Supplementary Table S1 *SYNGAP1* patients reported in the literature

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
Kothur et al (2018)[83]	F, Unk.	6 mo	c.439C > T p.Gln147 Nonsense	De novo mutation No familiarity	MAbE	Myclonic absence	NA	NA	NA
Sabatini et al (2018)[80]	M, Unk.	2/3 y	c.3722_3723del; p. Leu1241Argfs*4 Premature stop codon	Complex unbalanced rearrangement involving chromosome 21 No familiarity		Myclonic seizures	EEG: NA MRI: normal	Myopathic facial features, ataxia, global developmental delay, sleep disrupted with frequent awakenings	Antiepileptic medications not specified
von Stulpnagel et al (2018)[84]	M, 4 y	2 y and 6 mo	c.968T > C p.Leu323Pro	De novo mutation No familiarity	EMAS	DA, upward gaze, eyelid myoclonia, atonic head dropping	EEG: 1–3 sec lasting high amplitude 3/sec spike wave complexes with bilateral initiation and occipital predominance but never lateralized. MRI: slight frontal dilatation of the external spaces of cerebrospinal fluid and an age-appropriate myelination. Triggers: heat, fatigue, stress, orofacial stimuli	Moderate ID, ASD, tongue hypotonia, horizontal nystagmus, postaxial hexadactilia, hypospadia	VPA, LTG/VPA + LTG
	M, 14 y	20 mo	c.388C > T p.Gln130Ter	De novo mutation No familiarity	Not classified	Episodes characterized by loss of consciousness, backward eyeball rolling, eyelid myoclonia, myoclonic; generalized with head atonia, and eyelid myoclonia	EEG: slowed background activity (theta); spikes and polyspikes over the occipital regions. MRI: normal Triggers: autoinduced (pattern sensitivity), eating, photic stimulation	Moderate–severe ID, ASD, abnormal gait, poor coordination, dysarthria, dysmorphic features	VPA, LTG, LEV, CLB/VPA, LTG, LEV
	M, 9 y	7 y and 6 mo	c.121C < T p.Arg41Cys	De novo mutation No familiarity	Not classified	Myoclonic and tonic seizures, oculocephalic seizure	EEG: diffuse spikes MRI: normal Triggers: eating	Severe ID, muscular hypotonia, hyperkinesia, dysmorphic features	LTG, LEV, VPA, TPM/VPA + TPM
	F, 4 y	14 mo	c.1210G > C p.Ala40Pro	Parents not tested, presumed to be de novo	Not classified	Atypical abs, myoclonic body	EEG: spike-waves complexes biparieto-occipital right > left 1–4 sec and diffuse spike waves. MRI: normal Triggers: eating	Moderate–severe ID, muscular hypotonia, problem with coordination	Sultiame, LEV, methylprednisolone, VPA, LTG/VPA + LTG
	M, 5 y	4 y and 3 mo	c.3676C > T p.Gln1226Ter	De novo mutation No familiarity	Genetic epilepsy	Atypical abs, DA	EEG: spikes and spike-waves complexes, multiregional, continuous slowing and regional slowing parieto-	Moderate–severe ID, hypotonia (main orofacial), orofacial dystonia and dysarthria, abnormal gait	ETX

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
							occipital. MRI: normal Triggers: eating	with dyskinesia/coordination problems	
	F, 8 y	16 mo	c.433–445dup p.Leu150 Valfs Ter6	Mosaic parent	Not classified	Abs, eye flutters, generalized seizures, myoclonic jerks, atonic drops, myoclonic eyelid flutters	EEG: NA MRI: normal Triggers: chewing, photic stimulation	Moderate-severe ID, ataxia, problems with fine motor skills	Tried 15 anticonvulsant and ketogenic diet/ZNS + CLB
	F, 6 y	12 mo	c.433–445dup p.Leu150 Valfs Ter6	Mosaic parent	Not classified	Abs, eye flutters, generalized seizures, myoclonic jerks, atonic drops, myoclonic eyelid flutters	EEG: NA MRI: normal Triggers: chewing, photic stimulation	Moderate–severe ID, ASD, ataxia	Tried five anticonvulsant and modified Atkins diet/ZNS + CLB
Brimble et al (2018)[85]	M, 4 y	2 y and 7 mo	c.3583–9G > A (p. V1195Rfs*27)	De novo mutation No familiarity	EMAS	Absence seizures with myoclonic and atonic components	EEG Ictal: generalized 3 Hz spike and polyspike and slow waves with occipital and frontocentral predominance EEG background: mild diffuse slowing MRI: normal	Developmental coordination disorder, behavioral difficulties, poor sleep	Refractory to LTG, CBD, and ketogenic diet did not reduce seizure frequency
Cowley et al (2019)[48]	F, 7 y	8 mo	c.435_447dup Leu150Lysfs Ter6 Frameshift	Same variant in the sibling (case 2) Variant was absent in DNA extracted from the peripheral blood from both parents, consistent with gonadal mosaicism as the most likely explanation No familiarity	EMAS and EMA overlapping syndrome	EM (eyelid myoclonia with abs) EM with myoclonic-atonic seizures, myoclonic and myoclonic-atonic seizures. Triggers: eating, touch	EEG-ictal: 3 Hz GSW EEG-interictal: GSW, GPSW (posterior) MRI: normal	Delayed developmental milestones, developmental regression, language impairment, moderate ID, trouble sleeping, pica, hypotonia, ataxic gate, hearing loss, trichotillomania	VPA, LEV, TPM, ETX, PHT, CLB, ketogenic diet, LTG, lacosamide/ ZNS + CZP + CBD
	F, 5 y	12 mo	c.435_447dup Leu150Lysfs Ter6 Frameshift	Same variant in the sibling (case 1) Gonadal mosaicism in one of the parents. No parents history of epilepsy or ID No familiarity	EMAS and EMA overlapping syndrome	EM (eyelid myoclonia with abs) EM with myoclonic-atonic seizures, myoclonic and myoclonic-atonic seizures Triggers: eating	EEG-ictal: 3 Hz GSW EEG-interictal: 2.5–3.5 Hz GSW MRI: not performed	Delayed developmental milestones, language impairment, moderate ID, ASD, echolalia, trouble sleeping, pica, hypotonia, ataxic gate, hearing loss	CLB, ketogenic diet, lacosamide/ZNS + CZP + CBD
Vlaskamp (2019)[52]	M, 3 y and 10 mo	16 mo	p.Arg164* Nonsense	De novo mutation Paternal first cousin seizures, distant relative "institutionalized"	EMA	Myoclonic absence, myoclonic seizures, eyelid myoclonia with absence Triggers: sounds,	EEG-ictal and interictal: GSWs MRI: normal	Medium–low intellectual level	VPA

