Epilepsy Syndromes

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This is a quick reference for epilepsy syndromes that are listed by the International League Against Epilepsy (ILAE). Most of the syndromes are described in detail in the ILAE website**:** http://www.ilae-epilepsy.org/ctf/syn_frame.html. The following features are outlined for each epilepsy syndrome: seizure types; ictal EEG and interictal EEG features; activating effects of sleep, sleep deprivation (SD), photic stimulation (PS), hyperventilation (HV), and other factors; course; and etiology. AED=antiepileptic drug, GABA=γ-aminobutyric acid, epilepsia partialis continua=EPC, IED=interictal epileptiform discharge, PPR=photoparoxysmal response.

I. Encephalopathic Epilepsies

Early Myoclonic Epilepsy (EME)

seizure types: erratic focal myoclonus, focal clonic or tonic seizures, tonic spasms; less commonly: massive bilateral myoclonus, epileptic spasms

ictal EEG: onset of focal seizures are similar to neonatal seizures; generalized discharges are seen during massive myoclonus; no EEG correlate for erratic myoclonus

interictal EEG: burst-suppression with loss of normal background features; silent periods last 3-10 sec

activation: burst-suppression, almost limited to sleep

course: less predictable than OS; may persist as EME or evolve into focal or multifocal epilepsy; burst-suppression may persist or evolve into multifocal spikes or atypical hypsarrhythmia

etiology: metabolic: nonketotic hyperglycinemia, pyridoxine-dependency, methylmalonic academia, propionic acidemia, D-glyceric acidemia, molybdenum cofactor deficiency, etc.

Ohtahara Syndrome (OS)

seizure types: tonic spasms, focal clonic or hemiclonic seizures; less commonly myoclonus

ictal EEG: burst episodes may be accompanied by tonic spasms

interictal EEG: burst-suppression with loss of normal background features; silent periods last 10-20 sec

activation: burst-suppression is present in wake and sleep

course: infant who is usually normal develops seizures within the first 10 days postpartum; seizures progressively increase in frequency as psychomotor retardation develops; OS often evolves to WS; burst-suppression may evolve to hypsarrhythmia or multifocal spikes

etiology: malformations: hemimegalencephaly, diffuse cortical migrational disorders, Aicardi syndrome, dentato-olivary dysplasia, etc.; metabolic: nonketotic hyperglycinemia, pyridoxine dependency, carnitine palmitoyl-transferase deficiency, Leigh disease, etc.

West Syndrome (WS)

seizure types: epileptic spasms, tonic seizures, drop attacks; less commonly: focal clonic seizures

ictal EEG: high voltage slow wave followed by electrodecrement during epileptic spasms (slow wave correlates with spasm); low voltage fast activity; focal spikes may associated with cluster of spasms

interictal EEG: hypsarrhythmia or its variants (modified hypsarrhythmia); multifocal spikes

activation: epileptic spasms usually occur after awakening or on falling asleep; hypsarrhythmia is more continuous in wake and fragmented in sleep; focal or multifocal spikes spread and become bilateral in sleep; loud sound or touch may precipitate spasms but not PS

course: before onset: 1/3 are normal, 2/3 are neurologically impaired (some diagnosed with OS); progressive increase in seizure frequency and impairment in cognitive and motor function; many develop LGS later; hypsarrhythmia becomes organized and may evolve into slow spike-waves

etiology: malformations: tuberous sclerosis, hemimegalencephaly, lissencephaly, agenesis of the corpus callosum, focal cortical dysplasia, Sturge-Weber syndrome, arteriovenous malformation, etc.; perinatal hypoxia-ischemia, periventricular encephalomalacia; infections: congenital CMV, HSV encephalitis, meningitis, etc.; neoplastic lesions; metabolic: phenylketonuria, pyridoxine-dependence, neuronal ceroid lipofuscinosis, etc.; epilepsy genes: Xp22 ARX or STK9 genes (X-linked WS)

Lennox-Gastaut Syndrome (LGS)

seizure types: tonic seizures, atypical absences, atonic seizures, focal seizures, tonic status; less commonly tonic-clonic seizures, absence status; myoclonus in myoclonic variant of LGS

ictal EEG: paroxysmal fast activity or polyspikes during tonic seizures; various patterns including slow spike-waves, high-voltage spikes, low-voltage fast activity, electrodecrement, or no change during atypical absences

interictal EEG: slow spike-waves (<2.5 Hz); paroxysmal fast activity (10-25 Hz); low-voltage fast activity; slow and disorganized background in wake and sleep; multifocal slow waves; focal or multifocal spikes; atypical spike-waves, polyspike-waves

activation: sleep accentuates multifocal spikes, slow spike-waves, and paroxysmal fast activity; more spikes are bilateral and synchronous and spike-waves acquire a polyspike-wave appearance; sleep is activating for tonic seizures; tonic seizures may occur only in sleep; HV activates slow spike-waves but not multifocal spikes and paroxysmal fast activity; PS has no significant effect; sound, touch, or movement may precipitate tonic seizures

course: drop attacks in preschoolers and behavioral changes in older children usually occur first followed later by frequent seizures, episodes of status, and progressive cognitive decline

etiology: malformations: tuberous sclerosis, hemimegalencephaly, subcortical band heterotopia, focal cortical dysplasia, Sturge-Weber syndrome, dysembryoplastic neuroepithelial tumor, etc.; destructive lesions: perinatal hypoxia-ischemia, periventricular encephalomalacia, cerebral infarction, cardiac or respiratory failure, head injury, hypoglycemia, radiation injury, etc.; infections: HSV encephalitis, meningitis, etc.; metabolic: phenylketonuria, homocysteinuria, sialidoses, neuronal ceroid lipofuscinosis, Lafora body disease, etc.

