The American Journal of Human Genetics, Volume *105*

Supplemental Data

Sex-Based Analysis of *De Novo* Variants in Neurodevelopmental Disorders

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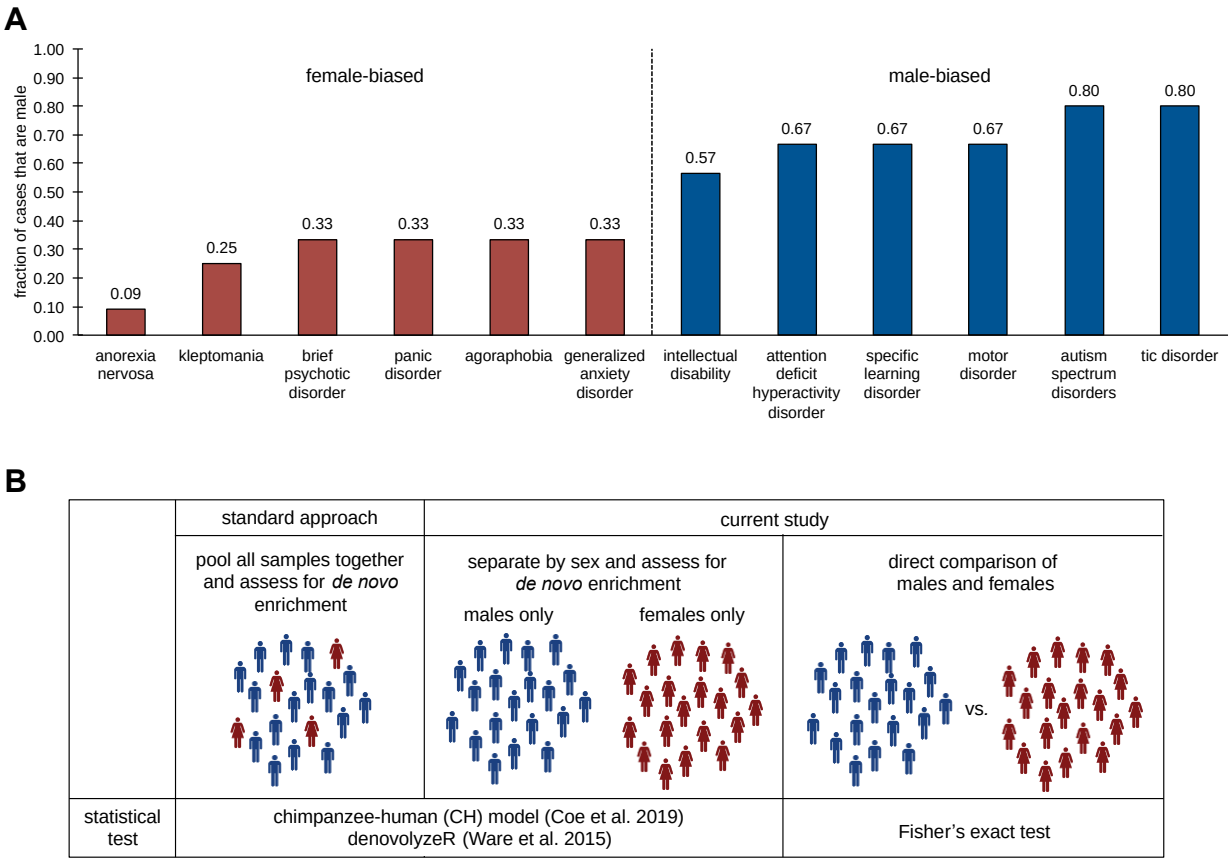
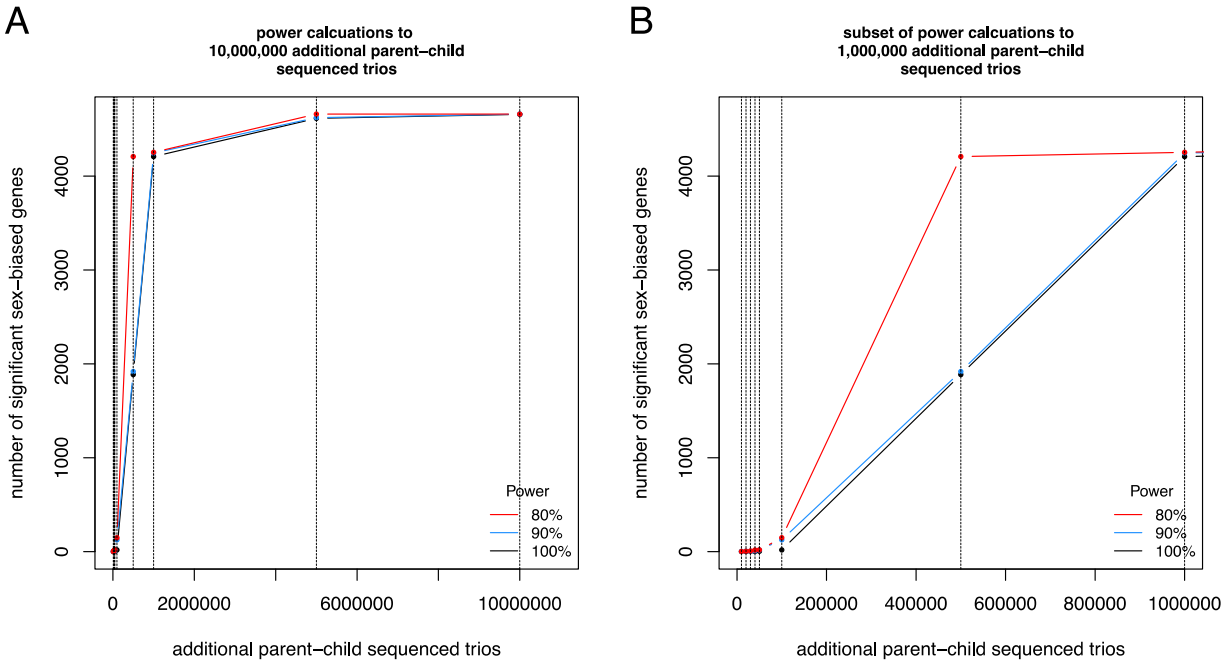
SUPPLEMENTAL FIGURES

