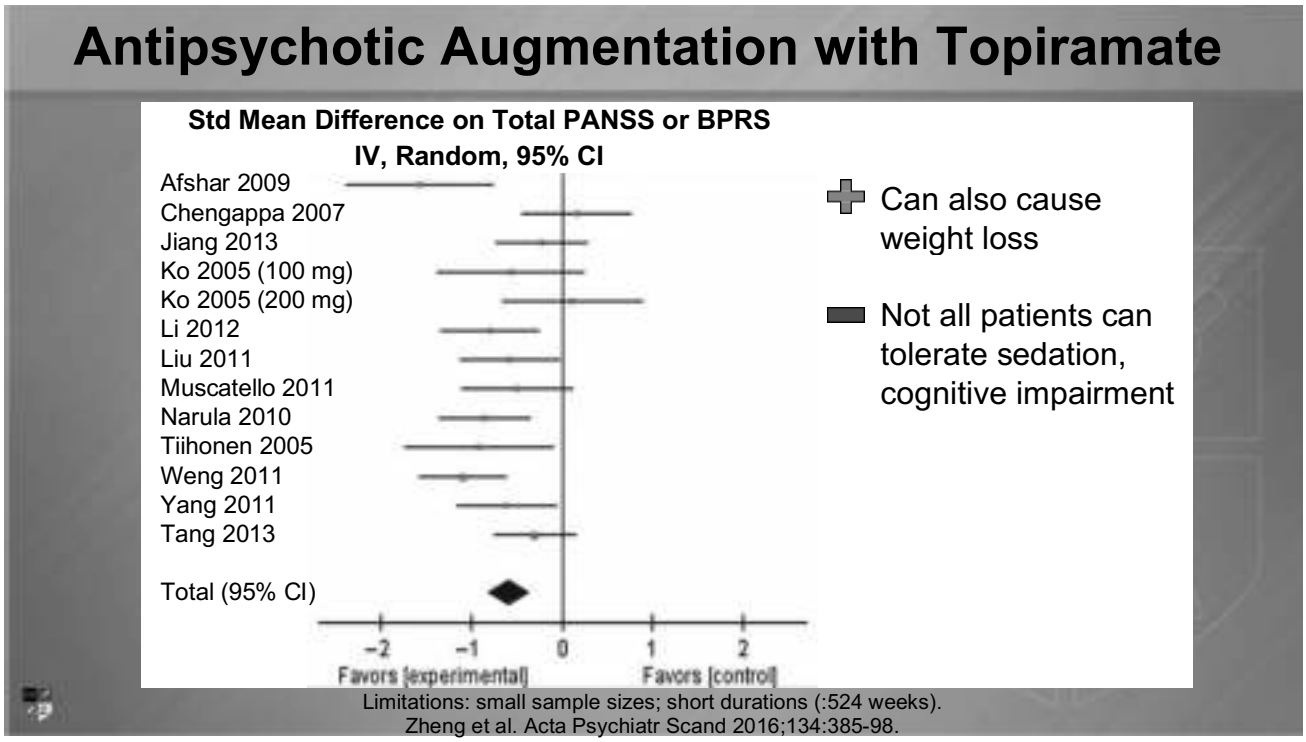
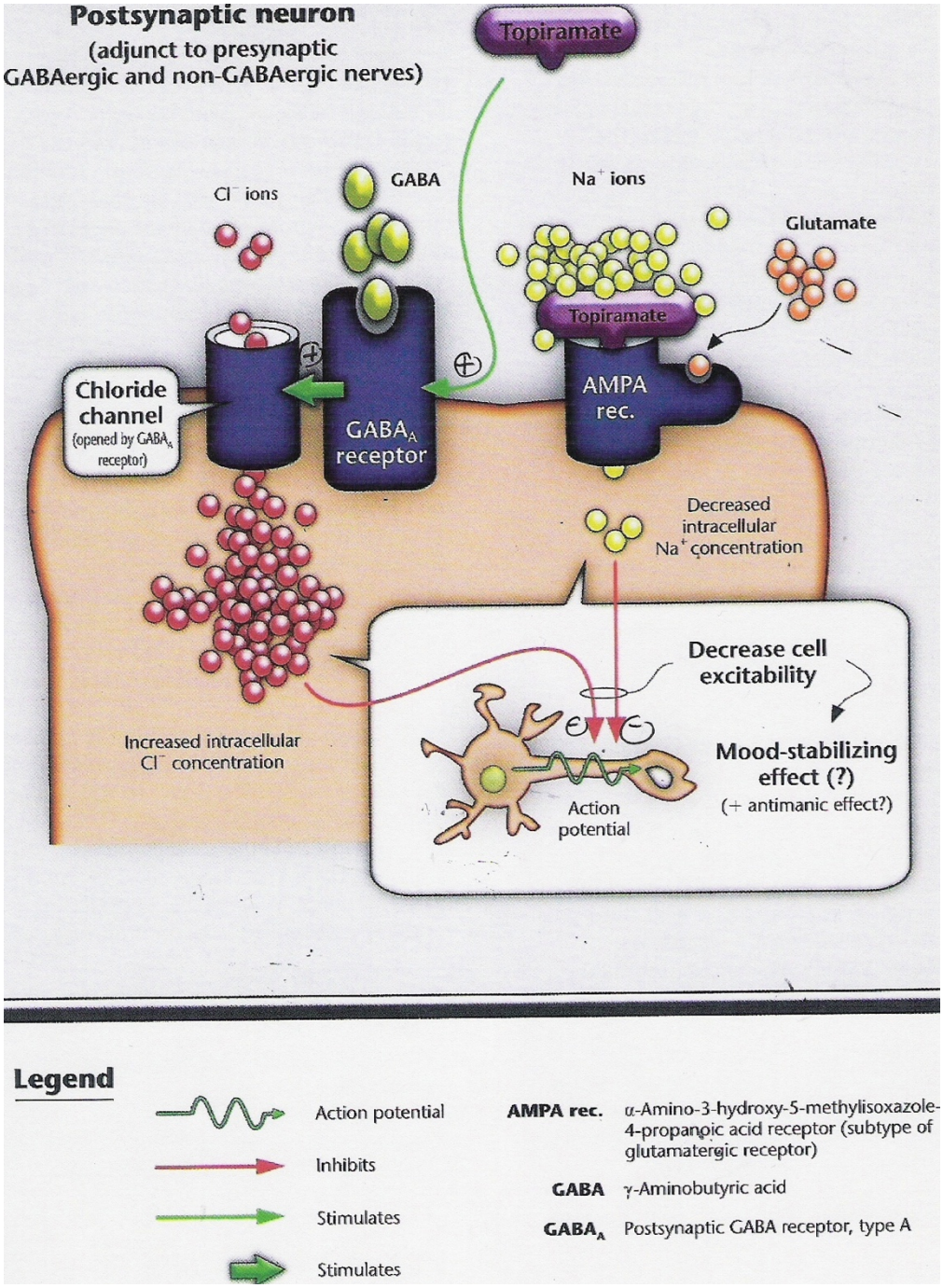
MARK W. WILSON, MD
330 WEST 58TH STREET, SUITE 313
NEW YORK, NEW YORK 10019

