

Supplementary Table 2. The raw data of the tria-WES-based genetic results and related clinical manifestations and neurodevelopmental phenotypes of the 38 s-NDDs cases in external validation set-1.

Genetic results	Sex	Age(y)	GDD/ID severity	ASD	ADHD	EP	Comorbidity condition	ICA	BM	Ocular/visual dysfunctions	Ear anomalies/hearing loss
negative	F	3.00	mild-moderate	N	Y	N	single	N	Y	N	Y
negative	F	1.00	mild-moderate	N	N	Y	single	N	N	N	N
positive	F	1.00	mild-moderate	N	Y	Y	single	N	N	N	N
negative	M	5.00	mild-moderate	Y	Y	N	single	N	Y	N	N
negative	M	11.81	mild-moderate	N	Y	N	single	N	N	N	Y
negative	M	5.00	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	12.39	mild-moderate	N	N	Y	single	N	N	N	N
negative	F	3.12	mild-moderate	Y	Y	N	single	N	Y	N	N
negative	M	8.21	mild-moderate	N	N	Y	single	N	Y	N	N
negative	F	14.97	mild-moderate	Y	N	N	single	N	Y	N	N
negative	F	1.54	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	3.50	mild-moderate	N	Y	Y	single	N	N	N	N
negative	M	1.85	mild-moderate	Y	N	Y	single	N	N	N	N
negative	M	13.13	mild-moderate	N	N	Y	single	N	N	N	N
negative	F	6.27	mild-moderate	N	Y	Y	single	N	N	N	N
negative	M	6.82	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	2.81	mild-moderate	Y	N	Y	multiple	N	N	N	N
positive	F	2.29	mild-moderate	N	N	Y	multiple	N	Y	N	N
negative	F	14.68	mild-moderate	Y	N	N	single	Y	N	N	Y
positive	F	0.75	severe-profound	N	N	Y	single	N	N	N	N
negative	M	2.27	severe-profound	Y	N	N	single	N	N	N	N
negative	M	1.33	severe-profound	N	N	Y	single	N	Y	N	N
positive	M	3.28	severe-profound	Y	N	N	single	N	Y	N	N
positive	F	11.05	severe-profound	N	N	Y	multiple	N	N	N	N
positive	M	0.80	severe-profound	N	N	Y	multiple	N	N	N	N
positive	M	4.48	severe-profound	Y	N	N	single	Y	Y	N	N
positive	M	8.10	severe-profound	N	Y	N	single	Y	N	N	N
positive	M	0.52	severe-profound	N	N	Y	single	Y	Y	N	N
positive	F	4.98	severe-profound	Y	N	Y	single	Y	Y	N	N
positive	F	2.49	severe-profound	N	N	Y	single	Y	N	N	N
positive	F	7.48	severe-profound	Y	N	Y	single	Y	Y	N	N
positive	F	0.80	severe-profound	N	N	Y	multiple	Y	Y	N	N
positive	M	0.76	severe-profound	N	N	Y	multiple	Y	N	N	N
positive	F	10.95	severe-profound	Y	Y	N	multiple	Y	N	N	Y
positive	M	2.00	severe-profound	Y	N	N	multiple	Y	Y	N	N
positive	M	6.60	severe-profound	Y	N	Y	multiple	Y	N	N	N
positive	F	0.88	severe-profound	N	N	Y	multiple	Y	N	N	N
positive	M	13.58	severe-profound	N	N	Y	multiple	Y	N	N	N

Abbreviations: s-NDDs, severe developmental disorders; GDD/ID, global developmental delay/intellectual disability; ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity; EP, epilepsy; ICA, head circumference abnormality; BM, brain malformation. Note: (1) M, male; F, female. (2) "Y" means "obvious abnormality on the clinical assessment", "N" means "no abnormality on the clinical assessment". (3) "single" means "only existing one type of neurodevelopmental comorbidity (ASD or ADHD or EP) in s-NDDs individuals", "multiple" means "existing two or three types of neurodevelopmental comorbidity (ASD or ADHD or EP) in s-NDDs subjects". (4) "positive" means patients with pathogenic/likely pathogenic variants detected by tria-WES; "negative" means patients with benign/intermediate significance variants detected by tria-WES.

