted brain connectivity patterns to post-ECT improvement in visuospatial learning and rumination/affective persistence

1. ECT "normalizes" the functional brain architecture linked to visuospatial learning

ECT-Corrected Connectivity Profile
(Specific to the Autobiographical Memory Task)

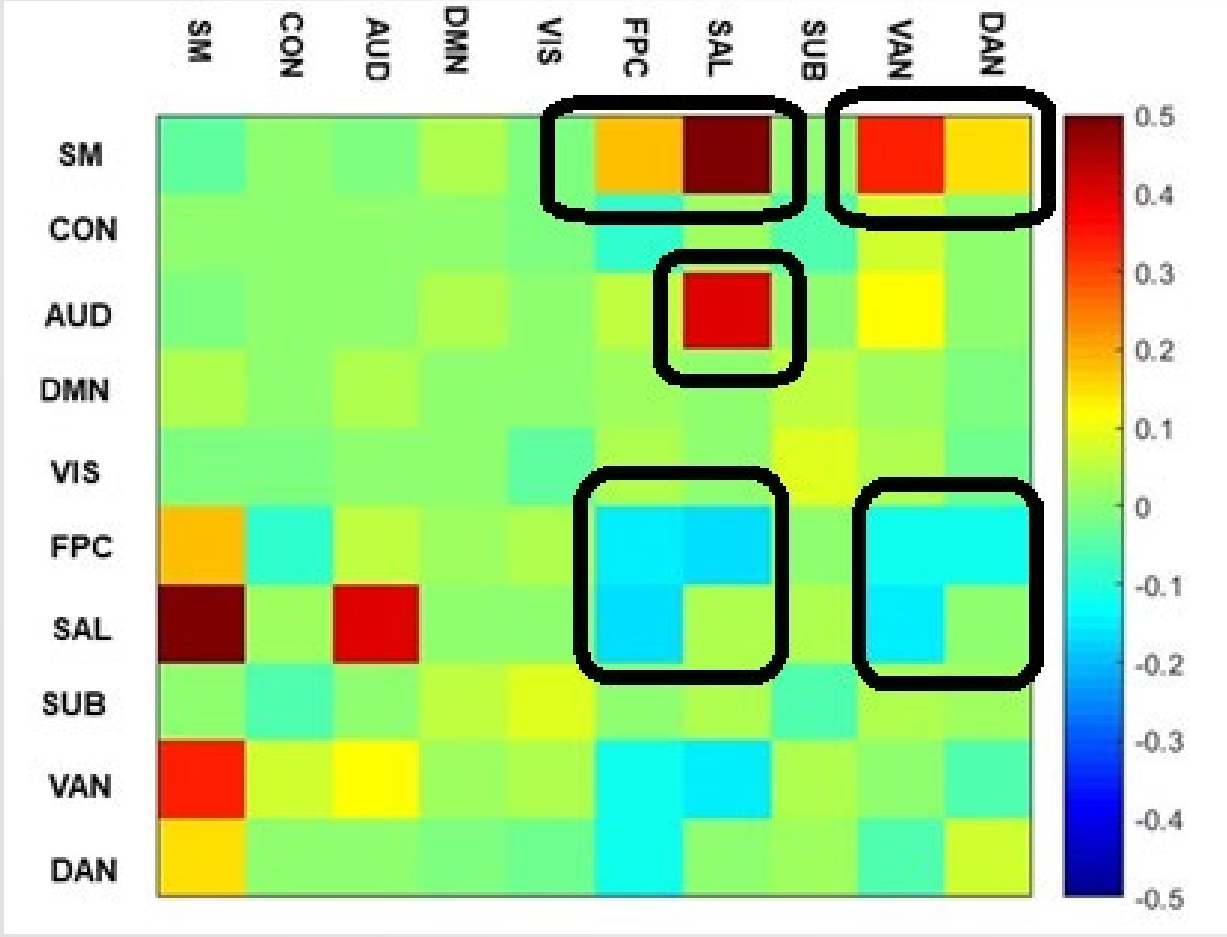


Greater expression of the ECT-corrected connectivity profile predicts post-ECT improvements in visuospatial learning