Epilepsy with Continuous Spike-Waves during Sleep (ECSWS)

►The *LKS form* of ECSWS (formerly Landau-Kleffner syndrome) is characterized by aphasia and temporo-parietal location of epileptic activity whereas the *non-LKS form* is characterized by cognitive and behavioral changes and frontal location of epileptic activity. In both forms, seizures occur in the majority (but not all cases) before or after the onset of aphasia or neurobehavioral manifestations and frequent bilateral spikes and/or CSWS (detected with all-night EEG, polysomnography, or video-EEG monitoring) is required for diagnosis.

seizure types (non-active phase): focal clonic or hemiclonic seizures, complex partial seizures, secondary generalized tonic-clonic seizures; **(active phase):** atypical absences, atonic seizure, drop attacks, most seizures with onset before the active phase persist and become more frequent during the active phase; interictal CSWS pattern (see EEG below):

ictal EEG: *non-active phase*: focal seizures are infrequent; onset of focal seizures (including those that are secondarily generalized) usually temporal or parietal in LKS and frontal in non-LKS; *active phase*: atypical absences and atonic seizures occur with or without ictal EEG correlate; focal seizures are frequent; seizure onset usually temporal or parietal in LKS and frontal in non-LKS

interictal EEG (non-active phase): in wake: focal slow waves, spikes, and spike-waves, temporoparietal in LKS, frontal in non-LKS; infrequent bursts of bilateral 2-3 Hz spike-waves, absent in many LKS and some non-LKS; in sleep: increase amount of bilateral 2-3 Hz spike-waves but still < 85% of slow wave sleep; sleep spindles may be attenuated or absent in non-LKS patients; **(active phase):** in wake: abnormalities as in non-active phase but in greater amounts; in sleep: CSWS – nearly continuous bilateral 2-3 Hz spike-waves occupying > 85% of slow wave sleep; fragment or disappear in REM sleep; sleep architecture is preserved; intracranial EEG in LKS: focus of interictal activity in the posterior temporal lobe (often in superior temporal gyrus) and occasionally within the sylvian fissure near Heschl's gyrus

activation: sleep, especially slow wave sleep, activates bilateral 2-3 Hz spike-waves

course: focal seizures initially occur at a low rate; the onset of atypical absences and drop attacks coincides with an increase in the frequency of focal seizures and correlates with the appearance of CSWS; seizure frequency declines over the course of the illness in CSWS

etiology: malformations: focal cortical dysplasia, unilateral or bilateral perisylvian polymicrogyria, schizencephaly, others: arachnoid cyst, neoplasms, etc.

Migrating Focal Seizures in Infancy (MFSI)

seizure types: focal seizures with variable motor and autonomic manifestations, secondary generalized tonic-clonic seizures (later); less commonly: myoclonic seizures, epileptic spasms

ictal EEG: focal rhythmic theta appears at seizure onset decreasing in frequency as it spreads; subclinical seizures are common; as the number of independent seizure foci increase, seizures may begin before other seizures end and seizures may overlap as they spread producing a "migrating" picture

interictal EEG: multifocal spikes, mainly temporal, occipital, and rolandic; background slowing at onset or develops later, usually shifting in laterality

activation: multifocal spikes are not clearly affected by sleep

course: initially, seizures arise from one area and seizure-free intervals are common; seizures increase in frequency, more foci appear, and neurological function deteriorates; in a few months, multifocal seizures occur nearly continuously ("migrating" pattern), an interictal state is no longer evident, and sleep-wake differentiation is loss.

etiology: unknown

Dravet Syndrome (DS)

seizure types: febrile seizures, clonic, hemiclonic or tonic-clonic seizures, erratic myoclonus, myoclonic absences, atypical absences, massive bilateral myoclonus, tonic seizures, myoclonic status, tonic-clonic status; non-epileptic segmental myoclonus

ictal EEG: electrodecrement followed by slow spike-waves are associated with tonic-clonic seizures; tonic-clonic seizures as in idiopathic epilepsies except initial tonic phase is vibratory due to high frequency clonic activity; polyspike-waves occur with myoclonic jerks; slow spike-waves (2-3.5 Hz) appear during atypical absences; no EEG correlate for multifocal erratic myoclonus

interictal EEG: slow spike-waves and polyspike-waves; focal or multifocal spikes, usually central or posterior; rhythmic central theta activity; background activity is usually normal at onset; may remain normal for years before becoming slow

activation: sleep and drowsiness enhance IED; fever, infection, and hot-water immersion trigger seizures; PS induces PPR or seizures in > 2/5 of cases; movement may elicit non-epileptic myoclonus

course: febrile and clonic seizures appear first; myoclonic jerks and developmental delay appear later; myoclonus frequently disappears with age but can persist; EEG becomes more disorganized and spike-waves and polyspike-waves increase in prominence

etiology: 2q24 SCN1A gene encoding α1-subunit of voltage-gated sodium channel

Myoclonic Encephalopathy in Nonprogressive Disorders (MEND)

seizure types: myoclonic status, erratic myoclonus, myoclonic absences, atypical absences, massive myoclonus, focal clonic seizures, hemiclonic seizures, generalized clonic or tonic-clonic seizures, febrile convulsions: non-epileptic paroxysms: massive startles, intentional tremor