- **Topamax (topiramate; since 1995)**
  - FDA-approved in 1998 (for epilepsy)
  - Evidence
    - Mania
      - 14 open-label studies in bipolar disorder with 279 patients—anti-manic response rate 58%
      - ***Double-blind RCTs: emerging evidence of lack of efficacy in mania/bipolar disorder in four double-blind studies; some recent evidence of safety and efficacy as an adjunct medication (2003) in treating mania.***
    - Youth
      - Tramontina et al., 2007, 10 patients, aged 11-17, non-adherent to medication treatment due to weight gain; medications were gradually tapered and patients were then started on open-label Topamax: 4 of 7 experienced 68-100% reductions in mania symptoms; average weight loss 6 pounds; side effects included loss of appetite, tiredness, sleepiness, forgetfulness, and slowness of thought
      - Barzman, DelBello et al, 2006:, 25 youth with bipolar disorder, inpatient
        - Significant improvement for all episodes, symptoms
        - No adverse events
      - DelBello, 2006: small case series of 9 youth with co-occuring bipolar disorder and disruptive behavior disorders—efficacious at doses of 50-150 mg/day (average 78 mg/day)
      - DelBello, 2005: 4-week, placebo-controlled trial in 56 youth with average age 13.8 yo (range 12.2-16.4yo) with bipolar I with acute mania or mixed mania; 59% also had ADHD; average dose 278 mg (range 150-400 mg)
        - Overall, Topamax was associated with a 30% reduction in symptoms and placebo was associated with a 16% reduction in symptoms
        - More pronounced in mixed mania.
      - DelBello, 2002: chart review of 26 youth with bipolar I or II; 13 with co-morbid ADHD; adjunctive or monotherapy; 1-30 months; 73% improvement in manic symptoms, 62% overall improvement, 38% with decreased ADHD symptom severity.
      - Pavuluri et al, 2002: Topamax 50 mg/day added to Risperdal 0.5 mg/day in a 4.5 yo with mania normalized mood swings and led to a 30 pound weight loss
      - Davanzo et al, 2001: case series; positive
    - May have antidepressant efficacy
    - May help ameliorate some symptoms of treatment-resistant schizophrenia (Tiihonen, 2005; Corell et al, 2013 meta-analysis)
    - Borderline personality disorder
      - Nickel et al, 2004, 2005
      - Loew et al, 2006
    - Double-blind, placebo-controlled RCTs demonstrated efficacy in binge eating disorder, obesity, bulimia, migraine headaches, post-traumatic stress disorder (Tucker et al, 2007) and alcohol dependence.
    - May be useful in chronic pain