Figure S1. Sex-biased neuropsychiatric disorders.



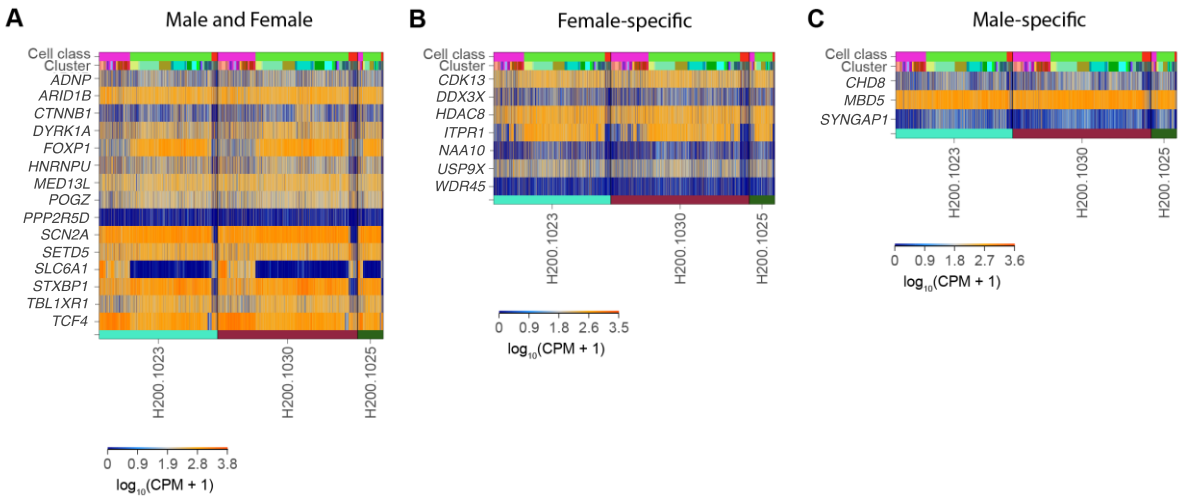
A) Disorders in the DSM with a known sex bias aggregated from "Understanding Mental Disorders, Your Guide to DSM-5 by the American Psychiatric Association." B) Standard study design for DNM enrichment contrasted with design employed in this study.

Figure S2. Power calculations for the male-versus-female test.



Power assessment using empirical DNM data from the discovery cohort. These estimates assume a 4:1 male-to-female ratio similar to ongoing large studies of autism and DD (e.g., SPARK). Large gains in sex-biased genes are predicted when cohort sizes reach ~50,000. Note in the gene counts *DDX3X* is included and already known to be significant at our current parent–child sequenced trio sizes. A) Results for all tests up to 10,000,000 additional parent–child sequenced trios and B) subset of the results (up to 1,000,000 additional parent–child sequenced trios) for ease of visibility. Vertical dotted lines occur at each of the data points.

Figure S3. Expression analysis.



Similar expression in cortical cell types from male and female donors. Heatmaps of log-transformed expression (CPM, counts per million) for NDD risk genes shared by males and females (A) and for female-specific (B) and male-specific (C) risk genes. Donor H200.1023 is female and donors H200.1030 and H200.1025 are male. Colored bars at top of heatmaps indicate cell class (inhibitory, pink; excitatory, green; non-neuronal, red) and cluster.