

The American Journal of Human Genetics, Volume 95

Supplemental Data

Cryptic and Complex Chromosomal Aberrations

in Early-Onset Neuropsychiatric Disorders

Harrison Brand, Vamsee Pillalamarri, Ryan Collins, Stacey Eggert, Colm O'Dushlaine, Ellen B. Braaten, Matthew Stone, Kimberly Chambert, Nathan D. Doty, Carrie Hanscom, Jill A. Rosenfeld, Hillary Ditmars, Jessica Blais, Ryan Mills, Charles Lee, James F. Gusella, Steven McCarroll, Jordan W. Smoller, Michael E. Talkowski, and Alysia E. Doyle

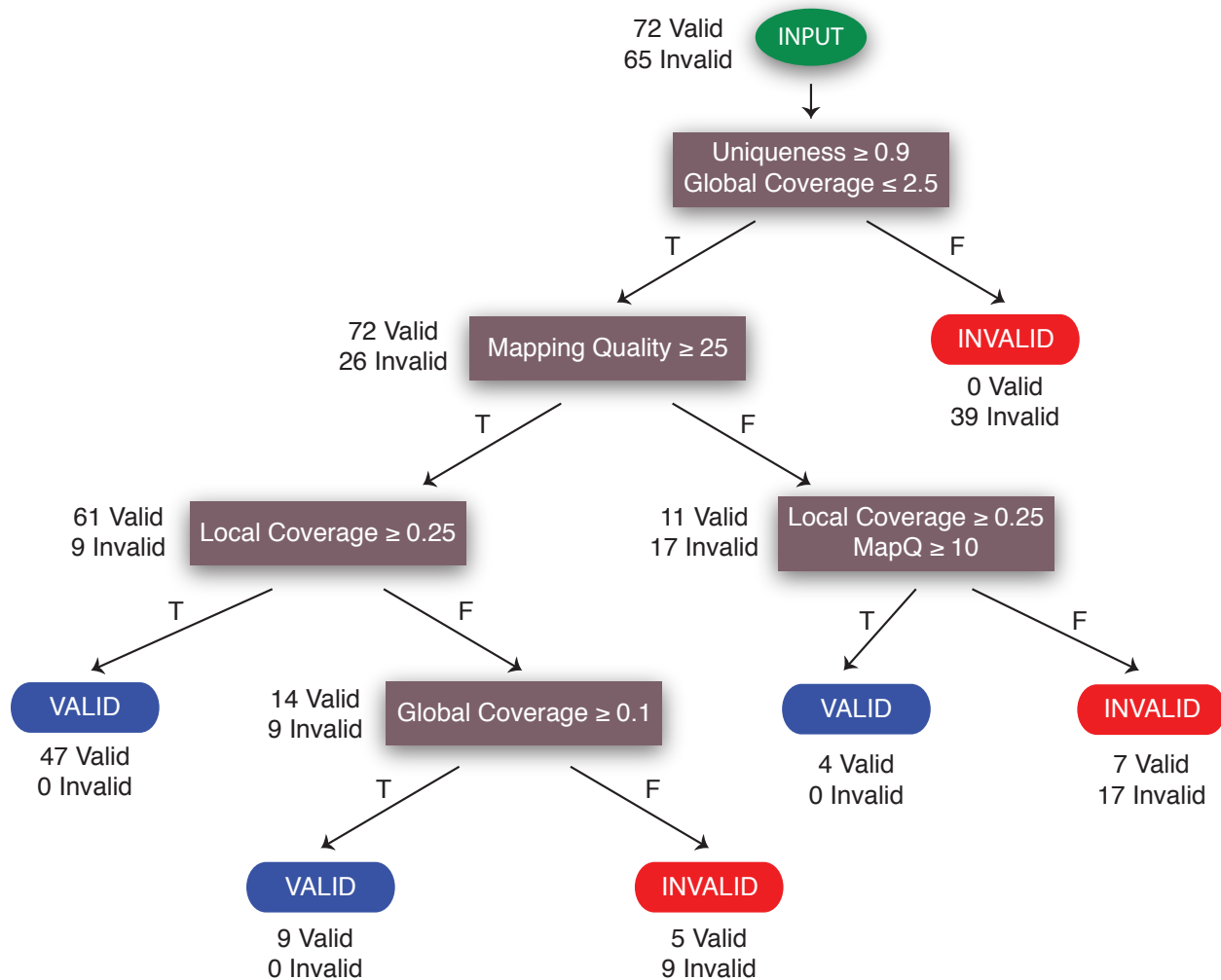


Figure S1. Classification algorithm. We implemented a decision tree classifier to predict high quality structural variation while mitigating false positive errors. We assessed seven metrics in each cluster as potential features for classification: 1) mapping quality, or average Phred-scaled aligner score across the reads within the cluster; 2) cluster uniqueness, or proportion of reads which mapped to unique positions; 3) local coverage, or ratio of cluster size to local insert coverage; 4) global coverage, or ratio of cluster size to the library's average haploid insert coverage; 5) span, or size of the regions spanned by the reads within the cluster, normalized by median library insert size; 6) GC content; and 7) mappability. GC content and mappability were both computed from their respective UCSC Genome Browser tracks as the average value within the regions spanned by the cluster. We compiled a set of training events ($n=137$), consisting of 72 valid events confirmed by Sanger sequencing and 65 invalid events which had previously failed Sanger validation, and computed these metrics across each cluster, retaining the four most discriminatory metrics for our classifier. Each branching point in the decision tree shows the number of valid and invalid training clusters which passed the previous filter.

Table S1. DSM –IV-TR diagnoses and other clinical features of the sample

Subject Characteristics	Total N=29 (%)
DSM-IV Diagnoses	
Autism Spectrum	
Autistic Disorder	1 (3.5)
Asperger's Syndrome	3 (10.3)
Pervasive Developmental Disorder NOS	7 (24.1)
Subclinical features of ASD	3 (10.3)
Mood Disorders	
Major Depressive Disorder	4 (13.8)
Bipolar Disorder	5 (17.2)
Mood Disorder NOS	6 (20.7)
Externalizing	
Attention-Deficit/Hyperactivity Disorder	18 (62.1)
Subclinical features of ADHD	3 (10.3)
Anxiety Disorders	
Generalized Anxiety Disorder	4 (13.8)
Obsessive Compulsive Disorder	1 (3.5)
Panic Disorder	0 (0)
Anxiety Disorder NOS	5 (17.2)
Psychosis	
Schizoaffective disorder	1 (3.5)
Psychotic symptoms	2 (6.9)
Intellectual/ Learning disorders	
Intellectual Disability	2 (6.9)
Borderline IQ	1 (3.5)
Language Disorder	1 (3.5)
Math Disorder	2 (6.9)
Reading Disorder	2 (6.9)
Numbers of full diagnoses	
One diagnosis	6 (20.7)
Two diagnoses	17 (58.6)
Three diagnoses	5 (17.2)
Four diagnoses	1 (3.5)
Past psychiatric hospitalization	
	11 (44.0)
Categories of illness	
Full psychiatric & autistic spectrum diagnoses	7 (24.1)
Full psychiatric diagnosis with autistic features	2 (6.9)
Psychiatric diagnosis only	16 (55.1)
Autistic spectrum diagnosis with learning disorder or ID	2 (6.9)
Autistic spectrum diagnosis with psychiatric features	1 (3.5)
Intellectual disability with psychiatric features	1 (3.5)