ictal EEG: slow spike-waves with bilateral myoclonus or myoclonic absences; bursts of bilateral spike-waves or slow waves alternating with periods of bicentral theta during myoclonic status; no EEG correlate for erratic myoclonus

interictal EEG: multifocal slow waves and spike-waves; intermittent bifrontal delta and bilateral parieto-occipital spike-waves; background slowing is also present

activation: drowsiness precipitates massive startles or myoclonic jerks; myoclonus disappear in slow wave sleep; multifocal spikes increase in frequency during slow-wave sleep and may mimic CSWS; epileptiform activity may occur only in sleep; other abnormal movements disappear in sleep; eye closure frequently elicits rhythmic bilateral parieto-occipital spike-waves

course: erratic myoclonus develops insidiously and may remain unrecognized for several months; atypical absences appear and increase in frequency; myoclonus increase in frequency, become more rhythmic and develops into myoclonic status

etiology: chromosomal disorder: Angelman syndrome, Wolf-Hirschhorn syndrome; metabolic disease: Rett syndrome; malformations: bilateral polymicrogyria, partial agenesis of the corpus callosum, microcephaly with vermis hypoplasia; destructive lesions: perinatal hypoxia-anoxia

Progressive Myoclonus Epilepsy (PME)

seizure types: focal or multifocal myoclonus, bilateral myoclonus, tonic-clonic seizures, atypical absence seizures, focal motor seizures, complex partial seizures, myoclonic status

ictal EEG: low-amplitude focal myoclonic jerks usually have *no EEG correlate* (both in the conventional and back-averaged EEG); *focal or multifocal spikes* may be present but are often independent interictal phenomena with no definite relation to the myoclonic jerks; large-amplitude focal myoclonic jerks may be associated with *focal slow waves, spike-waves, or polyspike-waves* in the conventional EEG and jerk-locked EEG back-averaging often reveals a large positive-negative *pre-myoclonic cortical potential* even when conventional EEG fails to show any change; with myoclonic jerk of the hand, the cortical potential has a latency of about 20 ms and a voltage maximum in the contralateral central region; bilateral myoclonus is often associated with *bifrontal slow waves, spike-waves, or polyspike-waves*; distinguishing the multifocal cortical myoclonus of PME from the thalamocortical myoclonus of idiopathic epilepsy can be difficult if there is rapid inter- and intrahemispheric spread of focal myoclonus.

EMG-EEG polygraphy: ballistic or tonic EMG pattern (50-300 msec agonist burst, asynchronous or synchronous antagonist burst) and absence of an EEG correlate indicates *non-epileptic myoclonus*; reflex EMG pattern (10-100 msec agonist burst, synchronous antagonist burst or silent period) and a cortical spike detected by routine EEG or burst-locked back-averaging indicates *epileptic myoclonus.*

interictal EEG: *focal* or *multifocal spikes*; the spikes are frequently independent interictal phenomena with no definite relation to the myoclonic jerks; vertex positive spikes suggest sialidosis; the background activity may be normal initially; with disease progression, mild slowing in the theta frequency range occurs in wake and the sleep background becomes disorganized; ultimately, both wake and sleep background activity become extremely slow and disorganized.

activation: *reflex myoclonus* evoked by proprioceptive (action or movement), tactile (touch), or acoustic (loud sound) stimuli is more common in PME than in JME; reflex myoclonus may be more prominent than spontaneous myoclonus early in the course of PME; *PPR* is frequently encountered in PME due to Lafora disease, Unverricht-Lundborg disease, and neuronal ceroid lipofuscinosis (NCL) but, as a rule, PPR is more common in JME than in PME; *PPR to single flashes* is consistent with NCL; *high-voltage photic driving* response to PS is most consistent with the late infantile and adult forms of NCL; *giant somatosensory evoked potentials* (SEPs) consisting of high-voltage P25, N30/P30 and/or N35 (N20/P20 is often normal) with median nerve stimulation is common in PME; it is unusual in JME and other syndromes where the main seizure type is bilateral thalamocortical myoclonus; *low intensity electrical stimulation* of the peripheral nerve (imperceptible and incapable of evoking cortical SEP in normal persons) may elicit responses in PME; the most prominent cortical SEPs early in the course of the disease occur in Unverricht-Lundborg disease; *long-loop reflexes* (especially C reflexes) are easily evoked by peripheral nerve stimulation (and often occur spontaneously); with median nerve stimulation, the C reflex latency is about 45 ms, thus C responses follow giant SEPs; *transcranial magnetic stimulation* (TMS)

course: myoclonus is the presenting seizure type in most patients (> 50%) but a large percentage of patients (~ 50%) initially manifest tonic-clonic seizures; initially, myoclonias may not be "spontaneous" and may occur only when activated by movement, noise, light, or other stimuli (see activation above); ultimately myoclonias occur "spontaneously"; myoclonus may generalize to a tonic-clonic seizure; some patients never manifest tonic-clonic seizures; other seizure types may also develop including absence seizures, dyscognitive seizures, and other focal (non-myoclonic) seizures; the "non-myoclonic" seizures are usually infrequent at the early stages of the disease, increase in frequency over a few years (3-7 years), and may entirely cease later; the myoclonic seizures tend to be progressive throughout life except in Unverricht-Lundborg disease wherein myoclonus may stabilize or even decrease in frequency with time.

etiology: *metabolic*: neuronal ceroid lipofuscinosis including infantile, late infantile, juvenile, and adult forms, the Finnish, Turkish, and early juvenile variants of the late infantile form, and the Northern epilepsy variant of the juvenile form, Unverricht-Lundborg disease, Lafora disease types A and B, sialidosis type 1, galactosialidosis, Gaucher disease type 3, dentatorubral-pallidoluysian atrophy, myoclonic epilepsy with ragged-red fibers, neuroaxonal dystrophy, β-galactosidase deficiency, GM2 gangliosidosis, celiac disease, juvenile Huntington disease, etc.

II. Idiopathic Generalized Epilepsies

Benign Myoclonic Epilepsy in Infancy (BMEI)

seizure types: bilateral myoclonus; simple febrile seizures preceding the myoclonus

ictal EEG: bisynchronous fast (>3-Hz) spike-waves and polyspike-waves with myoclonic jerks

interictal EEG: normal for age, central theta activity, bisynchronous spike-waves in REM sleep

activation: myoclonus occur in drowsiness and early stages of sleep; not favored by awakening; noise or contact induce myoclonus in some; PS trigger jerks in 10% of cases

course: normal before onset; jerks are initially subtle and increase in prominence, rarely cause falls; disappear in most but may persist in some if untreated; few develop tonic-clonic seizures in childhood

etiology: epilepsy gene has not been identified yet

Childhood Absence Epilepsy (CAE)

seizure types: typical absences only in childhood; tonic-clonic seizures may begin after childhood

ictal EEG: 3Hz spike-waves with typical absence (4–20 sec)

interictal EEG: 3Hz spike-waves (<4 sec) including fragments, bioccipital 3-Hz slow waves

activation: sleep activates and modifies expression of 3Hz spike-waves; SD is activating but not awakening from sleep, HV activate 3Hz spike-waves and absence seizures; hypoglycemia potentiates the effects of HV; PS elicits a PPR in some; eye-opening blocks bioccipital slow waves

course: complete remission in about 2/3 of cases; good to excellent response to AED; CAE evolving to JME becomes lifelong raising the possibility that this represents an early form of JME

etiology: 3q27 CLCN2 gene encoding voltage-gated chloride channel, 5q31 GABRG2 gene encoding γ2-subunit of GABA-A receptor; 8q24 candidate gene

Juvenile Absence Epilepsy (JAE)

seizure types: typical absences, tonic-clonic seizures, less commonly myoclonic seizures

ictal EEG: 3Hz spike-waves with typical absence, slightly faster and longer than in CAE; EEG correlate of myoclonus or tonic-clonic seizures (see JME)

interictal EEG: 3Hz spike-waves including fragments; background is usually normal

activation: tonic-clonic seizures usually occur on awakening, more likely with prior SD; sleep activates and modifies expression of 3Hz spike-waves; HV activates 3Hz spike-waves and absence seizures; PS is activating in a few cases

course: can be lifelong; good response to AED in the majority, some may be resistant

etiology: 3q27 CLCN2 gene encoding voltage-gated chloride channel

Juvenile Myoclonic Epilepsy (JME)

seizure types: bilateral myoclonus, fragments of bilateral myoclonus, tonic-clonic seizures, atypical absences, reflex myoclonus

ictal EEG: polyspike-waves with the spike component time-locked to the myoclonic EMG burst; similar discharges with rhythmic myoclonic jerks in the early clonic phase preceding tonic-clonic seizures; 3Hz spike-waves or rarely slow spike-waves during absences

interictal EEG: atypical spike-waves (4-6 Hz) including fragments; 3Hz spike-waves (1/5 of cases)

activation: awakening activates all types of seizure and IED; the effect is potentiated by prior SD, alcohol intake, or stress; drowsiness enhances polyspikes and spike-waves; SD precipitates seizures and IED; PS (10-20 Hz) triggers PPR, myoclonus, absences, or tonic-clonic seizures; eye closure may elicit polyspike-waves; talking or reading may induce peri-oral myoclonus; praxis is also activating

course: usually lifelong; good response to AED in the majority, some may be resistant

etiology: 3q27 CLCN2 gene encoding voltage-gated chloride channel, 2q22 CACNB4 gene encoding β4-subunit of voltage-gated calcium channel, 5q34 GABRA1 gene encoding α1-subunit of GABA-A receptor, 8q24 candidate gene (adult type); 6p12 EFHC1, 6p21 BRD2, and 15q14 susceptibility genes

Epilepsy with Generalized Tonic-Clonic Seizures Only (EGTCS)

seizure types: tonic-clonic seizures (no other seizure type)

ictal EEG: polyspikes during myoclonus or clonus in the pre-tonic phase of tonic-clonic seizures

interictal EEG: atypical spike-waves (4-6 Hz) including fragments; 3Hz spike-waves (1/5 of cases)

activation: tonic-clonic seizures occur within 1–2 h after awakening; a second evening peak may be present; polyspikes and spike-waves are more frequent after awakening; SD and alcohol can precipitate seizures and IED upon awakening; PS elicits PPR in 18% of cases

course: can be lifelong; good response to AED in the majority, some may be resistant

etiology: 3q27 CLCN2 gene encoding voltage-gated chloride channel

Generalized Epilepsy with Febrile Seizures Plus (GEFS+)

seizure types: typical febrile seizures (age < 6 years), febrile seizures plus (age > 6 years), afebrile tonic-clonic seizures; less commonly absences, myoclonus, atonic seizures; some members of GEFS+ families have EMAS or DS

ictal EEG: pattern consistent with tonic-clonic seizure during febrile seizures; 3Hz spike-waves with l absence seizures; polyspikes during myoclonus

interictal EEG: 3Hz spike-waves; atypical spike-waves; polyspike-waves

activation: fever commonly activates seizures early in life (age < 6 years); in some patients fever may still activate seizures even at an older age (age > 6 years); HV and PS may be activating.

course: remission of febrile seizures plus usually occurs around age 12 years; afebrile seizures occur rarely in some patients and frequently in others; spontaneous or AED-induced remission occur in many but not all patients; the range of interfamilial and intrafamilial variation in AED response or resistance can be broad.

etiology: 2q24 SCN1A gene encoding α1-subunit, 2q24 SCN2A gene encoding α2-subunit, and 19q13 SCN1B gene encoding β1-subunit of voltage-gated sodium channel; 5q31 GABRG2 gene encoding γ2-subunit of GABA-A receptor

Epilepsy with Myoclonic Absences (EMA)

seizure types: myoclonic absences, tonic-clonic seizures, less commonly typical absences, myoclonic absence status, atonic seizures

ictal EEG: 3Hz spike-waves with or without bifrontal delta waves at the end occur during myoclonic absences with the spike components time-locked to the myoclonic jerks (also 3 Hz)

interictal EEG: 3Hz spike-waves, focal or multifocal spike-waves, normal background

activation: awakening can precipitate seizures; seizures become less frequent as sleep deepens; PS and HV may precipitate seizures in some

course: may be associated with psychomotor impairment; AED resistance is common; myoclonic absences may evolve to typical absences and tonic seizures

etiology: chromosome lesions: Angelman syndrome, trisomy 12p

Epilepsy with Myoclonic-Astatic Seizures (EMAS)

seizure types: myoclonic-atonic seizures, myoclonic seizures, atypical absences, myoclonic status with obtundation, less commonly tonic-clonic seizures, tonic seizures

ictal EEG: 3-Hz polyspike-waves followed by EMG silence (up to 500 msec) during myoclonic-atonic seizures: the spikes are time-locked with the jerks and the EMG silence coincides with atonia.

interictal EEG: 3Hz spike-waves; parietal theta activity (4-7 Hz); occipital delta or theta (4-Hz)

activation: PS elicits a PPR in some; eye closure precipitates occipital theta (4-Hz)

course: outcome varies from complete remission to poor outcome with cognitive impairment; AED response varies from good to AED resistance; EEG background is usually normal at onset, becomes slow with disease progression, and may normalize with disease resolution

etiology: detected in a few patients with EMAS within GEFS+ families: 19q13 SCN1B gene encoding β1-subunit of voltage-gated sodium channel, 2q24 SCN1A gene encoding α1-subunit of voltage-gated sodium channel

III. Idiopathic Focal Epilepsies

Benign Familial Neonatal Seizures (BFNS)

seizure types: focal tonic or clonic seizures with or without automatisms, apnea is common and usually occurs first; seizure types are often mixed

ictal EEG: diffuse attenuation at the onset of focal seizure

interictal EEG: often normal; theta pointu alternant (~2/3 of cases); other non-specific abnormalities

course: onset in neonatal period, often in the first week (~1/2 of cases); remission around age 4 months is the rule; about 10% develop febrile or afebrile seizures in childhood

etiology: 20q13 KCNQ2 or 8q24 KCNQ3 gene encoding α-subunit of voltage-gated potassium channel

Benign Familial and Non-familial Infantile Seizures (BFNIS)

seizure types: focal, tonic, clonic, or hypomotor seizures with or without automatisms; apnea and other autonomic changes; bilateral motor activity may be due to focal frontal lobe activation (e.g. SMA) although this has been described as "secondarily generalized" seizures

ictal EEG: no correlate in about ½ of cases; focal temporal, bitemporal, frontal, parietal, or occipital rhythmic spikes or sharp waves seizure clusters are common (~3/4 of cases)

interictal EEG: normal interictal EEG is required for diagnosis

course: normal development (required) at onset; remission in early childhood in the majority; some (~1/10) develop mental retardation and persistent seizures requiring change in syndrome diagnosis

etiology: 2q24 SCN2A gene encoding α-subunit of voltage-gated sodium channel; 19q12 and 16q candidate genes

Benign Childhood Epilepsy with Centrotemporal Spikes (BCECTS)

seizure types: rolandic seizures manifesting as paresthesia of oral mucosa, hypersalivation, and contractions of face, tongue, and pharyngeal muscles resulting in dysarthria, dysphagia, and drooling; spread to motor cortex result in jerking of the arm, rarely the leg; secondary generalization

ictal EEG: focal centrotemporal attenuation or low-voltage fast activity at the onset of seizure may evolve into spike discharge and spike-wave activity; onset may shift sides; may also generalize

interictal EEG: rolandic or centro-midtemporal spikes; less frequently: bisynchronous spike-waves, occipital spikes, frontal spikes, multifocal spikes; background activity is usually normal

activation: NREM sleep (all stages) causes a dramatic increase in the density of rolandic spikes; in 1/3 of cases, rolandic spikes occur only in sleep; PS, HV, and eye closure have no significant effect

course: seizures and EEG manifestations usually resolve before age 16 years; very low risk of adult epilepsy (~ 3%); evolution to LKS-type of ECSWS is rare

etiology: 15q14 candidate gene; rare cases with associated cortical dysplasia or tumor