Supplementary Table 2: The raw data of the sex-WES-based genetic results and related clinical manifestations and neurodevelopmental phenotypes of the 97 s-NDDs patients in external validation set 2											
Genetic results	Sex	Age(y)	GDH ID severity	ASD	ADHD	EP	Comorbidity condition	HCA	BM	Ocular/visual dysfunction	Ear anomalies/hearing loss
positive	M	11.00	mild-moderate	N	N	Y	multiple	Y	N	N	N
negative	M	9.00	mild-moderate	Y	Y	N	single	N	N	N	N
positive	F	7.00	severe-profound	Y	Y	N	multiple	N	N	N	N
positive	F	2.50	severe-profound	Y	N	Y	single	Y	Y	N	N
negative	M	3.08	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	5.75	mild-moderate	N	N	Y	single	Y	N	N	N
positive	M	6.58	mild-moderate	Y	N	N	single	N	Y	Y	N
positive	M	6.50	mild-moderate	N	N	Y	single	Y	Y	N	N
negative	M	8.00	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	6.50	mild-moderate	N	N	Y	single	Y	Y	N	N
negative	M	2.17	mild-moderate	Y	N	N	single	Y	N	N	N
positive	M	6.08	severe-profound	Y	Y	Y	multiple	Y	Y	N	N
positive	M	3.5	severe-profound	Y	N	N	multiple	Y	N	N	N
positive	M	7	severe-profound	Y	Y	N	multiple	Y	N	N	N
negative	M	8	mild-moderate	Y	Y	N	multiple	N	N	N	N
negative	M	4.25	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	1.5	mild-moderate	N	Y	N	single	N	N	N	N
negative	F	2.08	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	8	mild-moderate	N	N	Y	single	N	N	N	N
negative	F	0.3	mild-moderate	N	N	Y	single	Y	N	N	N
negative	F	5	mild-moderate	N	Y	N	single	N	N	N	N
positive	F	3.5	severe-profound	Y	N	N	single	Y	Y	N	N
negative	M	8	mild-moderate	N	Y	N	single	N	N	N	N
negative	F	6.5	mild-moderate	N	N	Y	single	N	Y	N	N
positive	M	12.00	severe-profound	Y	N	Y	single	N	Y	N	Y
positive	F	10.00	mild-moderate	Y	N	Y	multiple	N	N	N	N
positive	F	9.00	severe-profound	Y	N	N	single	N	Y	N	Y
positive	F	1.17	severe-profound	N	N	Y	single	N	Y	N	N
positive	F	6.50	severe-profound	Y	Y	N	multiple	N	N	N	N
negative	M	11	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	5.75	mild-moderate	N	N	Y	single	N	Y	N	N
negative	M	1.17	mild-moderate	N	N	Y	single	N	N	N	N
positive	M	7	severe-profound	Y	N	N	single	N	N	N	N
negative	M	3.50	mild-moderate	Y	N	N	single	N	N	N	N
positive	M	5.08	severe-profound	Y	N	Y	multiple	Y	N	Y	N
negative	M	3.83	mild-moderate	N	N	Y	single	N	Y	N	Y
negative	F	1.25	mild-moderate	N	N	Y	single	N	Y	N	N
negative	M	2.83	mild-moderate	N	N	Y	single	N	Y	N	N
positive	M	1.50	severe-profound	Y	N	Y	single	Y	Y	N	N
positive	F	2.83	severe-profound	Y	N	Y	multiple	Y	Y	N	N
positive	M	2.83	severe-profound	Y	Y	N	multiple	Y	Y	N	Y
positive	M	2.00	severe-profound	Y	Y	N	multiple	Y	N	N	N
negative	F	1.00	mild-moderate	N	Y	N	single	N	N	N	N
positive	M	5.92	severe-profound	Y	N	Y	multiple	Y	Y	N	N
negative	M	1.92	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	1.92	mild-moderate	N	Y	N	single	N	N	N	N
positive	F	10.00	severe-profound	N	Y	N	single	N	Y	N	N
negative	M	13	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	6.75	mild-moderate	N	Y	N	single	N	N	N	N
negative	F	10	mild-moderate	N	N	N	single	N	N	N	N
positive	H	7.25	severe-profound	Y	N	N	multiple	N	N	N	N
positive	F	4.42	severe-profound	Y	Y	N	multiple	Y	N	Y	N