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
						photosensitivity, sleep deprivation, fatigue			
	M, 7 y and 7 mo	3 y and 10 mo	p.Thr855Serfs*14 Frameshift	De novo mutation No familiarity	EMAS	Atypical abs, myoclonic drop attack, bilateral TCS	EEG-ictal: 2–4 Hz GSWs EEG-interictal: GSWs and MFD photosensitivity MRI: normal	Developmental delay, borderline ID, plateauing of development with seizures, ADHD	LEV + TPM
	F, 8 y and 3 mo	2.5 y	p.Lys114Serfs*20 Frameshift	De novo mutation No familiarity	DEE	Eyelid myoclonia with abs, myoclonic seizures	EEG-ictal: no clinical seizures recorded EEG-interictal: Frequent 2.5–4 Hz GSW (posterior), after eye closure in trains, MFD photosensitivity MRI: normal	Developmental delay, mild ID, plateauing of development with seizures, traits of autism spectrum disorder, mild tantrums and aggression, high pain thresholds, hypotonia	LEV, LTG, ETX, VPA/CBD
	M, 11 y and 2 mo	11 mo	p.Lys142Glufs*31 Frameshift	De novo mutation No familiarity	EMAS and EMA overlapping syndrome	EM (eyelid myoclonia with abs), EM with myoclonic-atonic seizures, bilateral TCS Triggers: photosensitivity, fatigue, sleep deprivation	EEG-interictal: GPSW MRI: normal	Moderate ID, plateauing of development with seizures	VPA
	M, 17 y	2 y	p.Arg143* Nonsense	De novo mutation Sister, father and many paternal ralatives learning difficulties; maternal cousin ASD	EMAS and EMA overlapping syndrome	Bilateral TCS, EM (eyelid myoclonia with abs), myoclonic seizures, FIAS, DA Triggers: eye closure, photosensitivity, eating	EEG: NA MRI: NA	Severe ID, developmental delay with regression, ASD, severe tantrums, self-injury, aggression, sleep problems, high pain thresholds, hypotonia, unsteady gait with toe walking, severe reflux, constipation, benign bone tumor behind ear	VPA + CBZ + CZP
	M, 18 mo	17 mo	p.Arg164* Nonsense	De novo mutation Paternal first cousin seizures	DEE	Typical abs, myoclonic seizures with fever	EEG: NA MRI: NA	Severe ID, developmental delay, ASD, hypotonia, dysphagia, nasopharyngeal reflux, megalocornea, hypoplastic scrotum, high-pain thresholds	No

