The Psychoses of Epilepsy

- Psychosis occurs in up to 7% of patients with epilepsy. There is a bidirectional association between the two.
- Risk Factors for psychosis of epilepsy: early onset of epilepsy, autism spectrum disorder, family history of psychosis or mood disorder, temporal (or frontal) lobe epilepsy, L sided mesial hippocampal sclerosis, status epilepticus, refractory seizures/poor adherence

Differential diagnosis for psychoses of epilepsy

- Acute and transient psychotic disorder, schizophrenia, bipolar disorder, folie a deux, non-epileptic seizures, factitious disorder
- **Anti-seizure medication-induced**: **levetiracetam**, **zonisamide**, vigabatrin, **topiramate**, brivaracetam, multiple ASMs causing **cerebellar cognitive affective syndrome** (CCAS), or CCAS from cerebellar atrophy from chronic ASM exposure
- Post-ictal psychosis
- Ictal psychosis
- Schizophrenia-like psychosis of epilepsy (interictal psychosis)
- **Alternative psychosis** (also called **forced normalization psychosis** or **Landolt phenomena**). Occurs with improvement of seizures, normalization of EEG, emergence of psychosis

Phenomenology

- **Post-ictal psychosis:** most commonly in TLE or FLE, may be R sided lesions, typically occurs after a cluster of seizures, up to 6% of EMU admissions, lucid interval up to 72h, lasts between 1 day and 3 months, typically with grandiosity, religious delusions, sometimes hypersexuality (i.e. looks like mania). More persecutory themes have been described as well. Must either have clouding of consciousness and/or delusions and hallucinations.
- **Ictal psychosis:** most commonly in TLE or FLE – includes auditory, visual, olfactory hallucinations, paranoia, fear, excitement, aggression, transient, episodic, stereotyped, associated with other features (e.g. motor symptoms, autonomic symptoms, automatisms), may be amnestic for symptoms, or confused after
- **Schizophrenia-like psychosis of epilepsy (interictal):** not temporally associated with seizures, risk factors described above, can occur with same age of onset as primary 'schizophrenia' or later, may be clinically indistinguishable. Often thought to have less negative symptoms but pts with FLE often have apathy, withdrawal etc.
- More unusual symptoms should prompt evaluation for possible epilepsy or other neurological disorders: **delusions of misidentification** (Capgras, Fregoli, intermetamorphosis), **reduplicative paramnesia**, **Cotard syndrome**, **Alice in Wonderland Syndrome** (**macropsia**, **micropsia**, time distortion), **autoscopy** (subjective doubles)

Differential for seizures and psychosis:

- Vascular: stroke, cerebrovascular disease, cerebral amyloid angiopathy, primary angiitis of CNS, PRES (posterior reversible encephalopathy syndrome)
- **TBI, chronic traumatic encephalopathy**
- Autoimmune: SLE (e.g. lupus cerebritis or NP-SLE), **antiphospholipid syndrome**, **limbic encephalitidies** (e.g. anti-NMDA-R, anti-LGI1, anti-GABA-B, anti-AMPA-R), neurosarcoidosis, Sjögren's syndrome
- Inborn errors of metabolism: metachromatic leukodystrophy, **mitochondrial disease** (e.g. MELAS)
- Nutritional: Wernicke-Korsakoff syndrome
- Neoplastic: primary brain tumors, cerebral metastases, paraneoplastic limbic encephalitis
- Degenerative: **Alzheimer's disease**, bvFTD, less so DLB
- Substances/toxins: **alcohol** withdrawal, **benzo** withdrawal, gabapentin withdrawal, intoxication with cocaine, amphetamines, PCP, spice and other **synthetic cannabinoids**, disulfiram, **serotonin toxicity**

Management

- Establish temporality of psychosis and seizures and exposure/withdrawal of ASMs to establish diagnosis
- Rule out limbic encephalitis, TBI, neurodegenerative disease where history and exam point in that direction
- For post-ictal psychosis benzos (e.g. clonazepam) and low dose antipsychotics are helpful briefly. In refractory cases epilepsy surgery may be necessary
- For ictal "psychosis" treatment with ASMs and benzos most appropriate
- For schizophrenia like psychosis of epilepsy long-term neuroleptics may be needed. Try to avoid loxapine, clozapine, and chlorpromazine where possible.