To: The Editor of Nature Genetics

Date: 19th December 2023

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Subject: Article submission

Dear Editors,

It is our pleasure to submit a research paper titled: “Isolating transdiagnostic effects reveals specific genetic profiles in psychiatric disorders.” for your consideration.

In this article, we isolate genetic effects that are shared across 11 major psychiatric disorders to gain further insight into genetic specificity and comorbidity over and above that contributed by transdiagnostic effects, unique to each psychiatric disorder.

Genetic studies have challenged the current classification of psychiatric disorders as distinct categorical diagnoses by revealing overlaps in their genetic architectures. The positive genetic manifold between diagnoses is consistent with the idea of a general factor of psychopathology that describes the propensity to developing all forms of psychopathologies. Isolating these transdiagnostic effects could better capture the specific genetic effects associated with each psychiatric disorder and provide a more precise understanding of disorder-specific biology.

Here, we isolated transdiagnostic genetic effects across 11 major psychiatric disorders from genetic effects specific to each psychiatric condition. We uncovered differences in the genetic architecture of each disorder and specific changes in tissue enrichment. The greatest shift we observed was in the genetic relationships between disorders, which changed substantially after considering transdiagnostic effects. Genetic effects associated with individual disorders also showed a greater degree of specificity in their genetic correlations with external biobehavioral traits, particularly health-related and psychological traits. By separating genetic influences into a shared and specific components, we provide novel insight into the genetic architecture, biology and comorbidity between psychiatric conditions that can inform future diagnostic classification and treatment research.

Sincerely,

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