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	M, 6 y	4 y	p.Ile214Trpfs*9 Nonsense	De novo mutation No familiarity	EMAS and EMA overlapping syndrome	Myoclonic seizures, DA, EM Triggers: fever, infection	EEG-ictal: bilateral occipital sharps, followed by MFD EEG-interictal: MFD MRI: normal	Severe ID, developmental delay, aggression, high pain thresholds	VPA + LEV + TPM
	F, 4 y and 8 mo	23 mo	p.Phe231Leufs*14 Frameshift	De novo mutation No familiarity	EMAS and EMA overlapping syndrome	Myoclonic seizures, atypical abs, atonic seizures, EM	EEG-ictal: generalized poly-spike-wave (myoclonic), 1.5–2 Hz generalized spike-wave (atypical abs) EEG-interictal: GSW MRI: normal	Severe ID, developmental delay with regression, ASD, severe tantrums, self-injury, aggression, sleep problems, oral aversion, high-pain thresholds hypotonia, ataxia, severe reflux, constipation, enterovirus meningitis (6 wk)	CLB, TPM, nitrazepam/ LTG + VPA + CZP
	M, 7 y and 10 mo	2 y	p.Gln247* Frameshift	De novo mutation Maternal aunt and distant relative epilepsy, other distant relatives ASD	EMAS and EMA overlapping syndrome	Myoclonic, EM, EM-atonic, bilateral TCS Triggers: eating, fever, fatigue	EEG-ictal: no clinical seizures recorded EEG-interictal: GSW MRI: normal	Severe ID, developmental delay, obsessions, tantrums, aggression, oppositional, sleep problems, oral aversion, poor chewing, hearing loss, constipation, high-pain thresholds iron deficiency, clumsy, pes planus, strabismus	VPA + CLB
	F, 9.5 y	18 mo	p.Lys277Glnfs*7 Frameshift	De novo mutation No familiarity	EMAS and EMA overlapping syndrome	Bi- and unilateral TCS, EM, EM-myoclonic-atonic	EEG-ictal: FD left posterior (unilateral TCS) EEG-interictal: 3–4 Hz GSW (frontal, central), MFD (posterior) MRI: normal	Severe ID, developmental delay, traits of ASD (poor interaction and eye contact, obsessions), stereotypes, odontoprisis, high-pain thresholds, nystagmus	VPA, CZP, pyridoxin,/ LEV + TPM
	F, 15 y and 3 mo	y	p.Gly391Glnfs*27 Frameshift	De novo mutation half-sister with epilepsy	DEE	EM, FIAS Triggers: eating	EEG-ictal: frequent generalized bursts of spike-waves, frequent frontal and posterior spikes MRI: normal	Moderate–severe ID, developmental delay, traits of ASD (poor interaction and eye contact, obsessions), self-injury, aggression, sleep problems, eating difficulties, constipation, high-pain thresholds hypotonia,	LEV, VPA, CLB

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	F, 5 y and 2 mo	3.5 y	p.Gln456* Nonsense	De novo mutation No familiarity	EMA	EM with myoclonic jerks, myoclonic seizures	EEG-ictal: no clinical seizures recorded	ataxia with wide-based gait, scoliosis	LEV + VPA + CZP + CLB
							EEG-interictal: 1.5–3 Hz GSW, MFD (posterior) MRI: normal	Severe ID, development delay, odontoprisis, high-pain thresholds, congenital hip dislocation	
	M, 5 y and 10 mo	3 y	p.Leu465Phefs*9 Frameshift	De novo mutation Maternal granfather post-stroke epilepsy	EMA	EM Triggers: fatigue	EEG-ictal: Unk. EEG-interictal: 3 Hz GSW and bifrontal spike-wave MRI: normal	Severe ID, developmental delay, obsessions, self-injury, aggression, sleep problems, high-pain thresholds, drooling, hypotonia, unsteady gait and tip-toe gait with poor balance and coordination	VPA
	M, 5 y and 5 mo	2.5 y	p.Thr488Serfs*7 Frameshift	De novo mutation Maternal first cousin ASD	DEE	Atypical abs Triggers: eating (chewing)	EEG-ictal: 2 Hz GSW EEG-interictal: Unk. MRI: Mild prominence frontotemporal subarachnoid space	Severe ID, developmental delay, ASD, tantrums, high-pain thresholds, hypotonia, unsteady gait, orthotics for problems rotating feet, hyper reflexia with clonus, dystonic finger movements, strabismus, mildly tapered fingers	TPM, LEV, VPA/ LTG
	F, 15 y and 1 mo	12–24 mo	p.Tyr505* Nonsense	De novo Paternal uncle moderate ID	EMAS and EMA overlapping syndrome	Myoclonic abs, atonic DA, nocturnal tonic seizures, EM Triggers: photosensitivity, eating	EEG-ictal: GSW (myoclonic abs) EEG-interictal: MFD MRI: normal but with discrete hippocampal tissue loss, not progressive and without sclerosis	Moderate ID, development delay, ASD, self-injury, aggression, sleep problems, high-pain thresholds, oral hypersensitivity, hypotonia, wide-based gait, hypermobility, scoliosis, premature puberty	VPA, LEV/LTG
	F, 10 y and 5 mo	2 y	p.Glu578Alafs*74 Frameshift	De novo mutation No familiarity	EMAS and EMA overlapping syndrome	EM, EM-atonic, EM with myoclonic jerks, bilateral TCS	EEG-ictal: no clinical seizures recorded EEG-interictal: 3 Hz GSW (posterior), also following eye closure, FD (posterior right) MRI: normal	Moderate ID, development delay with regression, ASD, severe tantrums, self-injury, aggression, sleep problems, oral hypersensitivity, oral hypotonia, drooling, constipation, hypotonia, congenital nystagmus, few cafe au lait macules	VPA
	M, 13.5 y	18 mo			DEE				