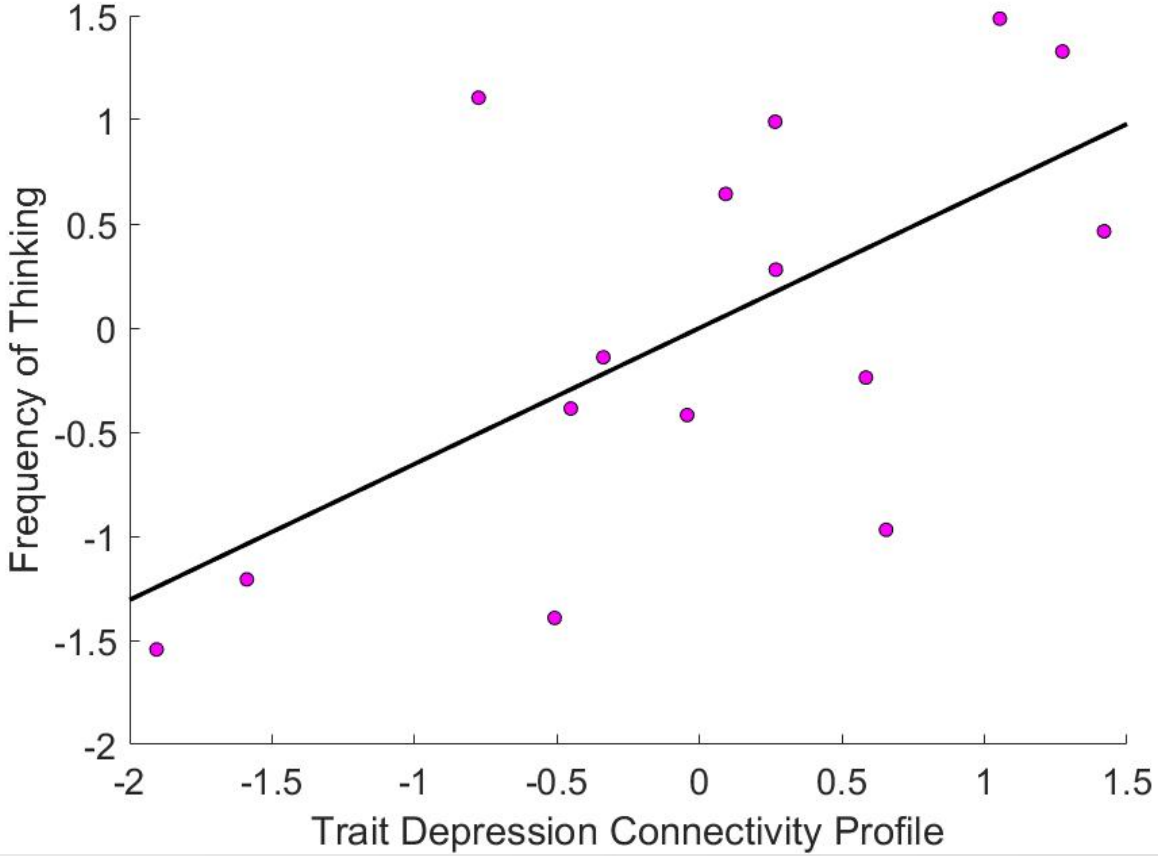


2. There are reliable functional brain organization patterns typical of trait depression

Trait Depression Connectivity Profile
(Task-General)



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 (8 Task Conditions)

- 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

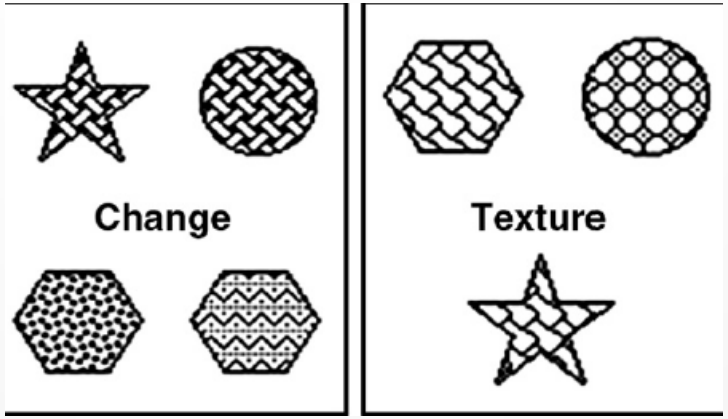
3. Brain-Behavior Associations

- 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

Relational Processing



Social Cognition

Story/Math

Aesop's fables

E.g., An eagle saves a man who had done him a favor.