- Side effects/risks (combined with data from Tucker et al, 2007)
  - 65% **decreased serum bicarbonate/metabolic acidosis**; serious in 3-11%
  - 26% change in taste perception vs. 0% in placebo
  - 24-37% headache vs. 26% placebo
  - 21% **stomach upset** vs. 11% placebo
  - 20-50% **weight loss**
  - 13-17 pounds with 100 mg/day over 12 weeks
    - Chengappa et al, 2006:
      - If normal weight
        - 4% with weight loss, 8% with weight gain on Topamax
        - 0% with weight loss and 13% with weight gain on placebo
      - If overweight
        - 53% with weight loss, 3% with weight gain on Topamax
        - 42% with weight loss, 8% with weight gain on placebo
  - 20% **cognitive dulling**
  - 15.4-24% **nausea** vs. 0-11.9% placebo
  - 14-23.1% **paresthesias** (numbness or tingling in extremities) vs. 3.5-3.7% placebo
  - 14-16.8% **diarrhea** vs. 7.4-8.4% placebo
  - 10.5% **dizziness** vs. 10.5% placebo
  - 10-21% **insomnia** vs. 3.7-16% placebo
  - 10% **rash** in youth vs. 3.7% placebo
  - 11-21% **poor concentration** vs. 4-16% placebo
  - 6-15.4% **sedation/fatigue** vs. 3.7-16.1% placebo
  - **word loss**
  - **memory problems**
  - **speech problems**
  - **difficulty with balance/unsteadiness**
  - 35 cases/million of **temperature instability** and ***risk of decreased sweating and elevated body temperature***
  - **kidney stones**
    - especially if on a ketogenic diet or taking a carbonic anhydrase inhibitor
    - 1.5%; 2-4X higher risk
    - Men>women; reported in some kids
    - Likely due to inhibition of carbonic anhydrase
    - drink plenty of water to minimize risk
  - vision problems
  - glaucoma (angle closure type)
    - signs: eye pain, decreased vision
    - 23 reported cases through 2001; mostly adults
  - cataracts

