Defining Cognitive-Affective Subgroups in Major Depressive and Bipolar Spectrum Disorders

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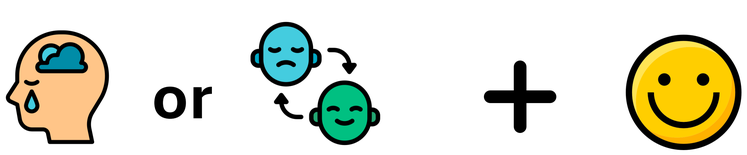
Background

- Alterations in cognitive-affective processes such as reward sensitivity and self-referential. processing are potential treatment targets in Major Depressive Disorder (MDD) and Bipolar Spectrum Disorders (BSD).
- Little is known about heterogeneity in these processes.
- **AIM:** Identify and characterize data-driven subgroups of cognitive-affective processing among acutely depressed individuals with MDD and BSD.

Methods

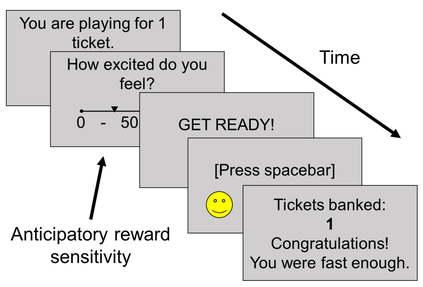
Moderate-to-severely depressed adults with:

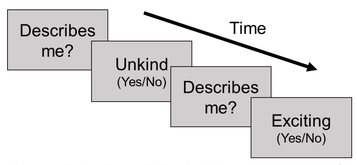


MDD	BSD	Healthy Controls [HC]
(n = 65, M_{age} = 40.7)	(n = 19, M_{age} = 34.5)	(n = 25, M_{age} = 38.1)

completed tasks of:

reward processing + *self-referential processing*





Immediate Recall Task: "Now tell me all of the words you can remember."

$$Self\text{-}Referent\ Memory\ Bias = \frac{(No.\ of\ negative\ traits\ endorsed\ and\ recalled)}{(Total\ no.\ of\ traits\ endorsed\ and\ recalled)}$$

- Participants also completed: Mini International Neuropsychiatry Interview (MINI, clinical interview) & Montgomery-Asberg Depression Rating Scale (MADRS, depressive symptom severity).
- K-means clustering was used to characterize subgroups based on task performance. Gap statistic and silhouette analysis was used to determine optimal cluster size.
- ANOVA & chi-squared was used to examine differences between clusters on basic demographic and clinical variables.

Results

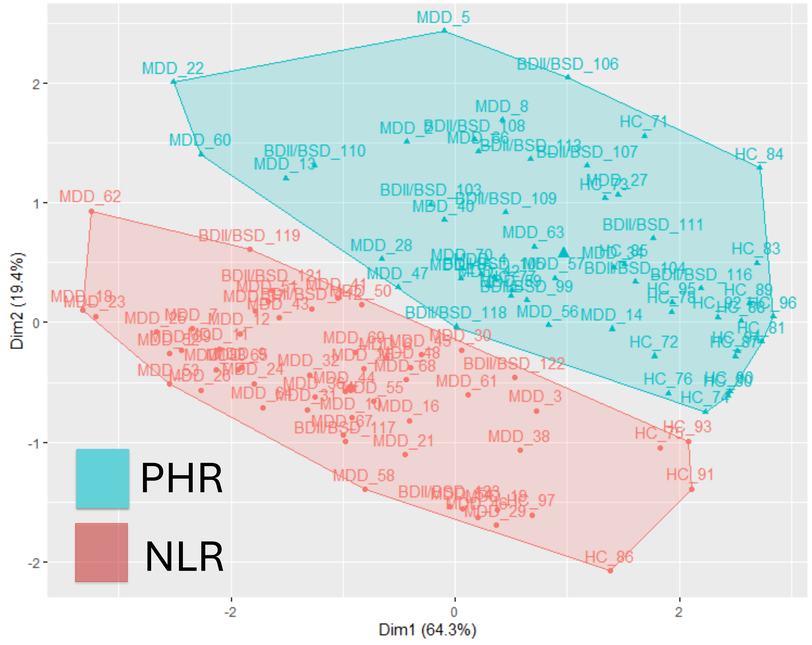
Gap statistics & silhouette analysis revealed a k = 2 cluster solution:

Negative Low Rewarder (NLR) n = 56

Positive High Rewarder (PHR) n = 53

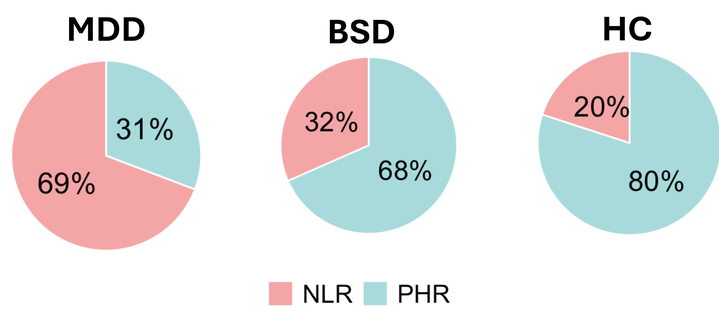
- Sig. lower reward anticipation (p <.001), positive encoding (p <.001) in NLR vs PHR.
- Sig higher negative encoding (p =.002), negative memory bias (p <.001) in NLR vs PHR.

Cluster Plot



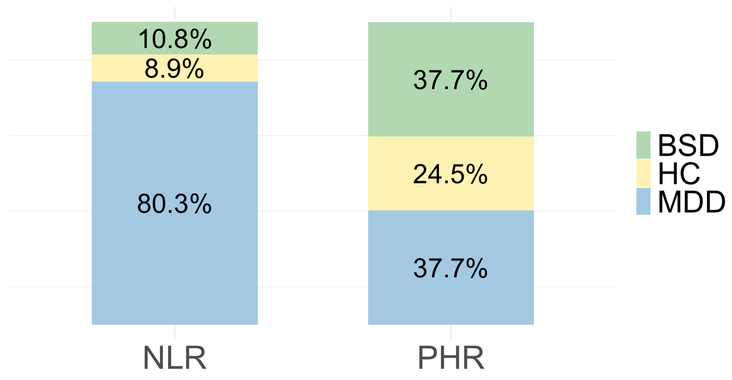
- NLR > PHR in MADRS "inability to feel" (*p* = .009) and "reported sadness" (*p* = .007).
- There were **no significant differences** between the clusters on:
  - Basic demographic variables: age (*F* = .597, *p* = .442), education (*F* = .238, *p* = .628), and gender (χ^2 = .745, *p* = .388).
  - Clinical variables: total symptom severity, comorbid anxiety disorder and suicidality.

Cluster Belonging by Diagnosis



- 31% of all participants with MDD performed similarly to most HCs and were classified as PHRs.
- Significantly more individuals with MDD were classified as NLRs vs. PHRs (χ^2 = 9.62, *p* = .002).
- Most HCs were PHRs (χ^2 = 9.00, *p* = .003)
- For BSD participants, there was no significant difference in proportion of NLRs vs. PHRs (χ^2 = 2.58, *p* = .003).

Diagnostic Classification by Cluster



Conclusions

- 2 cognitive-affective processing clusters were identified representing variation in reward sensitivity and self-referential encoding.
- Participants from all diagnostic categories are represented in both clusters.
- Personalized therapies might target specific alterations in cognitive-affective processes.

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