

	Case 1	Case 2	
Clinical data			
Sex	Female	Female	
Age	8y	14y	
Birth	Term	Preterm, 28 wk	
Developmental Delay	Yes	Yes	
Intellectual Disability	Yes (profound)	Yes (moderate)	
Motor impairment	Yes	Yes	
GMFCS level	V	II	
Epilepsy	Yes	No	
Microcephaly	Yes	Yes	
Occipital plagiocephaly	Yes	Yes	
Dysmorphic features	Yes	Yes	
Ocular manifestations	Nystagmus	Strabismus	
Other	Facial asymmetry	Scoliosis, hemifacial microsomia	
Brain imaging	Cerebellar atrophy	Cerebellar, pons hypoplasia Mild ventriculomegaly	
Genomic data			Case 3*
Genomic coordinates	chr11:62677434	chr11:62677299	chr11:62677944
Transcripts and variant (cDNA and protein)	(NM_000738.3):c.1139C>T (p.Pro380Leu)	(NM_000738.3):c.1274T>C (p.Phe425Ser)	(NM_000738.3):c.629G>T (p.Arg210Leu)
SIFT 4G (ref)	Damaging (0)	Damaging (0)	Damaging (0.011)
PolyPhen-2 (ref)	Probably damaging (1)	Probably damaging (0.998)	Possibly damaging (0.616)
Mutation Taster2 (ref)	Disease causing (1)	Disease causing (0.9994)	Disease causing (0.9999)
ACMG	Likely pathogenic	Uncertain significance	Uncertain significance
CADD_PHRED v1.4 (ref)	27.6	28.3	24.4
gnomAD	NA	NA	NA
De novo occurrence	Yes	Yes	NA

GMFCS: Gross Motor Function Classification System. * Satterstrom et al., 2020.

Supplementary Table 1: Clinical and genetic features of three patients with CHRM1-related neurodevelopmental disorders.

Sift 4G: Vaser R, Adusumalli S, Leng SN, Sikic M, Ng PC. SIFT missense predictions for genomes. Nat Protoc. 2016 Jan;11(1):1-9. <https://sift.bii.a-star.edu.sg/>

Polyphen-2: Adzhubei IA, Schmidt S, Peshkin L, Ramensky VE, Gerasimova A, Bork P, Kondrashov AS, Sunyaev SR. Nat Methods 7(4):248-249 (2010). <http://genetics.bwh.harvard.edu/pph2/>

Mutation taster2: Schwarz JM, Cooper DN, Schuelke M, Seelow D. MutationTaster2: mutation prediction for the deep-sequencing age. Nat Methods. 2014 Apr;11(4):361-2. <http://www.mutationtaster.org>

CADD: Rentzsch P, Witten D, Cooper GM, Shendure J, Kircher M. CADD: predicting the deleteriousness of variants throughout the human genome. Nucleic Acids Res. 2018 Oct 29. <https://cadd.gs.washington.edu/>