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
			p.Arg579* Nonsense (also maternally inherited 15q11.2 deletion)	De novo mutation No familiarity		Atypical abs Triggers: eating, fatigue, illness	EEG-ictal: slow GSW and GPSW with frontal predominance (atypical abs) EEG-interictal: Frequent generalized and MFD, MRI: normal	Moderate–severe intellectual disability, developmental delay, sleep problems, ataxia with wide-based gait, tremulous, heterochromia right iris, 0.5 cm pigmented birthmark left arm	Pyridoxine, VPA, ETX/CLB + TPM + LTG
	F, 11 y and 11 mo	2 y	p.Trp657* Nonsense	Unk.	EMAS and EMA overlapping syndrome	Febrile seizures, EM, EM-atonic, bilateral TCS	EEG-ictal: 2–3 Hz GSW with frontal maximum (EM-atonic) EEG-interictal: MFD MRI: normal	Severe ID, developmental delay with regression, ASD, tantrums, self-injury, aggression, sleep problems, difficulties with eating, high-pain thresholds hypotonia, clumsy gait	VPA/LEV
	F, 7 y	6 mo	p.Arg687* Nonsense	De novo Paternal grandmother GTCS 16–20 y. Distant relative ASD	EMAS and EMA overlapping syndrome	EM, bilateral TCS, atonic DA Triggers: fatigue, illness	EEG-ictal: no clinical seizures recorded EEG-interictal: 2.5 Hz GSW (posterior) MRI: normal	Severe ID, developmental delay with regression, ASD, aggression, sleep problems, difficulties with eating, high-pain thresholds, hypotonia, ataxic gait, congenital hip dysplasia (4 m), ankle-foot orthosis, chronic unresponsive iron deficiency	VPA + LEV
	M, 11 y and 7 mo	9.5 y	p.Arg687* Nonsense	De novo mutation No familiarity	EMA	EM Triggers: eating	EEG-ictal: no clinical seizures recorded EEG-interictal: Unk. MRI: normal	Moderate ID, developmental delay, ASD, self-injury, aggression, mild sleep problems, high-pain thresholds, hypotonia, unsteady gait, pes planus	No
	M, 6 y	2 y	p.Arg726Thrfs*33 Frameshift	De novo mutation No familiarity	EMA	EM triggers: hunger, self-induced with hyperventilation, fatigue, stress	EEG-ictal: GSW EEG-interictal: 2–3 Hz GSW, irregular, GPSW, MFD (L centro-parieto) MRI: patent cavum vergae	Severe ID, developmental delay with regression, ASD, high pain thresholds, unsteady gait	VPA, LEV, ketogenic diet, + ZNS, CBD/ETX + LTG
	F, 11 y and 10 mo	2 y	p.Arg967* Nonsense	Not tested	DEE	Typical abs, Triggers: touching nose, fatigue	EEG-ictal: no clinical seizures recorded EEG-interictal: Unk. MRI: normal	Moderate ID, developmental delay, traits of ASD, self-injury, aggression, sleep problems, high-pain thresholds, drooling, reflux, mild	VPA

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	F, 3 y and 11 mo	18 mo	p.Phe979Serfs*98 Frameshift	De novo maternal aunt ID	EMA	EM, TCS with fever Triggers: no	EEG-ictal: no clinical seizures recorded	constipation, chronic sinusitis, hypotonia, clumsy gait	No
				Paternal first cousin post-traumatic epilepsy			EEG-interictal: Unk. MRI: Atypical white-matter abnormalities	Severe ID, developmental delay, ASD, tantrums, self-injury, aggression, sleep problems, high-pain thresholds, chronic idiopathic thrombocytopenic purpura, drooling, constipation, hypotonia, unsteady gait	
	M, 11 y and 2 mo	2 y and 3 mo	p.Gln1136Profs*17 Frameshift	De novo Maternal uncle ID post-meningitis Distant relative epilepsy	EMAS and EMA overlapping syndrome	EM, atonic DA, Triggers: auditory triggers, fatigue, drop in temperature	EEG-ictal: irregular GSWs followed by slower discharges (EM), GPSW (EM) EEG-interictal: GSW, GPSW, bifrontal spike-wave, MFD MRI: normal	Severe ID, developmental delay with regression, ASD, tantrums, aggression, sleep problems, high pain thresholds, eating difficulties, hemangioma nasal cavity, borderline hypotonia, ataxia, borderline short stature	VPA, CLB, TPM/ketogenic diet + LTG
	F, 33 y	8 mo	p.Glu1169* Nonsense	De novo Maternal and paternal first cousins learning difficulties	EMA	EM, GTCS Triggers: photosensitivity	EEG-ictal: NA EEG-interictal: NA MRI: NA	Moderate–severe ID, developmental delay with regression, ASD, self-injury, aggression, poor concentration, high pain thresholds, eating difficulties, drooling, hypotonia, coordination disorder/ataxia	CBZ, TPM/VPA
	M, 15 y and 3 mo	18 mo	p.Tyr1219* Nonsense	De novo Distant relative ASD	EMA	EM Triggers: no	EEG-ictal: GSWs (EM) EEG-interictal: temporo-occipital spike-wave, 10% generalized activity in 24 h MRI: enlarged ventricles	Severe ID, developmental delay with regression, ASD, aggression, sleep problems, high-pain thresholds, eating difficulties, drooling, hypotonia, bilateral pyramidal syndrome, unsteady gait deteriorating since 15y (crouch gait), orthotics, hyperflexibility, right pes planus, left pes caves, epistaxis	LEV/VPA + LTG
	M, 9 y and 7 mo	3 y			DEE				ZNS/LTG