- **nervousness**
- a number of other side effects and risks in multiple organ systems
- 35 cases/million of **temperature instability** and ***risk of decreased sweating and elevated body temperature***
- **decrease the estrogen in birth control**



- Acts on GABA-A receptors, sodium channels; blocks kainate/AMPA glutaminergic receptors; weak carbonic anhydrase inhibitor
  - Pharmacodynamics
    - Dosing
      - Initial pediatric dosing: 1-3 mg/kg/day; maintenance 5-9 mg/kg/day
      - 50-150 mg for weight
      - 100-300 mg for binge eating disorder and obesity
      - 100-400 mg for mood
      - 400-1000 mg for seizure disorders
    - Comes in 25, 100, and 200 mg tabs and sprinkle caps 15 and 25 mg caps.
    - 30% liver metabolism; no induction of liver enzymes; inhibits 2C19
    - Half-life 18-30 hours
    - Steady state in 4-5 days

    - Levels 2-10.5 mcg/mL
    - 15 and 25 mg sprinkles; 25, 50, 100, 200 mg non-scored tabs
- Drug-drug interactions
    - Tegretol lowers Topamax by 50%
    - Depakote lowers Topamax by 15%
    - Topamax lowers Depakote by 15%
    - ***May reduce effectiveness of birth control pills.***

Efficacy for Psychopathology and Body Weight and Safety of Topiramate-Antipsychotic Cotreatment in Patients With Schizophrenia Spectrum Disorders: Results From a Meta-Analysis of Randomized Controlled Trials

Christoph U Correll, Lawrence Maayan, John Kane, Marc De Hert, Dan Cohen

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OBJECTIVE: To meta-analyze the efficacy and tolerability of topiramate-antipsychotic cotreatment in schizophrenia.

DATA SOURCES: PubMed/MEDLINE database were searched until September 5, 2015, using the keywords topiramate AND antipsych* OR neurolept* OR specific antipsychotic names.

STUDY SELECTION: Randomized controlled trials (RCTs) of topiramate-antipsychotic cotreatment versus placebo and ongoing antipsychotic treatment in patients with schizophrenia spectrum disorders were included.

DATA EXTRACTION: Two evaluators extracted data. Standardized mean difference (SMD), weighted mean difference (WMD), and risk ratio (RR) ± 95% CIs were calculated.

RESULTS: In 8 RCTs, lasting a mean ± SD of 13.6 ± 4.9 weeks, 439 patients were randomized to topiramate (100-400 mg/d) versus placebo (trials = 7) or ongoing antipsychotic treatment (trial = 1). Topiramate outperformed the comparator regarding total psychopathology (trials = 6, n = 269, SMD = -0.57 [95% CI, -1.01 to -0.14], P = .01), positive symptoms (trials = 4, n = 190, SMD = -0.56 [95% CI, -1.0 to -0.11], P = .01), negative symptoms (trials = 4, n = 190, SMD = -0.62 [95% CI, -1.13 to -0.10], P = .02) general psychopathology (trials = 3, n = 179, SMD = -0.69 [95% CI, -1.27 to -0.11], P = .02), body weight (trials = 7, n = 327, WMD = -3.14 kg [95% CI, -5.55 to -0.73], P = .01), and body mass index (BMI) (trials = 4, n = 198, WMD = -1.80 [95% CI, -2.77 to -0.84], P = .0003). Topiramate's efficacy for total psychopathology and weight reduction effects were not mediated/moderated by trial duration, topiramate dose, sex, age, inpatient status, baseline Positive and Negative Syndrome Scale, or baseline BMI. