

Setting the stage from diagnoses to dimensions

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The case-control method, where researchers compare patients with a particular disease to healthy control participants, has increased understanding of disease-related effects at a group level. However, psychiatric pathology complicates assumptions of the method – that the illness can be defined and that patients cleanly fit the definition. Although psychiatry has characterized different diagnoses, patients within a diagnosis vary widely and symptoms often overlap diagnostic labels.

To address this issue, the National Institute of Mental Health recently developed the Research Domain Criteria (RDoC), a new framework to move away from diagnostic categories in favor of linking symptom domains with biological systems. However, without a practical way to implement the criteria, psychiatric research studies continue to fit patients into predefined categories.

In a new study published in *Biological Psychiatry*, Andre Marquand, PhD, of the Donders Institute for Brain, Cognition and Behaviour in The Netherlands, and colleagues establish a new framework for studying psychiatric pathology without losing the heterogeneity of patients.

"In contrast to virtually all existing approaches, our approach does not require partitioning the cohort into groups," said Marquand, explaining that it instead aims to chart variation across the entire population. They achieve this by mapping the relationship between biology and behavior in each participant.

Because variation associated with disease often overlaps normal variation, the new framework offers a way to map healthy variation and determine where a patient falls on that continuum. According to Marquand, this approach is similar to the way normative growth charts are used to map child development.

The researchers demonstrated their approach by mapping variation in the relationship between trait impulsivity and reward-related brain behavior, which targets core features of many psychiatric disorders, in 491 healthy participants. The analysis not only identified participants that deviated from the rest of the group, but could infer how each individual differed.

"This study exemplifies the power of understanding the range of normal variation when attempting to characterize psychiatric pathology," said John Krystal, Editor of *Biological Psychiatry*.

"This approach enables us to move beyond the case–control framework and make statistical inferences in a way that matches the clinical view: where diseases in individual [patients](#) are recognized as deviations from a healthy pattern of functioning," said Marquand. The researchers believe this new approach will become an instrumental tool to understand individual variation in many [psychiatric disorders](#).

More information: The article is "Understanding Heterogeneity in Clinical Cohorts Using Normative Models: Beyond Case-Control Studies," by Andre F. Marquand, Iead Rezek, Jan Buitelaar, and Christian F. Beckmann ([DOI: 10.1016/j.biopsych.2015.12.023](https://doi.org/10.1016/j.biopsych.2015.12.023)). It appears in *Biological Psychiatry*, volume 80, issue 7 (2016)

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