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	M, 4 y and 9 mo	2 y and 1 mo	c.190–2A > G; p.? Missense probably affecting splicing p.Arg1240* Nonsense	De novo mutation, no familiarity De novo Maternal cousin ASD	EMA	EM Triggers: eating Typical abs, atypical nocturnal frontal seizures, myoclonic seizures Triggers: photosensitivity, sound, eating	EEG-ictal: two single event with eye blinking no ictal correlate EEG-interictal: in sleep occassional focal sharp waves MRI: normal	Moderate-severe intellectual disability, developmental delay, ASD, aggressive, sleep problems, high-pain thresholds, eating difficulties, mild hypotonia	No
	F, 8 y and 11 mo	<2 y	p.Ser129Ser Non-synonymous probably affecting splicing	De novo mutation, no familiarity	EMAS and EMA overlapping syndrome	EM, EM-myoclonic-atonic Triggers: eye closure, hunger, fatigue	EEG-ictal: generalized spike EEG-ictal: generalized dis-(myoclonic) charges (EM-myoclonic- EEG-interictal: FD, generalatonic) ized spikes and polyspikes EEG-interictal: 2–3 Hz GSW, MRI: Hyperintensity on T2 in very frequent general dis- bilateral posterior centrum charges, induced by eye semiovale and subcortical closure white matter in bifrontal MRI: normal lobes	Mild ID, developmental de- Mild intellectual disability, lay with regression, traits of developmental delay, ASD, ASD (no eye contact, ADHD, OCD, tantrums, op- obsessions), tantrums, self- positional defiant disorder, injury, aggressive, few café aggressive, sleep problems, au lait macules over trunk high-pain thresholds, eating and right arm difficulties, hypotonia,	CLB/VPA + LTG
	F, 4 y and 11 mo	3 y and 3 mo	c.388–2A > T; p.? Missense probably affecting splicing	De novo mutation, no familiarity	DEE	Atypical abs Triggers: no	EEG-ictal: no clinical seizures recorded EEG-interictal: 2–2.5 Hz GSW, MFD MRI: normal	wide-based gait, hyperflexi- ble, high reflexes (clonus bilateral), plagiocephaly, pronated feet (braces), strabismus (had surgery), constipation, PANDAS	VPA
								Severe ID, developmental delay with regression, traits of ASD, tantrums, self-injury, high-pain thresholds, ataxia, varus deformity	
	F, 6 y and 8 mo	4.5 y	c.1677–2_1685del; p.? Inframe del probably affecting splicing	De novo mutation, no familiarity	EMA	EM, typical abs Triggers: no	EEG-ictal: GSW and GPSW (EM) EEG-interictal: no MRI: mega cisterna magna fossa posterior	Moderate-severe intellectual disability, developmental delay with regression, ASD, sleep problems, high-pain thresholds, hypotonia	ZNS, rufinamide/LEV + VPA
	M, 6.5 y	2.5 y	p.Cys282Arg Missense	Unk.	DEE	Myoclonic seizures, febrile convulsions Triggers: no	EEG-ictal: no clinical seizures recorded EEG-interictal: MFD (right temperature), MRI: normal	Severe ID, developmental delay with regression, traits of ASD, sleep problems, eating difficulties, spasmus nutans (6 m, disappeared), hypotonia (needs CPAP in winter), constipation, lactose intolerance	VPA/LTG

