

Deadline March 31

- Summarize experience with NDD, ASD, ID, and epilepsy exome testing over a 5-year period.
- Assess what reported P/LP variants would/would not be captured on our current NeuroDev panel.
 - How this stratifies by REA, sex, and age at testing
- Report outcomes by trio/non-trio
- Evaluate specialty ordering trends by demographics and outcomes.

Exome cohort

-NDD NOS, epilepsy, ID, ASD

-2016-2021

Abstract (250-word maximum) structured.

Consider the Net You Cast: Multigene Panel Testing Misses 15% of Diagnostic Results Compared to Exome Sequencing

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OBJECTIVE:

Exome sequencing (ES) is recommended as a first-tier test for patients with a neurodevelopmental disorder (NDD), autism spectrum disorder (ASD), intellectual disability (ID), and epilepsy by professional organizations; however, multigene panel testing (MGPT) is still widely used. We assessed the probability that pathogenic/likely pathogenic (P/LP) variants reported in an ES cohort would have been detected on MGPT.

METHODS:

We analyzed data from individuals ≤ 21 years who underwent ES at a diagnostic laboratory between 2016-2021 for an indication of NDD, ASD, ID, or epilepsy. Report outcomes (positive, uncertain, negative) were assessed. For positive cases, genes with P/LP variants were compared to the laboratory's current MGPT offerings. Fisher's exact test was used for statistical analysis.

RESULTS:

Overall ES diagnostic yield was 25% (1046/4205). Trios comprised 77% of orders and resulted in a 30% increase in diagnostic yield (26% vs. 20%) and a 40% decrease in uncertain results (15% vs. 25%) compared to non-trio ES. Of positive cases, 15% (161/1046) would have had ≥ 1 P/LP variants missed if only MGPT was ordered. Overall, 29 patients had two diagnoses reported, and 59% (17/29) would have had one (n=13) or both (n=4) variants missed on MGPT alone. Individuals were more likely to have a variant missed by MGPT if they were male (p=0.026) or had a primary indication of ASD (p=0.006).

CONCLUSIONS:

We found 15% of ES patients would have had one or more P/LP missed by MGPT alone. Trios provide additional clarity for interpreting results and improve diagnostic yield while decreasing uncertain results.