Early-onset Benign Childhood Occipital Epilepsy (BCEOS-1)

seizure types: autonomic seizures: ictal nausea ± emesis ± other autonomic changes, deviation of eyes ± head; visual seizures less common than BCEOS-2; rolandic and other focal seizures; secondary generalization; focal status epilepticus (common); ictal syncope (rare);

ictal EEG: occipital rhythmic theta or delta activity at the onset of seizure; bifrontal ictal onset

interictal EEG: IED morphology resembles rolandic spikes but with variable foci including occipital, rolandic, frontal, and bifrontal; frequently multifocal; normal wake and sleep background activity

activation: NREM sleep activates occipital spikes and seizures; elimination of visual fixation activates occipital spikes (fixation-off sensitivity or scotosensitivity); PS and HV have no significant effects

course: first seizure around age 5 years; most have only a few seizures; seizures are usually controlled with monotherapy; EEG normalizes around age 10 years; risk of adult epilepsy is not increased

etiology: epilepsy genes suspected but not yet identified; part of the BCECTS-BCEOS spectrum

Late-onset Childhood Occipital Epilepsy (BCEOS-2)

seizure types: visual seizures; spread to rolandic area, motor cortex or temporal lobe; secondary generalization; focal status epilepticus; *postictal headache* common and misdiagnosed as migraine

ictal EEG: occipital and posterior temporal fast spike discharge at onset of seizure

interictal EEG: occipital spikes with stereotyped morphology and prominent occipital voltage peak; background activity is usually normal in wake and sleep

activation: NREM sleep activates occipital spikes and seizures; REM sleep is inhibitory; elimination of visual fixation activates occipital spikes (fixation-off sensitivity or scotosensitivity); PS has no effect in most patients, in a few PS either activates or inhibits occipital spikes; HV has inconsistent effects

course: first seizure around age 8 years; significant risk of adult epilepsy (~20%); continuation of AED is often necessary

etiology: epilepsy genes suspected but not yet identified; part of the BCECTS-BCEOS spectrum

Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE)

seizure types: frontal lobe seizures manifesting as paroxysmal arousal, nocturnal paroxysmal dystonia, episodic nocturnal wanderings (rare); secondary generalization

ictal EEG: often obscured by artifacts; no correlate (~1/2 of cases); seizure onset in NREM sleep: focal frontal/frontotemporal attenuation, rhythmic theta/delta, or fast activity; temporal-onset (~14%)

interictal EEG: no IED (~1/2 of cases); wake IED (~1/3 of cases), sleep IED (~1/2 of cases); frontal or frontotemporal (~2/3), temporal (~1/3); wake-sleep background is usually normal

activation: NREM sleep, especially stage 2, is activating resulting in nocturnal preponderance; seizures in wake occur in about 1/3 of cases (usually when seizure control is poor) but are not frequent

course: response to AED (carbamazepine) is good in ~2/3 of cases; ~1/3 are carbamazepine-resistant

etiology: 20q13 CHRNA4 gene encoding α4-subunit and 1q21 CHRNB2 gene encoding β2-subunit of nicotinic acetylcholine receptor; 15q24 candidate gene; sporadic cases with ADNFLE phenotype.

Familial Temporal Lobe Epilepsy (FTLE)

seizure types: mesial temporal lobe seizures, lateral temporal lobe seizures, secondary generalization; history of febrile seizures is common in mesial-FTLE; déjà vu is a common aura in some mesial-FTLE series and auditory auras are common in lateral-FTLE

ictal EEG: The two FTLE phenotypes, mesial-FTLE and lateral-FTLE, share the electroclinical features of MTLE and LTLE, respectively

interictal EEG: frequently normal; occasionally, anterior temporal or posterior temporal spikes or sharp waves

activation: inconsistent activation with NREM sleep (needs further studies)

course: age of onset is variable, seizures are easily controlled with antiepileptic drugs (AEDs).

etiology: 10q24 LGI1 gene encoding leucine-rich glioma inactivated protein in lateral-FTLE; sporadic cases with lateral-FTLE phenotype; lateral temporal malformation in lateral-FTLE; 4q13 candidate gene in mesial-FTLE; hippocampal sclerosis present in ~1/2 of mesial-FTLE cases

Familial Focal Epilepsy with Variable Foci (FFEVF)

seizure types: frontal lobe seizures, temporal lobe seizures; rarely occipital and parietal lobe seizures; seizures types are constant for each individual, vary among members of the same family

ictal EEG: variable and depends on the seizure type

interictal EEG: frequently normal; occasionally, spikes or sharp waves are detected in the frontal, temporal, or other areas

activation: much less consistent activation with NREM sleep compared to ADFLE (needs further studies)

course: intrafamilial heterogeneity in seizure outcome; *compared to ADNFLE*: seizures are less frequent, clusters and auras are rare, and daytime seizures and secondary generalization are more frequent

etiology: 22q11 candidate gene

IV. Symptomatic Focal Epilepsies

Mesial Temporal Lobe Epilepsy (MTLE)

seizure types: mesial temporal seizures, mesial temporal auras, mesial temporal seizures with spread to lateral temporal neocortex, mesial temporal seizures with extratemporal spread, mesial temporal seizures with secondary generalization; less commonly complex partial status, tonic-clonic status, or aura continua; history of febrile seizures

ictal EEG: rhythmic theta or alpha activity in one or both temporal regions within 30 sec of the clinical onset; initial change can be voltage attenuation or low-voltage fast activity; slower (2-5 Hz), more polymorphic, bilateral or diffuse patterns are possible but more common in LTLE

interictal EEG: temporal spikes with maximal anterobasal (FT9, FT10, or sphenoidal) negativity and broad vertex positivity; independent bitemporal spikes may be present (~ 1/3 of cases); middle or posterior temporal spikes are possible but more consistent with LTLE; spikes are absent in (~ 10% of cases); interictal abnormality may be limited to focal slow-waves or asymmetries; rarely, the interictal EEG is normal

activation: sleep and SD are activating,

course: variable depending on etiology; intractability is common with hippocampal sclerosis, focal cortical dysplasia and other malformative lesions, and certain neoplasms (e.g. dysembryoplastic neuroectodermal tumor, ganglioglioma)

etiology: hippocampal sclerosis, cortical malformations, vascular malformations, neoplasms, meningitis, encephalitis, traumatic brain injury, dual patholgy (often hippocampal sclerosis and focal cortical dysplasia), etc.