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	M, 10 y M, 3 y and 2 mo	2 y and 9 mo 2.5 y	p.Gly344Ser Missense p.Leu323Pro Missense	De novo mutation, no familiarity De novo paternal uncle epilepsy and behavioral problems	EMAS and EMA overlapping syndrome EMAS and EMA overlapping syndrome	EM, EM-myoclonic-atonic Triggers: visual patterns (crossing/netting) EM, myoclonic-atonic seizures, myoclonic seizures, atonic DA Triggers: eating, stress	EEG-ictal: no clinical seizures recorded EEG-interictal: GPSW, 3 Hz GSW, MFD MRI: normal EEG-ictal: unk. EEG-interictal: unk. MRI: normal	Moderate ID, developmental delay with regression, ASD, tantrums, OCD, echolalia, eating difficulties, high-pain thresholds, mild cerebral palsy with hypotonia, pes planus, mild muscle weakness, clinodactyly toes, celiac disease, constipation	VPA + LTG
	M, 18 y and 10 mo	4 y	p.Ala404Pro Missense	De novo Distant relative epilepsy and ID	DEE	Typical abs Triggers: no	EEG-ictal: unk. EEG-interictal: unk. MRI: normal	Severe ID, developmental Severe ID, developmental delay with regression, traits of ASD (obsessions, tantrums, compulsive, sleep problems, eating difficulties without routine), sleep problems, eating difficulties, high-pain thresholds, hypotonia, nystagolds, hypotonia, clumsy mus since, hypospadias, 6th gait, drooling toe	no
	F, 14 y and 10 m	3 y	p.Tyr417Cys Missense	De novo mutation, no familiarity	DEE	Typical abs Triggers: photosensitivity	EEG-ictal: no clinical seizures recorded EEG-interictal: GPSW, 3.5–4 Hz GSW (post), MFD (central) MRI: normal	Moderate ID, developmental delay	ETX, CZP, steroids/VPA
	M, 5 y and 8 mo	14 mo	p.Asp463_Leu465delinsVal Inframe deletion / insertion	De novo mutation, no familiarity	EMAS	FIAS, atonic DA Triggers: no	EEG-ictal: no clinical seizures recorded EEG-interictal: FD (temporo-occipital), diffuse spike-wave and polyspike-wave MRI: thin corpus callosum, mild hypomyelination (11 m), left frontal subcortical nodular heterotopia	Moderate ID, developmental delay, self-injury, aggression, motor stereotypes, mild dysphagia	LEV/VPA
	M, 15 y and 1 mo	2.5 y	p.Leu465dup Inframe deletion / insertion	De novo Mother febrile seizures. Paternal uncle learning difficulties	EMAS and EMA overlapping syndrome	EM, EM-atonic, typical abs, bilateral TCS (with fever) Triggers: noise, photosensitivity	EEG-ictal: no clinical seizures recorded EEG-interictal: MFD, GSW, GPSW MRI: normal	Severe ID, developmental delay with regression, ASD, obesity with high appetite, poor chewing, ataxia with wide-based gait	Hydrocortison, VGB, nitrazapem
	F, 8 y and 3 mo	18 mo	p.Cys599Trp Missense	De novo mutation, no familiarity	EMAS and EMA overlapping syndrome	EM, EM-atonic Triggers: eating, eye closure, fatigue	EEG-ictal: unk. EEG-interictal: GSW		LEV, ETX, CZP/VPA + LTG + CLB

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	F, 7 y and 8 mo	2.5 y	p.Ile630Asn Missense	De novo mutation, no familiarity	EMAS and EMA overlapping syndrome	EM, EM-atonic Triggers: illness fatigue	EEG-ictal: no clinical seizures recorded EEG-interictal: MFD MRI: normal mild enlarged ventricles and pineal cyst	Mild ID, language delay with, ASD, tantrums, aggressive, sleep problems, hypotonia, developmental delay with regression, ASD, tantrums, self-injury, sleep problems, eating difficul-	ZNS, VPA, LEV, perampanel/CBD + ketogenic diet
	M, 2 y and 4 mo	20 mo	6p21.32 chr6:33,296,711—33,389,795 × 1 deletion	De novo Monozygotic twin SYNGAP1 (patient 42), brother ASD	DEE	Atypical abs Triggers: no	EEG-ictal: 2 Hz GSW (atypical abs) EEG-interictal: frequent GSW MRI: no	Severe ID, developmental ties, macrocephaly, hypo- delay with regression, traits tonia, wide-based gait with of ASD (handflapping), tan- poor balance, knee hyper- trums, sleep problems, extension, pes planus, pro- high-pain thresholds, eating nated feet difficulties, tone	LTG/VPA
								dysregulation	
	M, 2 y and 4 mo	20 mo	6p21.32 chr6:33,296,711—33,389,795 × 1 deletion	De novo Monozygotic twin SYNGAP1 (patient 41), brother ASD	DEE	Atypical abs Triggers: no	EEG-ictal: No clinical seizures recorded EEG-interictal: paroxismal activity MRI: no	severe ID, developmental delay with regression, traits of ASD (handflapping), self-injury, aggression sleep problems, high-pain thresholds, eating difficulties, tone dysregulation	VPA
	M, 5 y	12 mo	6p21.32-p21.31 chr6:33,329,945—34,163,248 × 1 deletion	De novo distant relative ASD	DEE	EM, with myoclonic jerks, typical abs Triggers: fever	EEG-ictal: 2–3 Hz GSW followed by following for 2—5 sec (EM) EEG-interictal:2–3Hz GSW, MFD MRI: normal	severe ID, developmental delay with regression, traits of ASD (obsessions), tantrums, eating difficulties, hypotonia, intermittent horizontal nystagmus, joint laxity, reflux oesophagitis	LEV, ZNS, lacosamide, rufinamide/ VPA+ CLB + ketogenic diet
	F, 7 y and 11 mo	2.5 y	6p21.32 chr6:33,343,159—33,435,947 × 1 deletion	Unk Father GTCS secondary to TBI	EMAS (epilepsy with myoclonic-atonic seizures)	Atypical abs, atonic DA Triggers: photosensitivity, hunger	EEG-ictal: 2–3 Hz GSW followed by following for 2—5 sec (atypical abs) EEG-interictal: 2–3 Hz GSW MRI: normal	Severe ID, developmental delay with regression, ASD, self-injury, aggressive, eating difficulties, hypotonia, mild hand tremor, history of strabismus (surgery at 8 years), constipation, drooling	ETX/LTG
	M, 7 y and 2 mo	Unk.	c.121C > T; p.? Missense variant of unknown significance	Unk. Maternal first cousin ID, distant relative single seizure	EMAS (epilepsy with myoclonic-atonic seizures)	Unknown seizures type and atonic seizures Triggers: unk	EEG-ictal: 1–2 Hz GSW (myoclonic) EEG-interictal: 1–2 Hz GSW, MFD MRI: unk.	ID (unknown severity), language regression, probable ADHD, stereotypes, self-injury, aggression, strabismus convergens, constipation	LTG, LEV/VPA + TPM

