Drug exposure and EEG/qEEG findings

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General comments:

There is a generally reciprocal effect between alpha and beta, as brain stem stimulation desynchronizes the alpha generators, beta is seen. During states of under-arousal, this relationship is not seen, as when the subject is alerted, when both alpha and beta increase.

The point is that *the arousal level changes the EEG responses expected*, as when a stimulant is given to an under-aroused subject, increasing alpha. In a normally aroused subject, stimulants decrease alpha, and in an anxious (low voltage fast EEG variant) subject alpha will not be seen as changed by a stimulant.

Though there is a *response stereotype* for each medication, there are also individual responses, which vary. Mixtures of medications become too complex to evaluate each individual medication's contribution, not to speak of *synergistic effects* not seen with any single medication, which may be seen in polytherapy.

The following pages represent a summary of many articles, papers, reviews and books on medications and the CNS function, and finally nearly 30 years of experience in clinical and research EEG. The difficulty in this area is the definitions of bands varies, the methods of analysis range from visual inspection of the raw EEG to quantitative measures, not all of which are clearly defined… and thus the need for a brief summary which puts this into a concise form for reference.

I will use the following definitions for the EEG bands. *Delta* is .5-3.5 Hz.; *theta* is 3.5-7 Hz, with slowing describing activity starting in the delta band, fading out in amplitude through the theta band. *Alpha* is 7-13 Hz, with "*high alpha*" being 11-15 or 16 Hz. *Beta is* from 13 Hz to the high frequency response of the system.

Due to the difficulty in visually detecting many of the changes reported, even small but significant changes can be missed. Don't expect to "see" every change noted in each patient, or when using only visual inspection.

Marijuana/ Hashish/ THC:

There is increased frontal alpha, with increased frontal interhemispheric hypercoherence and phase synchrony. These findings are reported in chronic exposures.

Effects on the evoked potentials have been noted as well.

Lysergic acid diethylamide (LSD-25):

The baseline EEG seems to determine the effect, with decreased alpha and increased beta from a normal background. With slower EEGs, there is an increase in alpha and fast activity. The low voltage fast EEG shows little change in spectral profile with exposure.

The increase in *conditioned inhibition* seen with lower doses corresponds to the decrease in paroxysmal activity. The stimulant effects of this powerful drug may cause convulsions at higher doses, such as the early government studies. In these studies, *milligram* doses were supplanted for the *microgram* recommendations from Switzerland, where the LDS was produced.

PCP, Phencyclidine, or angel dust:

There is a marked increase in slow activity, with paroxysmal activity and extreme voltages noted with increased dosage. Convulsions have been reported.

Barbiturates:

Rhythmic 18 to 26 Hz activity is noted, initially frontally, spreading with time to the entire cortex. With increased dose there is an increase in slowing, with further increases the faster activity is decreased and the slowing predominates, progressing to a decreased voltage and even a recoverable iso-electric pattern, in barbiturate coma.

Morphine/Opiates/Heroin:

Shortly following administration, there is increased alpha, with slowing of alpha during the euphoric high, with increased dose there is increased slowing, and like barbiturates the EEG may go iso-electric. There is an increase in REM sleep noted with opioids.

Alcohol:

Ethanol at higher levels causes slowing to occur, with the depressant effect seen behaviorally. In the low voltage fast type EEG (seen in anxious, nervous and in many chronic alcoholics and their family members), the initial alcohol exposure causes the sudden occurrence of alpha. With severe chronic alcoholism, there can be an abnormal pattern *of periodic lateralized epileptiform discharges (PLEDS)* seen with obtundation. This is not true underlying epilepsy, but rather disappears with the treatment of the alcoholism.

Neuroleptics:

"Tranquilizers" such as *chlorpromazine*, or it's equivalent, increase the coherence of the EEG and decrease beta, however they increase temporal and frontal sharp morphologic theta transients. There is a reduced alpha blocking with sensory stimulation, likely corresponding to the memory disturbance reported with these medications.

In cases of *dopamine receptor hypersensitivity* (tardive dyskinesia) there are prolonged bursts of mixed fast/sharp transients and slowing. There is a potentiation of latent epileptiform activity, even with lower doses.

Thioridazine also increases faster activity, accounting for its commonly reported antidepressant effects.

Clozapine, or Clozaril, shows the typical neuroleptic pattern, though with an increase in epileptiform discharges and increasing possibility with duration of medication usage, reaching as high as 30% of patients with epileptogenic EEGs after 3 years of use.

Anxiolytics:

Meprobamate was the first anxiolytic, or anti-anxiety, medication. It decreases alpha and increases beta over 20 Hz, also slightly increasing theta, while not increasing epileptiform activity or paroxysms. The *benzodiazapines,* like *Valium or Ativan* also decrease alpha and increase the 20-30 Hz band, with a sinusoidal hyper-rhythmic spindling waveform. Paroxysmal and epileptiform discharges are reduced with these medications. The effect of decreasing neural has been used for its anti-epileptic qualities, especially in cases of *status epilepticus*, where Intravenous Valium has the apparently "comatose" patient sitting up wondering what has been happening.

Hormones:

Vasopressin, usually in the form of DDAVP (desomopressin acetate), increases the high alpha band. *Cyproterone acetate* is an anti-androgen with clinical effects on premenstrual complaints, though the qEEG effects predicted its strong anti-anxiety and mood elevating side effects. The decrease in frontal alpha and increased beta are noted.

Antidepressants:

Imipramine:

This drug produces an increase in slow activity, a decrease in alpha and high alpha, with an increase in the faster beta frequencies in the mid to upper 20 Hz range and up.