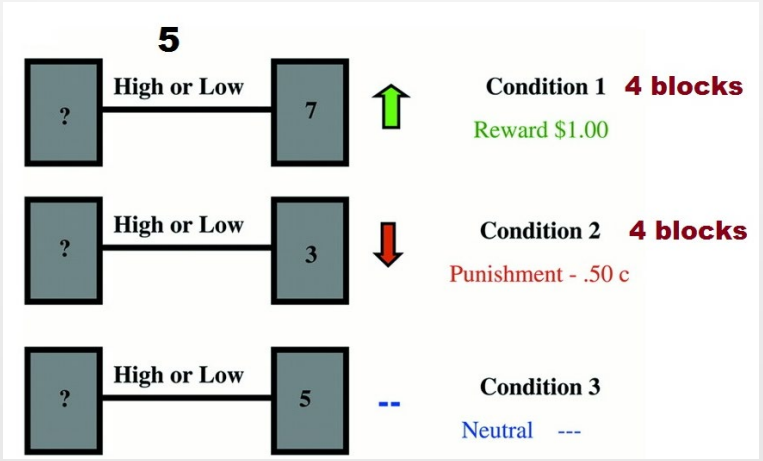
TEST: 'That was about revenge or reciprocity?'

Math

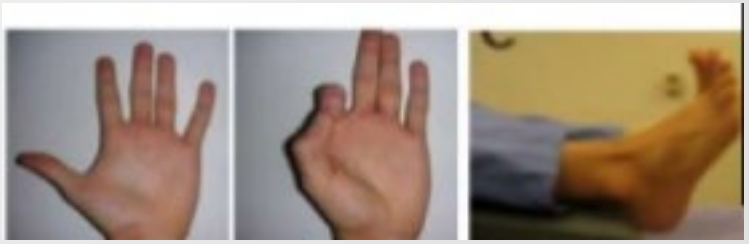
14 + 18 =

32 28

Incentive Processing

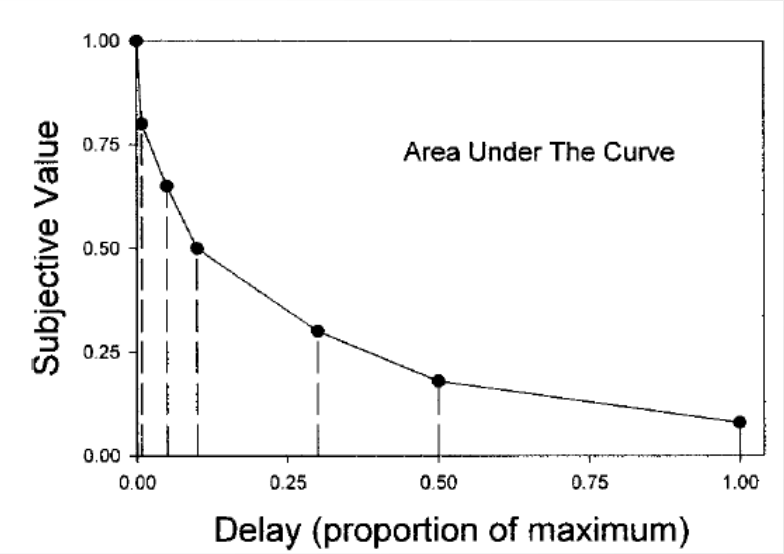


Motor Processing

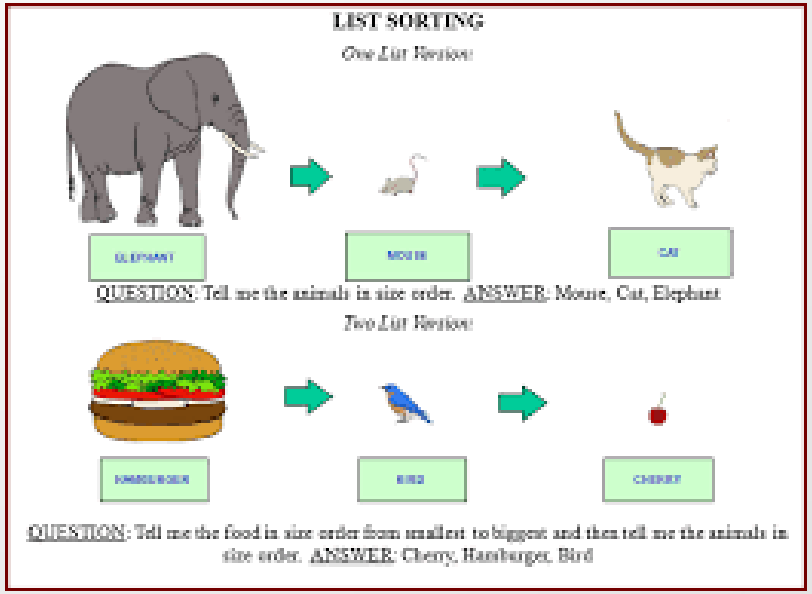


Part II : Cognitive Measures (out-of-scanner)

1. Affective Persistence: Reward Discounting Task



2. Visuospatial Learning: NIH Toolbox List Sorting Test



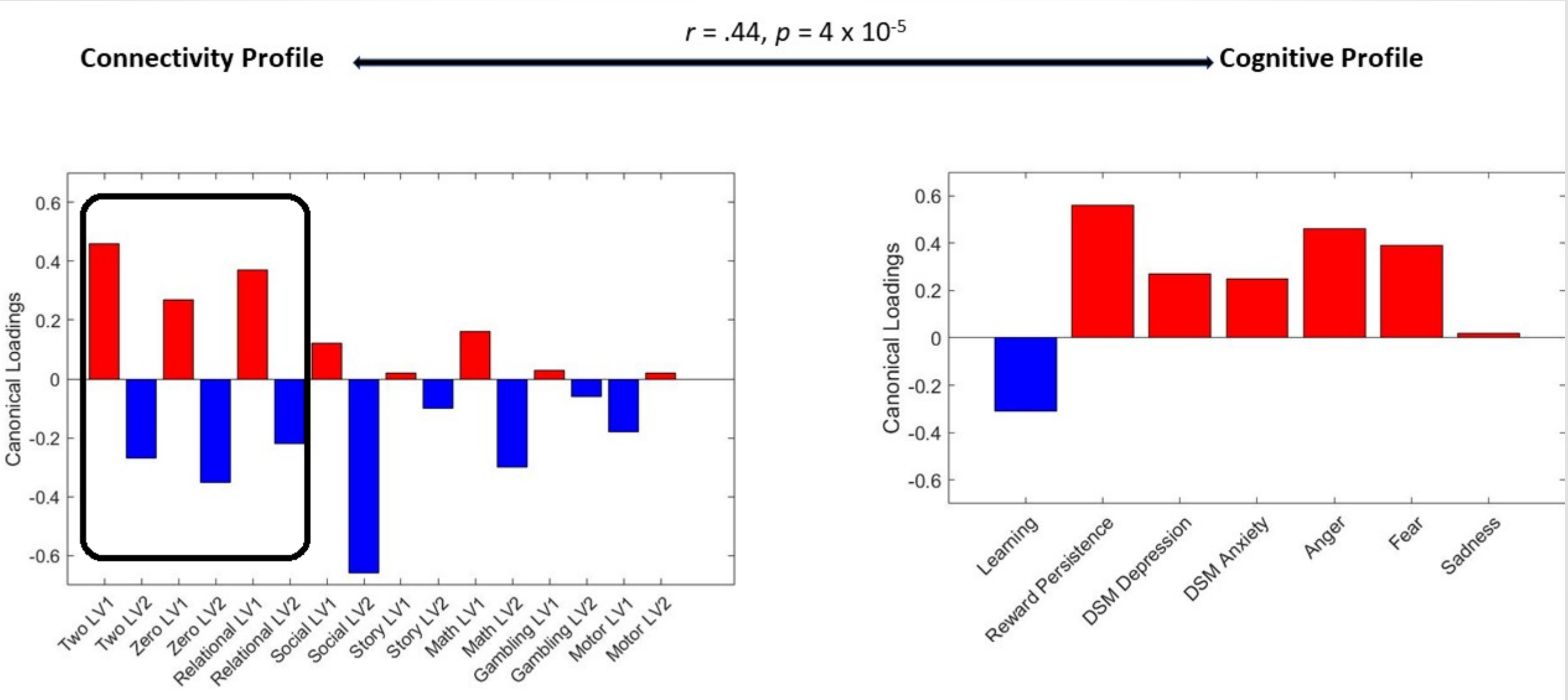
(Estle, Green, Myerson, & Holt, 2006; Green et al., 2007; Myerson, Green, & Warusawitharana, 2001)

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



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)

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Thank you!

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HUMAN Connectome PROJECT

Baycrest
Rotman Research Institute