Suicidality and AEDs: View from epileptologists

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Epilepsy and Suicidality

- **Suicidality in epilepsy is a multifactorial phenomenon:**
  - Bidirectional relationship between suicidality and epilepsy.

  Can Occur:
  - As a consequence of seizure occurrence
    - Post-ictal mood, anxiety and psychotic episodes
  - As a consequence of change in seizure diathesis
    - Psychosis or depression when seizures cease (forced normalization)

Suicidality as consequence of therapy

- Could occur simply as a result of change in seizure frequency
- Could occur as result of interaction between CNS active compound and pre-disposed patient
- Probably just as likely (or more likely) to occur with AED withdrawal as with AED introduction!
  - In placebo-controlled study of AED withdrawal, 38% of pts developed moderate-severe psychopathology![1]

Ketter et al, *Anticonvulsant-Emergent withdrawal psychopathology.* Neurology, 1994,44:55-61

Issues

- Inclusion of trials that are add-on therapy, rather than no treatment vs active drug
  - Request stratified analysis in these two groups
- Reporting bias of suicidality, which was not systematically collected
  - Request analysis using item 3 from HAM-D in psychiatric subgroup
- The analysis of trials with no events cannot report confidence intervals
  - Request bayesian analyses

Consequences of AED non-compliance

- Potential for injury, status epilepticus, death
- Recent study of AED non-compliance using large medicaid claims database
  - 3-fold increase in death with apparent non-compliance, as well as increase in ED visits, hospitalizations, auto acccidents, injuries.

Faught E et al, Neurology. 2008 Jun 18. [Epub ahead of print]

Conclusions

- Changes in medicine regimen should be a time of closer observation for changes in mood
- Label should at least emphasize that AEDs themselves have **not** been proven to be direct cause of suicidality in absence of other factors (emphasize that association does **not** mean cause!)
- Risks of not taking/withdrawing AEDs when they are warranted far outweigh risks of AEDs association with increase in suicidality- **labeling change could cause serious harm.**
- Analysis issues still of concern to AES and AAN