Electroclinical Syndromes of Adolescence (and Adulthood)

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References and Further Reading

ILAE Classification: https://www.epilepsydiagnosis.org/

Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, Engel J, French J, Glauser TA, Mathern GW, Moshé SL, Nordli D, Plouin P, Scheffer IE. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia. 2010 Apr;51(4):676-85. doi: 10.1111/j.1528-1167.2010.02522.x. Epub 2010 Feb 26. PubMed PMID: 20196795.

Geithner J, Schneider F, Wang Z, Berneiser J, Herzer R, Kessler C, Runge U. Predictors for long-term seizure outcome in juvenile myoclonic epilepsy: 25-63 years of follow-up. Epilepsia. 2012 Aug;53(8):1379-86. doi: 10.1111/j.1528-1167.2012.03526.x. Epub 2012 Jun 12. PubMed PMID: 22686598.

Marson AG, Al-Kharusi AM, Alwaidh M, Appleton R, Baker GA, Chadwick DW, Cramp C, Cockerell OC, Cooper PN, Doughty J, Eaton B, Gamble C, Goulding PJ, Howell SJ, Hughes A, Jackson M, Jacoby A, Kellett M, Lawson GR, Leach JP, Nicolaides P, Roberts R, Shackley P, Shen J, Smith DF, Smith PE, Smith CT, Vanoli A, Williamson PR; SANAD Study group. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet. 2007 Mar 24;369(9566):1016-26. PubMed PMID: 17382828; PubMed Central PMCID: PMC2039891.

Nicolson A, Appleton RE, Chadwick DW, Smith DF. The relationship between treatment with valproate, lamotrigine, and topiramate and the prognosis of the idiopathic generalised epilepsies. J Neurol Neurosurg Psychiatry. 2004 Jan;75(1):75-9. PubMed PMID: 14707312; PubMed Central PMCID: PMC1757463.

Nicolson A, Chadwick DW, Smith DF. A comparison of adult onset and "classical" idiopathic generalised epilepsy. J Neurol Neurosurg Psychiatry. 2004 Jan;75(1):72-4. PubMed PMID: 14707311; PubMed Central PMCID: PMC1757447.

Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, Hirsch E, Jain S, Mathern GW, Moshé SL, Nordli DR, Perucca E, Tomson T, Wiebe S, Zhang YH, Zuberi SM. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017 Apr;58(4):512-521. doi: 10.1111/epi.13709. Epub 2017 Mar 8. PubMed PMID: 28276062; PubMed Central PMCID: PMC5386840.

Shih JJ, Whitlock JB, Chimato N, Vargas E, Karceski SC, Frank RD. Epilepsy treatment in adults and adolescents: Expert opinion, 2016. Epilepsy Behav. 2017 Apr;69:186-222. doi: 10.1016/j.yebeh.2016.11.018. Epub 2017 Feb 23. Review. PubMed PMID: 28237319.

Shorvon SD, Bermejo PE, Gibbs AA, Huberfeld G, Kälviäinen R. Antiepileptic drug treatment of generalized tonic-clonic seizures: An evaluation of regulatory data and five criteria for drug selection. Epilepsy Behav. 2018 Mar 27;82:91-103. doi: 10.1016/j.yebeh.2018.01.039. [Epub ahead of print] Review. PubMed PMID: 29602083.

Vorderwülbecke BJ, Kowski AB, Kirschbaum A, Merkle H, Senf P, Janz D, Holtkamp M. Long-term outcome in adolescent-onset generalized genetic epilepsies. Epilepsia. 2017 Jul;58(7):1244-1250. doi: 10.1111/epi.13761. Epub 2017 May 2. PubMed PMID: 28464258.

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Electroclinical Syndromes of Adolescence

	Classification	Age at onset	Clinical
Juvenile Myoclonic Epilepsy	Genetic Generalized Epilepsy	8-25 years (5% start as Childhood Absence Epilepsy)	normal birth, development, cognition, exam, head size; 5-10% with febrile seizures
Juvenile Absence Epilepsy	Genetic Generalized Epilepsy	9-20 years (peak 9-13)	normal birth, development, cognition; may have ADHD and learning difficulties
Epilepsy with Generalized Tonic Clonic Seizures (GTCS) Alone	Genetic Generalized Epilepsy	5-40 years (peak 11-23)	normal birth, development, cognition, exam, head size
Familial Temporal Lobe Epilepsies	Genetic Focal Epilepsies	> 10 years (median 25)	seizures often unrecognized; normal birth, development, cognition, exam, head size
Autosomal Dominant Epilepsy with Auditory Features*	Genetic Focal Epilepsy	4-40 years	normal birth, development, cognition, exam, head size

