Treatment of Autism with Anticonvulsants & Mood Stabilizers

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Comorbid disorders in ASD

- Prevalence of seizure in ASD 5-38.3% (Tuchman & Rapin 2002)
- Bimodal distribution > small peak ~5 and big peak in adolescence.
- Risk increase ~ degree of MR & receptive language deficit (Tuchman & Rapin 2002)

Comorbid disorders in ASD

- 50% of patients with epileptiform discharges ~ cognitive impairment (Shewmon & Erwin 1988)
- Good examples
  - Electrical status epilepticus during slow-wave sleep (ESES) ~ DD before syndrome
  - Landau-Kleffner Syndrome (LKS) ~ DD after syndrome
- Treatment (corticosteroid +/- anticonvulsants) improvement in cognition after treatment

Comorbid disorders in ASD

- Language regression ~ 30% of children with PDD/ASD (Shinnar 2001)
- Within this group ~ 30-40% PDD + Language regression have EEG abnormality
- Autistic Regression with Epileptiform EEG (AREE) ~ Controversal as AREE ∝ MR & regression
- ??? Treatment of subclinical seizure in PDD/ASD may improve behavioural/cognitive outcomes

Comorbid disorders in ASD

- Aggression & Irritability (Arnold et al. 2003)
- ~ 25% of adults with PDD/ASD have hx of Irritability (Allen et al.2001)
- High-functioning PDD/ASD have more manic-like symptoms
- Elevated rate of affective disorders in 1st degree relatives (Sverd 2003)
- Neurobiological relation PDD/ASD & mood disorder (DeLong 2004)

Action of Anticonvulsants

- Blockade of voltage-sensitive Na channels (Dilantin, Tegretol, Lamictal, Epival)
- Enhancement of inhibitory activity through GABA (maninly Benzo, phenobarb)
- Inhibition of excitatory glutamatergic transmission (phenobarb, topamax, lamictal)

Action of Anticonvulsants

- Treating subclinical seizure
- Mood-stabilizing

- NO ALL ANTICONVULSANTS HAVE BEEN USED IN PDD/ASD TREATMENT

Valproate

- Good for partial, absence seizures & manic episodes
- Good for impulsivity, irritability & aggression in various populations with psychiatric disorder (Hollander 1999, 2002, 2003, 2005) (McElroy et al. 2004)

Valproate

- Case series ~ valproate may be effective in preventing/ treating behavioural activation associated with SSRI use in PDD/ASD (Anagnostou et al. 2006) (Duggall et al. 2003)

- Open-label trial (Hollander et al. 2001) ~ valproate in PDD/ASD
  - Improvement in social, stereotypies, aggression, mood
  - Children with abnormal EEGs are responders

Levetiracetam (Keppra)

- As adjunctive for partial seizure & myoclonic seizure
- Unknown mechanism
- Markedly suppress kindling
- Persist even after dicontinuation
- Nootropic

Levetiracetam (Keppra)

- ONLY one open label study with PDD/ASD (Rugino & Samsock 2002)
- Improvement in hyperacticity, impulsivity, mood lability & aggression
- Wasserman et al. 2006 ~ trial result indicate otherwise

Topiramate

- Weight reduction for PDD/ASD on psychotropics (Canitano 2005)
- Side effects is the problem for the subjects in the study

Carbamazepine

- NO STUDIES for use in autism
- Only one case report ~ 20yr normal EEG ASD, started med for aggression treatment, developed seizure

Lithium

- No RCT
- Case report 2 young children with ASD & Fam Hx of Bipolar disorder with lithium
- Improvements n emotional lability
- (more studies of lithium on non-ASD DD population)