Neuroimaging-Based Profiling Identifies Distinct Transdiagnostic Subtypes of Youth with Mood and Anxiety Disorders at the Transition to Adolescence

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INTRODUCTION

- Clinical overlap between mood and anxiety disorders is pronounced in youth.¹
- Research into the neurobiological correlates of mood and anxiety disorders has identified transdiagnostic neuroimaging and genetic features.²
- Research effort has shifted towards new approaches that use data-driven methods to identify subgroups of individuals with mood and anxiety disorders based on their shared biological properties. This approach has yielded promising findings in adults.³

WORKING HYPOTHESIS

Pre-adolescents with mood and anxiety disorders can be partitioned into data-driven biologically informative subtypes based on neuroimaging features.

METHODS

Sample from the ABCD study⁴ (N=4,754; 53% female)

- Neuroimaging measures include:
  1. Cortical Thickness (CT)
  2. Cortical Surface Area (CSA)
  3. Subcortical Volume (SV)
  4. Gray/White Matter Contrast (GWC)
  5. Cortical Neurite Density (Cort-ND)
  6. Subcortical Neurite Density (Subc-ND)

- HYDRA (https://github.com/evarol/HYDRA) was applied to neuroimaging measures to identify homogenous clusters (i.e., subtypes).⁵

- Optimal cluster solution was chosen following 5-fold cross-validation based on the Adjusted Rand Index (ARI).

- Each subtype was compared to the typically developing (TD) group in terms of:
  1. Neuroimaging features at PFDR<0.005; psychopathology and cognition measures; prenatal and obstetric history; parental socioeconomic status and psychopathology; exposure to adverse life events and quality of family; school and neighbourhood environment at PFDR<0.005.⁶,⁷

RESULTS

- Each subtype showed a different brain maturational profile relative to the typically developing (TD) group:
  1. Subtype 1 showed a pattern of advanced brain maturation;
  2. Subtype 2 showed a pattern of delayed brain maturation;
  3. Subtype 3 showed an atypical brain maturational pattern.

  ① Exposure to adverse life events, family conflict and parental psychopathology were higher for all subtypes compared to TD.
  ② Subtype 1 had higher socioeconomic status and higher cognition measures.
  ③ Subtype 2 had greater socioeconomic adversity and lower cognition measures compared to TD and subtype 1 but not subtype 3.
  ④ Subtype 3 had the highest levels of adversity compared to other subtypes and TD across multiple domains of family and neighborhood socioeconomic disadvantage, exposure to maternal drug/alcohol use during pregnancy, and lower cognition measures.

CONCLUSIONS

- Pre-adolescents with mood and anxiety symptoms are heterogeneous at the neuroanatomical level.
- The identified subtypes transcended clinical diagnostic boundaries reinforcing the importance of redefining diagnostic approaches.

REFERENCE