*is a distinct type of familial temporal lobe epilepsy

Electroclinical Syndromes of Adolescence

	Seizure Types		
	Must Have	May Have	Must Not Have
Juvenile Myoclonic Epilepsy	myoclonic seizures (esp. upon awakening)	GTCS (>90%); absence (33%) which are infrequent and brief (< 3 sec)	any other types
Juvenile Absence Epilepsy	absence (infrequent as compared to Childhood Absence Epilepsy, may have incomplete loss of awareness)	GTCS (80%)	any other types (esp. myoclonic)
Epilepsy with Generalized Tonic Clonic Seizures (GTCS) Alone	GTCS, predominantly within 1-2 hours of awakening	n/a	any other types
Familial Temporal Lobe Epilepsies	focal seizures with temporal lobe features, often with retained awareness (often mild and experiential)	GTCS (infrequent and controllable, seen in 66% prior to treatment)	n/a
Autosomal Dominant Epilepsy with Auditory Features	auditory aura may be elementary (humming, buzzing, ringing), illusions (sound distortions), or hallucinations (specific songs or voices); receptive aphasia	reflex seizures (auditory); nocturnal GTCS (uncommon)	n/a

Electroclinical Syndromes of Adolescence

	EEG			
	Background	Interictal	Activation	Ictal
Juvenile Myoclonic Epilepsy	normal	generalized spike-and-wave (incl. fragments); generalized polyspike-and-wave (3.5-6 Hz)	photoparoxysmal response (33%); myoclonus upon awakening; hyperventilation (less common)	3-6 Hz generalized spike-and-wave or polyspike-and-wave (single discharge with myoclonic seizure)
Juvenile Absence Epilepsy	normal, or occipital intermittent rhythmic delta activity (OIRDA)	generalized spike-and-wave (incl. fragments); generalized polyspike-and-wave (NOT < 2.5 Hz)	hyperventilation; discharges upon awakening	3-6 Hz generalized spike-and-wave or polyspike-and-wave (rhythmic run)
Epilepsy with Generalized Tonic Clonic Seizures (GTCS) Alone	normal	generalized spike-and-wave (incl. fragments); 50% of patients have abnormalities only in sleep	n/a	EEG obscured by artifact during GTCS; may start with generalized fast rhythmic activity
Familial Temporal Lobe Epilepsies	focal slow activity in 33%; otherwise normal	temporal epileptiform discharges in 20%; otherwise normal	n/a	[not well published]
Autosomal Dominant Epilepsy with Auditory Features	normal	temporal abnormalities in 30%; otherwise normal	n/a	mid, anterior, or fronto-temporal discharges

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	Imaging	Genetics		
		Inheritance	Genes*	Family History
Juvenile Myoclonic Epilepsy	normal (not required in typical cases)	complex or Mendelian	CACNB4, GABRA1, CLCN2, GABRD, EFHC1, 15q13.3 microdeletion	occasional
Juvenile Absence Epilepsy	normal (not required in typical cases)	complex	GABRG2, CACNA1A	occasional
Epilepsy with Generalized Tonic Clonic Seizures (GTCS) Alone	normal	complex	CLCN2	common (20%); febrile seizures (10%)
Familial Temporal Lobe Epilepsies	normal (uncommonly may show hippocampal diffuse temporal abnormality)	autosomal dominant (60% penetrance)	DEPDC5	high (though seizures are mild and may not be recognized)
Autosomal Dominant Epilepsy with Auditory Features	normal (rarely may show nonspecific temporal findings)	autosomal dominant (high penetrance)	LGI1 (50%)	very high (though seizures are mild and may not be recognized)

*these are examples of genes that may be mutated in some (but not most) cases

Electroclinical Syndromes of Adolescence

	Psychosocial Prognosis	Seizure Prognosis	First Line Treatment	Alternative Treatments	AEDs to avoid	Treatment if Medically Intractable
Juvenile Myoclonic Epilepsy	good	seizures often easily controlled; (probable) lifelong treatment	LEV, LTG, VPA	TPM, ZNS, CLB, PER	GBP, PGB, CBZ, OXC, ESL, PHT	VNS, diets
Juvenile Absence Epilepsy	variable	often intractable; lifelong treatment	LEV, LTG, VPA	TPM, ZNS, CLB, PER, ESM as add-on only	GBP, PGB, CBZ, OXC, ESL, PHT	VNS, diets
Epilepsy with Generalized Tonic Clonic Seizures (GTCS) Alone	good	seizures often easily controlled; lifelong treatment	LEV, LTG, VPA	TPM, ZNS, CLB, PER	GBP, PGB, CBZ, OXC, ESL, PHT	VNS, diets
Familial Temporal Lobe Epilepsies	good	seizures often mild and easy to control	LEV, LTG, OXC	CBZ, ESL, LCM, GBP, PGB, TPM, ZNS	ESM	resection
Autosomal Dominant Epilepsy with Auditory Features	good	seizures often mild and easy to control	LEV, LTG, OXC	CBZ, ESL, LCM, GBP, PGB, TPM, ZNS	ESM	resection

LEV, levetiracetam; LTG, lamotrigine; VPA, valproate; OXC, oxcarbazepine; TPM, topiramate; ZNS, zonisamide; CLB, clobazam; PER, perampanel; ESM, ethosuximide; CBZ, carbamazepine; ESL, eslicarpazepine; LCM, lacosamide; GBP, gabapentin; PGB, pregabalin; PHT, phenytoin; VNS, vagus nerve stimulator