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
	F, 14 y	5 y and 3 mo	p.Asp201Glu Missense variant of unknown significance	Unk. (parents NA)	DEE	EM Triggers: no	EEG-ictal: 2–3Hz GSW, GPSW (EM) EEG-interictal: Right centro-temporal spikes MRI: unk	mild ID	LTG, CLB, CZP/VPA + ETX
	M, 16 y and 2 mo	7 mo	p.Arg293Cys Missense variant of unknown significance	Not maternal, father NA father focal epilepsy	DEE	Epileptic spasms, myoclonic seizures, GTCS Triggers: no	EEG-ictal: no clinical seizures recorded EEG-interictal: MFD MRI: thin corpus callosum, ventricular enlargement (R > L)	Severe ID, developmental delay, self-injury, eating difficulties (nasogastric tube) spastic quadriplegia	VPA, phenobarbital, VGB ACTH, TPM, LEV, PHT/CBZ + ZNS
	F, 11 y	3 y	p.Asp845Tyr Missense variant of unknown significance	De novo mutation, no familiarity	DE (developmental encephalopathy) with focal seizures	focal seizures Triggers: yes (not specified)	EEG-ictal:unk EEG-interictal: unk MRI: no	ID (unknown severity)	VPA
	M, 10 y and 8 m	5 y	p.Pro1320His Missense variant of unknown significance	Parents NA Father focal epilepsy, brother febrile seizures, mother BPD	Focal epilepsy	Focal seizures, bilateral GTCS Triggers: no	EEG-ictal: No clinical seizures recorded EEG-interictal: FD (fronto-temporal) MRI: normal	Developmental delay, OCD, eating difficulties	CBZ, CLB, CZP, VPA, LEV, TPM, OXC, rufinamide/ ETX + LTG
Mignot et al (2016)[26]	M, 14 y	24 mo	c.68–1518-?_1530 + ?del p.? intragenic deletion	De novo mutation, no familiarity	EMA	Myoclonic jerks, myoclonic abs, eyelid myoclonia Triggers: no	EEG: generalized burst of spikes MRI: normal	Severe ID, developmental delay with regression, ASD, truncal hypotonia, broad-based gait, hypotonic-atactic movements	VPA
	F, 15 y	24 mo	.348C > A p.Tyr116* Nonsense	De novo mutation, no familiarity	EMAS (epilepsy with myoclonic-atonic seizures) and atypical GGE (genetic generalized epilepsy)	DA, GTCS, clonic seizures, DA, myoclonic jerks Triggers: photosensitivity	EEG: GPSW MRI: normal	Mild ID, developmental delay, truncal hypotonia, broad-based gait, hypotonic-atactic movements	VPA/LEV
	F, 8.5 y	22 mo	c.403C > T p.Arg135* Nonsense	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy)	Febrile seizures, atypical abs, myoclonic jerks, atonic seizures Triggers: no	EEG: frontal and GSW and polyspike-wave MRI: normal	Moderate ID, developmental delay, Global hypotonia, gait ataxia	LEV
	F, 10.8 y	4 y	c.427C > T p.Arg143* Nonsense	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy) with abs	GTCS, abs Triggers: no	EEG: irregular spike-slow-wave complexes: generalized, maximum frontal; β-waves MRI: normal	Severe ID, developmental delay, ASD, truncal hypotonia	VPA
	F, 15 y	3 y							

(*Continued*)

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
			c.455_459del p.Arg152Glnfs*14 Frameshift	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy)	Tonic seizures febrile and afebrile, myoclonic jerks, myoclonic abs Triggers: no	EEG: generalized bursts of spikes, spike-waves in posterior areas; slow background activity, frontotemporal bursts of spike-waves	Severe ID, developmental delay with regression, ASD, nystagmus during the 1st year possibly caused by myopia), clumsy gait	VPA, OXC, LTG, LEV, CLB/VPA + LTG
	M, 15 y	30 mo	c.490C > T p.Arg164* Nonsense	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy) with abs	Abs and not defined seizures Triggers: no	EEG: bi-occipital slow spikes, spikes and spike-wave, bi-central anomalies MRI: normal	Severe ID, developmental delay, ASD, facial and truncal hypotonia, broad-based gait	VPA, CLB
	F, 5 y	5 y	c.509 + 1 G > T p.? Splice site	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy) with abs	Abs Triggers: NA	EEG: NA MRI: normal	Moderate ID, developmental delay with regression, truncal hypotonia	LTG
	F, 9.8 y	33 mo	c.828dup p.Lys277Glnfs*7 Frameshift	Parents not tested	Unclassified GGE (genetic generalized epilepsy) with abs	Abs Triggers: NA	EEG: GSW and GPSW	Moderate ID, developmental delay, truncal hypotonia, facial hypotonia with drooling, gait ataxia	VPA, LTG/LTG
	F, 5.5 y	30 mo	c.1057delC p.Leu353Trpfs*13 Frameshift	Parents not tested	Unclassified GGE (genetic generalized epilepsy) with abs	Head nodding, abs, myoclonic jerks (mainly arms) Triggers: chewing, emotions	EEG: GSW and GPSW posterior regions	Moderate ID, developmental delay, truncal hypotonia, walking with inward rotation of hips	VPA, ETX, LEV, CZP, ketogenic diet
	M, 5 y	3.5 y	c.1253_1254del p.Lys418Argfs*54 Nonsense	De novo mutation, no familiarity	NA	Not defined nonfebrile seizures Triggers: no	EEG: no abnormalities MRI: normal	severe ID, developmental delay with regression, ASD, Truncal hypotonia, broad-based gait, hypotonic-atactic movements	no
	M, 3 y	24 mo	c.1630C > T p.Arg544* Nonsense	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy)	Febrile seizures, eyelid myoclonia Triggers: photosensitivity	EEG: Abnormal background, generalized slowing, recorded seizures with eyelid myoclonia and generalized seizure patterns MRI: normal	Severe ID, developmental delay, Truncal hypotonia, swallowing difficulties	VPA
	F, 22 y	12 mo	c.1685C > T p.Pro562Leu Missense	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy)	Febrile seizures, eyelid myoclonia, atypical abs, myoclonic jerks	EEG: bursts of spikes and slow spikes in the occipital region after	Severe ID, developmental delay with regression, mild gait ataxia, flexion	VPA, CLB, CBZ, zonisamde/LEV + TPM

