Medical Xpress

New approach can help detect, predict mental health symptoms in adolescents by analyzing brain-environment interactions

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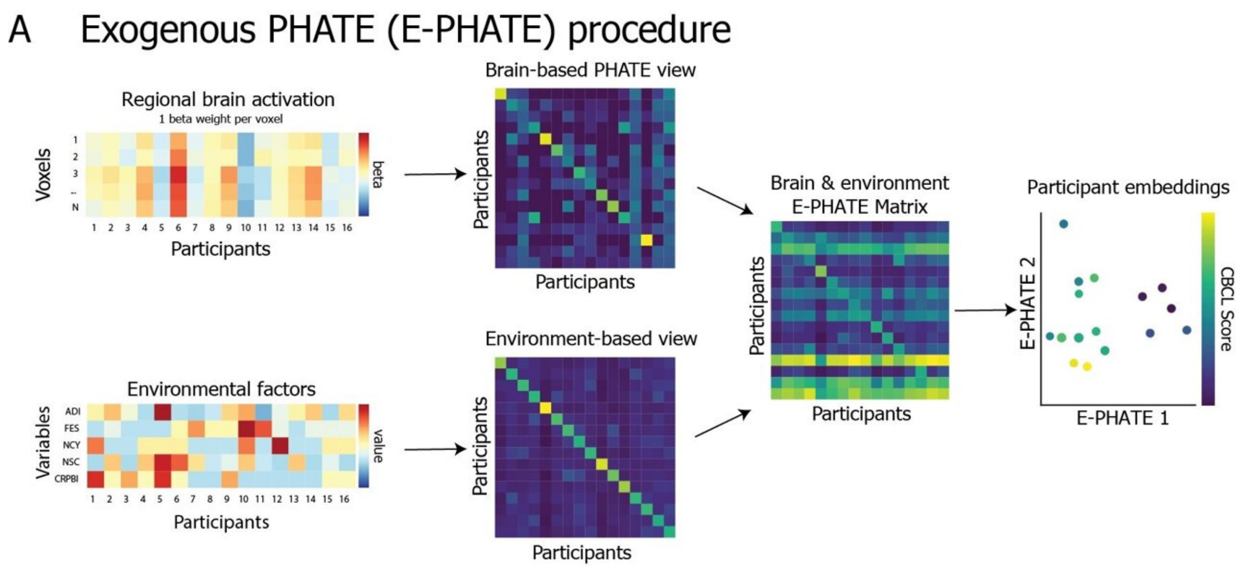

In this schematic, the first view of E-PHATE takes as inputs a vector of brain activation for each participant and computes a PHATE-based affinity matrix. The second view takes a vector of environment scores for each of those participants and builds an environment-based affinity matrix. These two views are combined into the E-PHATE diffusion matrix, which now captures both brain and environmental relations among participants and can be embedded into lower dimensions for visualization. Here, participants' coordinates in E-PHATE dimensions visually reflect individual differences along externalizing problem scores. Credit: *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*

The majority of mental health disorders manifest during adolescence and relate to a multiple interplay of neurobiological and environmental factors. Instead of considering these factors in isolation, a newly developed manifold learning technique can model brain–environmental interactions, which vastly improves detection of existing mental health symptoms and prediction of future ones compared to current methods.

The study in *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* underscores the importance of considering the adolescent brain in conjunction with the environment in which it develops.

There is an increasing need to build more complex, yet nuanced, models of human biology and behavior, particularly as they relate to the development of mental health symptoms. Despite the importance of this problem, most work still considers the brain and environment in isolation or as univariate and linear interactions.

May I. Conley, MS, MPhil, Ph.D. candidate, Yale University, Department of Psychology, co-lead author of the study says, "For a long time, developmental scientists have faced the challenge of testing theories that in many ways are hiding in plain sight. From the neighborhood to the family, we recognize youth's experiences in their environments and neurobiology both influence emotional and behavioral development. Yet, we haven't had methods that capture the complexity of this interaction precisely."

To address this, the investigators turned to manifold learning, a promising class of algorithms for uncovering latent structure from high-dimensional biomedical data like functional magnetic resonance imaging (fMRI). They developed the exogenous PHATE (E-PHATE) algorithm to model brain–environment interactions. Using the Adolescent Brain and Cognitive Development (ABCD) dataset, they used E-PHATE embeddings of participants' brain activation during emotional and cognitive processing to predict individual differences in cognition and emotional and behavioral symptoms, both cross-sectionally and longitudinally.

One of the most noteworthy findings of the study was the effect of combining additional environmental variables into the exogenous view of E-PHATE. Researchers saw a greater correlation of brain activity with mental health symptoms through modeling either the neighborhood or familial environments in E-PHATE, but by combining those metrics along with others, the model kept improving its representation. This was specific to adding environmental information, though, rather than an effect of the number of variables (which was tested with additional analyses). This finding reinforces the need to consider the multiple environments youth navigate in conjunction with how their brain takes in information from those environments.

Erica L. Busch, MS, MPhil, Ph.D. candidate, Yale University, Department of Psychology, first author of the study, continues, "I was excited to see that the principles of modeling neuroimaging data I'd been developing for basic science questions could be quickly adapted for clinical applications and yielded such striking results and mechanistic insights. It also underscored how fruitful interdisciplinary collaborations can be; my fellow graduate student May Conley and her advisor Dr. Baskin-Sommers are experts in biopsychosocial models of mental health symptoms, and combined with my computational experience, we each played key roles in defining the question and approaches of this project."

The work highlights the clinical applications of new machine learning and signal processing approaches. Specifically, it underscores the significance and complexity of the relationship between adolescent brains and environments as they relate to emotional and behavioral symptoms. The investigators present a general-purpose method with broad applications in both clinical and non-clinical domains.

Editor-in-Chief of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* Cameron S. Carter, MD, University of California Irvine, comments, "Decades of developmental work suggests that both neurobiology and environmental context shape the development of mental health symptoms. This study demonstrates the suitability of more computational methods, like manifold learning, for modeling complex multimodal developmental data, and they have great potential to enhance research on the neurobiology of emotional and behavioral symptoms in adolescents."

The current study is novel along three main dimensions:

1. By characterizing both neural and environmental data as multivariate measurements.
2. By considering the interaction between them as nonlinear and lower-dimensional (i.e., existing along a latent manifold, like most real-world data does).
3. By allowing for simultaneous hypothesis- and data-driven discovery of a meaningful representation of these signals.

Senior author Arielle Baskin-Sommers, Ph.D., Yale University, Department of Psychology, concludes, "It is important that as a field, we improve our ability to capture the complex transactions between the person and their environment. However, to estimate these transactions, new methods are needed to handle multiple types of data and estimate their interactions within individuals. The method produced from this interdisciplinary collaboration is one example of how we can estimate these complex transactions."

More information: Erica L. Busch et al, Manifold learning uncovers nonlinear interactions between the adolescent brain and environment that predict emotional and behavioral problems, *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging* (2024). DOI:

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