Amitriptyline: This drug produces more slowing than imipramine, though the other effects are similar. This corresponds to an increased initial sedative effect and its use as a sleeping medication for sleep onset as well as the usual wakefulness effects of antidepressants. In epileptics, there are increases in paroxysmal discharges, which can be controlled normally with adjustments to the anti-epileptic medications.

Ipronazid: This drug produces a slight increase in slower activity, though it produces a marked increase in faster activity. Paradoxically, this antidepressant does not produce an increase epileptiform profile or promote convulsions, even with this beta increase.

MAO Inhibitors: These medications have a wider variation of response than the other antidepressants. *Isocarboxazide* increases 30-20 Hz and decreases slower and higher frequencies, similar to a stimulant profile. *Nialamide and Tranylcypromine produce* a more typical profile, though with more variability.

SSRIs: These more modern antidepressants, such as Prozac, Paxil and Zoloft have fewer changes in the slow activity (associated with less viscero/autonomic side-effect), with a mild fronto-central beta increase in the range of 18-25 Hz and a decrease in alpha anteriorly.

Stimulants:

Stimulants increase the activity in the RAS, with the Raphe nucleus releasing norepinephrine, decreasing the polarization in the reticular nucleus of the thalamus and thus increasing the "clocking" or peak frequency of the rhythmic alpha activity and increasing faster activity.

Amphetamines: Both *dextro and methamphetamines* like *Dextrostat or Adderal* are similar in effect, with decreased slower activity and increased beta from 12-26 Hz. There is a paradoxical increase in alpha noted in the CEEG work of Itil (Itil et al., 1980). This is likely from the increased activation effect mentioned in the opening section.

Methylphenidate: *Ritalin* produces a decrease in delta and theta, with a more pronounced posterior alpha increase and an increase in low beta, with effects delayed up to 6 hours, compared to the rapid effects of the amphetamines.

Caffeine: This moderate stimulant has a moderate length of effect, but has surprisingly little research on its EEG effect. A fairly current study of its withdrawal effects (Clinical EEG, Vol. 26 No.3, July 1995) shows an alpha increase frontally, with suppression following resumption. The study also shows theta increases with withdrawal, maximal the second day, resolving with resumption. The degree of change in both frequencies corresponds well to the subjective withdrawal severity.

Nicotine: This drug has similar effects to caffeine, including the withdrawal study (Itil et al., 1971).

Cocaine: The effects of cocaine differ from the amphetamines in that cocaine decreases *synaptic reuptake,* and amphetamines increase the release of the neurotransmitters in the *dopamine/norepinephrine* systems in the brain. With lower to moderate doses, there is increased alpha and beta. With increased doses there is a *desynchronization* of the EEG and faster activity predominates.

The alpha increase frontally is seen during the euphoric phase of the subjective report. Cocaine is a well-known *epileptic potentiator*. Chronic abuse causes a "burned out" dopamine system, with delta decreases and slower alpha noted with little improvement even one year later

Antimanics:

Lithium carbonate is used extensively to treat bipolar depression, reducing the manic behavior and being prophylactic to depressive recurrences and further mania. The EEG shows an increase in theta, mild decrease in alpha as well as increased faster activity, with a strong potentiation of latent epileptiform activity. This mimics the tricyclic anti-depressant profile, though with slower slows and more fast activity.

Overdoses produce a marked slowing of the EEG, with *triphasic* discharges reported, likely associated with the liver toxicity and the associated metabolic disturbances, similar to the findings in *hepatic encephalopathies*. These slower findings may be noted many weeks

following discharge from the hospital. Slowing of alpha (rhythmic background that responds to eye opening) down to 4 and 5 Hz two weeks after discharge from hospitalization, with normal 9 Hz alpha in the child returning only after many months is reported in a case study (NeuroNet Neuroscience Centers, 1999).

Tuburculostatics:

INH, *Isonicotinic acid hydrazide*, is an irritant to the CNS. Large doses can hypersensitize the CNS. The EEG shows bursts of paroxysmal activity with photic stimulation.

Methanol:

The EEG shows marked slowing, which correlates with the extent of *acidosis* more than the blood levels of methanol. This has been shown to be quite *neuro-toxic*, with optic nerve blindness noted commonly in chronic abuse/exposure.

Solvents:

The EEG show slowing, though the etiology remains uncertain, it is not without possibilities. *Polyneuropathy, dendritic degeneration and demyelination* have been seen in industrial exposures, any and/or all of which can cause slowing.

Mercury:

With initial exposure to this neurotoxin (and many other heavy metals) there is an increase of faster activity, though with increased concentrations there is an increase in fast and slow activity, with eventual paroxysmal activity of an epileptiform nature.

Organo-phosphates:

The insecticides are known to form *peripheral neuropathies*, though also have central actions. The EEG shows slowing and paroxysmal bursts, though in coma there is a paradoxical spindling fast activity.

Chlorinated hydrocarbons:

Also insecticidal, these chemical compounds are fat soluble, stored and accumulating to a toxic level they are known to cause convulsions. Neurologically, there are bi-temporal sharp discharges and anterior slowing, rarely are spikes noted, with or without convulsions.

Lead, organic:

Cerebrotoxic effects are strong, with IQ points dropped significantly even with trace measurable exposure. Dementia progresses with increased exposure, with eventual convulsions. The EEG shows diffuse slowing in sub-acute exposure, with increased exposure leading to paroxysmal discharges. Inorganic lead has weak cerebrotoxicity.

Aluminum:

Commonly seen in *dialysis encephalopathies*, with *myoclonic* activity seen behaviorally. Though not well documented, the EEG shows slowing with excessive fast activity, in my experience. At autopsy, the aluminum is found concentrated anteriorly.