Individual	1	2	3	4	5	6	7	8	9	10	11	12	13	14 (brother of 15)	15 (brother of 14)	16	17	18
Age at last visit (years), sex	3.8, f	1, m	9.3, m	4, m	16, f	12.5, m	13, m	2, f	8, m	3.8, m	1.6, m	13.5, m	3, m	7, m	9, m	7, m	10, m	5, f
Genetic variant	c.2051_2052dup p.(Glu685*)	c.2107G>T p.(Glu703*)	c.3034C>T p.(Gln1012*)	c.4279C>T p.(Gln1427*)	c.65del p.(Gly22Valfs*7)	c.1099_1103dupCAGTT p.(Glu369Serfs*25)	c.1646_1650del p.(Ile549Argfs*6)	c.2164_2167del p.(Lys722Valfs*17)	c.2714dup p.(Met906Tyrfs*15)	c.4829dup p.(Leu1610Phefs*259)	c.5054dup p.(Pro1686Serfs*183)	c.183_186+2del p.?	c.264A>G p.(Glu88=)	c.768+1G>A p.?	c.768+1G>A p.?	c.2848-2A>C p.?	arr[hg19] 7q22.3(104,696,686-105,407,628)x1	arr[hg19] 7q22.3(104,730,300-104,791,108)x1
Inheritance	dn	dn	dn	dn	n/a*	paternal	dn	dn	dn	dn	dn	dn	dn	paternal	paternal	n/a*	dn	dn
Dysmorphic features																		
Macrocephaly (Z>2.0)	+	+	+	+	+	-	+	-	-	+	+	-	-	-	-	-	+, in infancy	+
→ OFC Z-Score at last visit	+3.0	n/a	+2.7	+3.3	n/a	+1.0	+2.5	+1.2	n/a	+3.5	n/a	n/a	n/a	+0.9	-0.3	n/a	+1.8	n/a
Dolichocephaly	-	-	-	-	-	-	-	+	n/a	-	+	-	-	-	-	-	-	-
Large forehead	+	-	+	+	+	-	+	+	n/a	+	+	-	-	-	-	-	+	+
Epicanthal folds	+	+	+	+	-	-	-	-	n/a	-	+	-	-	-	+	-	-	+
Deep-set eyes	+	-	+	-	+	-	+	-	n/a	+	-	-	-	-	-	+	+/ -	-
Prominent nasolabial folds	-	-	-	-	+	-	-	+	n/a	-	+	-	-	-	-	-	-	-
Full cheeks	+	-	+	-	+	-	-	+	n/a	+	+	-	-	-	+	+	+	-
Small ears	+	-	-	-	+	-	+	-	n/a	-	-	-	-	+	-	-	-	-
Finger/toe clinodactyly	+	-	+	-	+	-	-	n/a	-	-	-	-	-	+	-	-	-	-
Neurodevelopmental features																		
Developmental motor delay	+	+	-	+	+	+	+	+	+	+	+	-	-	-	-	+	+	+
→ Walking unsupported at	24 months	n/a	n/a	23 months	n/a	23 months	n/a	n/a	23 months	19 months	no walking so far	14 months	11 months	15-16 months	>12 months	23 months	n/a	18 months
Developmental speech delay	+ (after regression)	+	+	+ (after regression)	+	+	+	+	+	+	+	+	+	-	+	+	+	+
→ First words with	10 months	n/a	n/a	15 months	n/a	30 months	n/a	n/a	normal	24 months	n/a	18 months	no speech	n/a	n/a	no speech	n/a	45 months
Developmental regression	+	-	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Intellectual disability	n/a	+	-	+	n/a	+	+	n/a	-	-	n/a	+	-	-	-	n/a	+	n/a
→ IQ	n/a	n/a	n/a	n/a	n/a	n/a	69 (VIQ: 71, PIQ: 65)	n/a	n/a	83	n/a	n/a	n/a	high average IQ	n/a	n/a	VIQ: 71, PIQ: 63	n/a
Autism spectrum disorder	-	-	-	+	+	-	-	n/a	-	+	-	-	+	+	+	+	-	-
Pathological EEG	+	-	-	-	n/a	-	n/a	n/a	-	-	-	-	n/a	-	-	-	-	-
→ Epilepsy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
→ Febrile seizures	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-	+
Muscular hypotonia	+	-	-	+	+	-	-	+	-	+	+	-	-	-	-	+	-	+
Behavioral																		
ADHD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	+	-	-
Stereotypical behavior	-	-	-	+	+	-	-	+	-	+	-	-	-	+	-	+	-	-
Self-injurious behavior	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	+	-	-
Aggressive behavior	-	-	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Sleep disturbances	+	-	+	+	+	-	n/a	-	-	+	-	-	+, normal at 3y	-	-	+	+	-
Organ malformations																		
Corpus callosum hypoplasia	-	+	-	+	n/a	-	-	n/a	+	-	-	n/a	n/a	-	-	-	-	-
Ventriculomegaly	+	-	-	-	n/a	-	-	n/a	+	-	-	n/a	n/a	-	-	-	-	-
Reduced brain volume	+	-	-	-	n/a	-	-	n/a	-	-	-	n/a	n/a	-	-	-	-	-
Cerebral cysts	-	+	+	-	n/a	-	-	n/a	-	-	-	n/a	n/a	-	-	-	+	-
Delayed myelination	+	+	-	+	n/a	+	-	n/a	-	-	-	n/a	n/a	-	-	-	-	-
Gastrointestinal features																		
Constipation	+	+	+	+	-	+	-	+	+	-	-	+	-	-	-	-	-	-
Gastroesophageal reflux	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Vomiting	+	+	-	-	-	-	-	-	-	-	+	-	-	-	-	-	-	-
Other	Hyperalaninemia, borderline elevated serum lactate, strabismus	26wk premature, large VSD, ROP, recurrent ALTE/BRUE, multiple ependymal nodules and small pituitary on brain MRI	Aphasia, dysphasia, additional *MYH8* variant segregating with trismus-pseudocampto-dactyly in the family, central apnea, brachycephaly	Mild left eye strabismus, hypertelorism, polycythemia at birth. Additional *de novo* variant: *CHD8* c.3340G>T, p.(Glu1114*)	Diarrhea	Almost daily headaches	Mega cisterna magna, sensory integration disorder, verbal dyspraxia, high pain threshold	Congenitally adducted thumbs requiring splinting	Headaches, insensitivity to pain	Supernumerary nipple	Failure to thrive, recurrent respiratory infections, double hair whorl, ears posteriorly rotated, full lips	Brachymetacarpia, Brachymetatarsia. Anxiety disorder, selective mutism. High-arched palate, cutis marmorata. Obesity	None	Preauricular sinus on left ear, sinus at crus helix on right ear, pervasive developmental disorder, bleeding tendency, mild to moderate sensorineural hearing impairment (homozygous variant: *GJB2* c.109G>A, p.(Val37Ile))	Atypical autism, bleeding tendency	None	Everted lower lip, low-hanging columella, pervasive developmental disorder	Bilateral periventricular heterotopia, pachygyria

* The mother does not carry the variant, father unavailable for testing

n/a: not available, VIQ: Verbal IQ, PIQ: Performance IQ, VSD: ventricular septal defect, ROP: retinopathy of prematurity, ALTE/BRUE: apparent life-threatening event/brief resolved unexplained event