Supplementary Table S1 (*Continued*)

Study (Year)	Sex and age	Age at first seizure	Genetic variant	Family history	Epilepsy syndrome	Clinical manifestations	Instrumental Findings	Comorbidities	Treatment
						Triggers: fixation-off sensitivity	eye closure MRI: normal	deformity of left hip, hyperlordotic lumbar spine	
	M, 12 y	<2 y	c.1995T > A p.Tyr665* Nonsense	Parents not tested	EMAS (epilepsy with myoclonic-atonic seizures)	Astatic seizures, myoclonic astatic seizures Triggers: photosensitivity	EEG: GSW MRI: normal	Severe ID, developmental delay, hyperactive deep tendon reflexes, unsteady gait	VPA, ZNS, LTG
	F, 8 y	5 y	c.2214_2217del p.Glu739Glyfs*20 Frameshift	De novo mutation, no familiarity	Unclassified GGE (genetic generalized epilepsy)	Eyelid myoclonia, myoclonic abs Triggers: photosensitivity, fixation-off sensitivity	EEG: ictal bursts of diffuse GPSW with posterior predominance after eyes closer and photic stimulation MRI: normal	Mild ID, developmental delay with regression, ASD, Motor slowness and moderate akinesia, ataxic gait, truncal hypotonia, dystonic postures of hands and feet, plastic hypertonia	VPA/LEV + ETX
	M, 8.2 y	22 mo	c.2933del p.Pro978Hisfs*99 Frameshift	De novo mutation, no familiarity	EMAS (epilepsy with myoclonic-atonic seizures)	Atonic seizures, GTCS, focal, atypical abs., myoclonic jerks Triggers: no	EEG: focal spike-wave in central-parietal areas, GSW and GPSW MRI: normal	Moderate ID, developmental delay, Truncal hypotonia, orthostatic truncal tremor, slight pyramidal tetraparesis, gait ataxia	VPA, LTG LEV, CZP, ACTH
	M, 29 y	27 mo	c.3406dup p.Gln1136Profs*17 Frameshift	Parents not tested	Unclassified GGE (genetic generalized epilepsy)	Myoclonic seizures, Myoclonic jerks, GTCS, atypical abs. Triggers: no	EEG: GPSW and frontal slow spikes MRI: normal	Severe ID, developmental delay with regression, ASD, Truncal hypotonia	VPA, CLB, TPM/ketogenic diet
	M, 10 y	8 y	c.3408 + 1G > A p.? Splice site	De novo mutation, no familiarity	Unclassified	Atypical abs Triggers: photosensitivity	EEG: multifocal slow spikes MRI: normal	Severe ID, developmental delay with regression, ASD, Truncal hypotonia, orofacial hypotonia, wide-based gait	VPA

Abbreviations: abs, absences; CBD, cannabidiol; CBZ, carbamazepine; CLB, clobazam; CZP, clonazepam; DA, drop attacks; DEE, developmental and epileptic encephalopathy; EM, eyelid myoclonia with absences; EMA, epilepsy with eyelid myoclonia; EMAS, epilepsy with myoclonic-atonic seizures; ETX, ethosuximide; FD, focal discharges; FIAS, focal impaired awareness seizures; GD, generalized discharges; GGE, genetic generalized epilepsy; GPSW, generalized poly-spike-wave; GSW, generalized spike-wave; GTCS, generalized tonic-clonic seizures; ID, intellectual disability; LEV, levetiracetam; LTG, lamotrigine; MFD, multifocal discharges; NA, not available; OXC, oxcarbazepine; PHT, phenytoin; TCS, tonic-clonic seizures; TPM, topiramate; Unk., unknown; VGB, vigabatrin; VPA, valproic acid; ZNS, zonisamide