

CONCURRENT PARENTAL ANALYSIS ON NEURODEVELOPMENTAL MULTI-GENE PANELS RESULTS IN FEWER VARIANTS OF UNKNOWN SIGNIFICANCE REPORTED

OBJECTIVE

The objective of this study was to evaluate the effectiveness of concurrent parental analysis at reducing the rate of variants of unknown significance (VUS) found on multi-gene panels (MGP) for patients with neurodevelopmental disorders.

METHODS

The results of the first 40 consecutive MGPs submitted to our laboratory with at least one parent provided for concurrent parental analysis (PA) were reviewed. Genetic variants identified were classified according to a 5-tier system using previously validated algorithms. Only VUS in autosomal dominant (AD) genes were routinely analyzed in PA as these were most likely to be informative. We compared the number of VUS identified before and after PA.

RESULTS

52.5% (21/40) of cases had VUS in AD genes and PA was informative in 28.6% (6/21) of cases. In these cases, a total of 27 VUS were identified in AD genes. 22.2% (6/27) of these were classified as likely benign (18.5%; 5/27) or likely pathogenic (3.7%; 1/27) based on PA of at least one parent. PA was informative in 33.3% (4/12) of VUS when both parents were provided compared to 13.3% (2/15) of VUS when only a single parent was provided. 14.3% (3/21) of cases resulted in completely positive (4.8%; 1/21) or completely negative (9.5%; 2/21) reports after PA.

CONCLUSION

Concurrent PA for MGPs for patients with neurodevelopmental disorders results in a decrease of VUS in AD genes in over 25% of cases, which results in less complicated and more informative initial reports for patients. PA is most beneficial when both parents are provided for concurrent analysis.