Lateral Temporal Lobe Epilepsy (LTLE)

seizure types: lateral temporal seizures, lateral temporal seizures with mesial temporal spread, lateral temporal seizures with extratemporal spread and/or secondary generalization; less commonly complex partial status, tonic-clonic status, history of febrile seizures is much less prominent than MTLE

ictal EEG: rhythmic theta or delta activity in one or both temporal regions appear 30 sec or more after the clinical onset; voltage attenuation or low-voltage fast activity may appear initially; slower (2-5 Hz), more polymorphic, bilateral or diffuse patterns, and absence of EEG correlate are more common in LTS than in MTS.

interictal EEG: temporal spikes with broad temporal negativity and no vertex positivity; occasionally maximal mid-temporal (T7/T8) or posterior temporal (P7/P8) negativity; independent bitemporal spikes may be present; interictal changes may be limited to focal slow-waves or background asymmetry; interictal EEG can be normal

activation: sleep and SD are activating

course: variable depending on etiology; intractability is common with focal cortical dysplasia and other malformative lesions

etiology: cortical malformations, vascular malformations, neoplasms, hippocampal sclerosis (less frequently associated with LTLE compared to MTLE), meningitis, encephalitis, traumatic brain injury, brain infarction, etc.

Frontal Lobe Epilepsy (FLE)

seizure types: focal clonic seizures, jacksonian seizures, asymmetric tonic seizures, frontal lobe complex partial seizures, frontal lobe seizures (mixed type), frontal lobe seizures with spread outside the frontal lobe and/or secondary generalization; less commonly tonic-clonic status, focal status

ictal EEG: normal, obscured by artifact, non-localizing (due to rapid generalization), or any of these patterns: frontal low-voltage fast activity or rhythmic spike-waves with focal clonic seizures, low-voltage fast activity or attenuation near the vertex with supplementary motor area seizures, bifrontal voltage attenuation often followed by rhythmic theta/delta with mesiofrontal or orbitofrontal seizure, frontopolar rhythmic alpha/beta with orbitofrontal seizures

interictal EEG: normal, non-epileptiform EEG patterns, non-lateralizing/non-localizing IEDs, or localizing/lateralizing IED (~1/2 of cases); secondary bilateral synchrony is common and often due to mesial-FLE; midline spikes also suggest a mesial frontal focus; lateralized frontal intermittent delta waves suggests an orbitofrontal focus

activation: propensity to occur in NREM sleep (nocturnal predominance)

course: variable depending on etiology

etiology: cortical malformations, vascular malformations, neoplasms, traumatic brain injury, brain infarction or hemorrhage, meningitis, encephalitis, other destructive lesions.

Parietal Lobe Epilepsy (PLE)

seizure types: parietal lobe seizures, parietal lobe seizures with posterior spread, anterior spread, or inferior temporal lobe spread, parietal lobe seizures with secondary generalization; less commonly limbic or tonic-clonic status

ictal EEG: parietal lobe seizures often begin as a somatosensory aura with no EEG correlate; any subsequent discharge is often due to seizure spread to the temporal region, supplementary motor area, or other parts of the frontal lobe.

interictal EEG: parietal lobe spikes are elusive; patients with symptomatic PLE can manifest non-localizing or falsely-localizing temporal or frontal IED

activation: inconsistent activation by sleep and SD (insufficient data)

course: variable depending on etiology; some

etiology: cortical malformations, vascular malformations, neoplasms, traumatic brain injury, brain infarction or hemorrhage, meningitis, encephalitis, auto-immune disorders, other destructive lesions.

Occipital Lobe Epilepsy (OLE)

seizure types: occipital lobe seizures, occipital lobe seizures with infrasylvian or suprasylvian spread, occipital lobe seizures with secondary generalization; less commonly tonic-clonic or focal status

ictal EEG: occipital or temporo-occipital discharge may coincide with onset of visual seizure; a falsely-localizing EEG (e.g. temporal onset) is not uncommon.

interictal EEG: a wide array of IEDs is found in symptomatic OLE, including occipital or bioccipital spikes, widely distributed IEDs, and falsely-localizing IEDs (e.g. temporal or frontal spikes).

activation: sleep and SD may be activating (insufficient data)

course: variable depending on etiology

etiology: cortical malformations, vascular malformations, neoplasms, traumatic brain injury, brain infarction or hemorrhage, meningitis, encephalitis, auto-immune disorders (e.g. celiac disease), other destructive lesions

Hemiconvulsion-Hemiplegia Syndrome (HHS)

seizure types: hemiclonic status, hemiclonic seizures, tonic-clonic status, temporal lobe seizures, temporal lobe seizures with extratemporal spread, secondary generalization; extratemporal and other focal seizures

ictal EEG: focal onset (usually central or occipital) spikes or fast rhythms contralateral to the jerks with rapid spread; unihemispheric or lateralized (often posterior) high-voltage rhythmic 2-3 Hz slow waves or spike-waves.

interictal EEG: focal spikes or sharp waves; unihemispheric or lateralized slow waves.

course: abrupt onset of hemiclonic status (may alternate between sides); hemiplegia develops early and is permanent in most cases (moderate to severe in >80%); full recovery is rare; recurrent focal seizures develop 1-3 years after onset (hemiconvulsion-hemiplegia-epilepsy syndrome) in about 80% of cases; mild cognitive impairment is common.

etiology: prenatal or perinatal lesions, acute meningitis, subdural effusions, head trauma, etc.; *idiopathic cases*: may be due to prolonged febrile convulsions inducing brain injury in genetically susceptible children.