positive	M	7.25	severe-profound	Y	Y	N	multiple	Y	N	Y	N
positive	H	2.00	severe-profound	Y	Y	N	multiple	N	N	N	N
positive	H	4.83	severe-profound	Y	N	Y	multiple	N	N	N	N
positive	H	6.00	severe-profound	Y	Y	Y	multiple	N	Y	Y	N
negative	H	3.50	mild-moderate	Y	N	N	single	N	N	N	N
positive	H	3.83	severe-profound	Y	Y	N	multiple	N	N	Y	N
positive	H	3.25	mild-moderate	Y	Y	N	multiple	Y	Y	N	N
positive	H	5.00	severe-profound	Y	N	Y	multiple	N	N	N	N
negative	H	5.33	mild-moderate	Y	Y	N	multiple	N	N	N	N
negative	F	5.17	severe-profound	Y	N	N	single	N	N	N	N
negative	M	3.5	mild-moderate	Y	N	N	single	N	N	N	N
negative	F	7.58	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	3.67	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	3.42	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	3.5	mild-moderate	Y	N	N	single	N	N	Y	N
negative	M	4.25	mild-moderate	Y	N	N	single	N	N	Y	Y
negative	M	6.75	mild-moderate	Y	Y	N	multiple	N	N	N	N
negative	M	14.5	mild-moderate	Y	Y	N	multiple	N	N	N	N
negative	H	3.42	severe-profound	Y	N	N	single	N	N	N	Y
positive	M	4.83	severe-profound	Y	N	Y	multiple	N	Y	N	Y
negative	F	3.92	mild-moderate	Y	N	N	single	N	N	Y	N
negative	M	5.17	mild-moderate	Y	N	N	single	N	N	N	N
negative	M	4.17	mild-moderate	Y	N	N	single	N	N	N	N
positive	F	4.17	severe-profound	Y	N	N	single	Y	Y	N	Y
positive	F	1.5	severe-profound	Y	N	N	single	Y	Y	N	N
negative	F	3.67	mild-moderate	Y	N	N	single	N	N	N	N
positive	F	7	severe-profound	N	N	Y	multiple	Y	Y	N	N
negative	M	5.08	mild-moderate	N	Y	N	single	N	N	N	N
negative	M	1.67	mild-moderate	N	N	Y	single	N	N	N	N
negative	M	6.08	mild-moderate	N	Y	N	single	Y	N	N	N
negative	M	10	mild-moderate	N	Y	N	single	N	N	N	N
negative	M	1.7	mild-moderate	N	Y	N	single	N	N	N	Y
negative	M	4	negative	Y	N	Y	single	N	Y	N	N
positive	F	4.00	mild-moderate	Y	N	N	single	N	N	N	N
positive	F	1.66	mild-moderate	N	N	Y	single	N	Y	N	N
negative	M	2.83	mild-moderate	Y	Y	N	single	N	N	N	N
positive	M	4.33	severe-profound	N	N	Y	single	N	N	N	N
positive	M	3.33	mild-moderate	Y	N	N	single	N	Y	N	N
negative	F	3.00	mild-moderate	Y	N	N	single	N	Y	N	N
positive	M	4.58	severe-profound	N	Y	N	single	N	N	N	N
negative	M	3.25	mild-moderate	Y	N	N	single	N	Y	N	N
negative	F	1.56	mild-moderate	N	N	Y	single	N	Y	N	N
positive	M	6.00	mild-moderate	Y	Y	N	single	N	Y	N	N
negative	M	4.92	mild-moderate	N	N	N	single	N	N	N	N
negative	M	5.00	mild-moderate	Y	Y	N	multiple	N	N	N	N

Abbreviations: s-NDDs= syndromic neurodevelopmental disorder; GDH ID, global developmental delay/intellectual disability; ASD, autism spectrum disorder; ADHD, attention deficit hyperactivity; EP, epilepsy; HCA, hand circumference abnormality; BM, brain malformation; Note: (1) M, male; F, female; (2) "Y" means "abnormality on this clinical assessment"; "N" means "no abnormality on this clinical assessment"; (3) "single" means "only coexisting one type of neurodevelopmental comorbidity (ASD or ADHD or EP) in s-NDDs individuals"; "multiple" means "coexisting two or three types of neurodevelopmental comorbidity (ASD or ADHD or EP) in s-NDDs individuals with pathogenic variants detected by sex-WES"; "negative" means patients with benign genetic significance variants detected by sex-WES.