Rasmussen Syndrome (RS)

seizure types: focal motor seizures, hemiclonic seizures, EPC (focal myoclonic status epilepticus), complex partial seizures, tonic-clonic seizures, focal status other than EPC, tonic-clonic status.

ictal EEG: focal seizures are lateralized but not easy to localize; subclinical seizures are common; EPC consists of asynchronous jerks or twitches in different parts of the body; focal seizures and EPC are independent: activation occurs in the rolandic sulcus before the myoclonic jerk and in the neocortical convexity before the focal seizure.

interictal EEG: focal spikes are initially unilateral; with time, the number of independent spike foci increase; eventually spikes occur bilaterally but remain lateralized; bisynchronous spike-waves also occur (~ 50% of cases); background slowing and focal slow waves which are initially unilateral become bilateral but are always lateralized.

course: initially, focal seizures are prominent and hemiparesis is transient; seizures increase in frequency, EPC develops, and hemiparesis becomes permanent; seizure frequency increase further and neurologic deficits worsen; finally, the disease "burns out" - seizures become less frequent and neurological disability reaches a plateau.

etiology: unknown; inflammatory, auto-immune, and infectious etiologies have been implicated.

V. Reflex Epilepsies

Idiopathic Photosensitive Occipital Lobe Epilepsy (IPOLE)

seizure types: reflex occipital lobe seizures; rarely with temporal spread or secondary generalization

ictal EEG: photic-induced occipital lobe seizures: onset in Oz and shifting laterality; PPR followed by buildup of occipital ictal discharge; exaggerated driving evolving to a self-sustained ictal activity

interictal EEG: spontaneous focal occipital spikes, rarely bisynchronous spike-waves; no spontaneous interictal spikes in some; wake and sleep background is usually normal (including alpha rhythm)

activation: flicker (TV, video games, sunlight, strobe lights) induce seizures; PS evokes symmetric or lateralized bioccipital spikes; enhanced by eye closure; PPR occurs in some patients

course: most only have a few seizures, achieve AED-induced remission, and can be allowed moderate use of the computer and TV; despite AEDs some may have occasional seizures, especially if their *photosensitivity range* is wide; PPR persists through early adulthood in > 2/3 of patients with photosensitivity (no IPOLE-specific data)

etiology: unknown; genetic mechanism suspected but not yet established

Visual Pattern Sensitive Epilepsy (VPSE)

seizure types: reflex tonic-clonic, myoclonic, or absence seizures

ictal EEG: seizures evoked by pattern stimulation

interictal EEG: pattern-induced PPR; other responses are not specific can be confined to posterior regions; no PPR in some; wake and sleep background is usually normal (including alpha rhythm)

activation: visual patterns (stripes, etc) induce seizures; vibrating > stationary; photosensitivity is common; eye closure (fixation-off) sensitivity in some; self-induction of seizures can be pleasurable and is common

course: most patients achieve AED-induced remission; relapse is likely with early AED withdrawal (especially around teens); seizure control is less satisfactory in patients with a wide *range of photosensitivity*; photosensitivity disappears in only ~25% (usually around the third decade)

etiology: unknown; genetic mechanism suspected but not yet established

Primary Reading Epilepsy (PRE)

seizure types: reflex myoclonic jaw jerks, bilateral myoclonus, aphasic seizures, absence seizures, tonic-clonic seizures

ictal EEG: bisymmetric, lateralized, or focal left temporoparietal or frontocentroparietal spikes, spike-waves, or rhythmic theta during myoclonic jaw jerks; bisynchronous spike-waves during bilateral myoclonus or absences

interictal EEG: without activation: normal (80%), spontaneous bisynchronous spike-waves (10%) or focal temporal spikes (5%); wake and sleep background is usually normal

activation: language tasks induce seizures and/or spikes or spike-waves; PPR may occur (~10% of cases)

course: good seizure control in most patients with valproate or clonazepam; some adapt by learning to stop reading immediately at the onset of seizures

etiology: genetic mechanism suspected but not yet established; may be related to JME and other idiopathic epilepsies

Epilepsy with Startle-Induced Seizures (ESIS)

seizure types: reflex tonic, tonic-atonic, or myoclonic seizures; in patients with hemiparesis, the weak side is preferentially involved; infrequent spontaneous seizures occur in all cases

ictal EEG: scalp vertex spikes followed by flattening or low-voltage activity during reflex seizures; intracranial EEG: motor evoked responses followed by ictal discharge in the motor-premotor areas

interictal EEG: spontaneous or startle-induced focal spikes or spike-waves; often lateralized especially when unilateral lesions and hemiparesis are present; background asymmetries and slowing are common

activation: stimulus (usually auditory) triggers a startle response followed by seizure; habituation may occur

course: seizure control is usually incomplete or only temporary; intractable epilepsy is common; many have cerebral palsy (especially hemiparesis) and cognitive impairment; AED-induced remission is possible in mild cases

etiology: birth-related or congenital destructive brain lesions or encephalopathy early in life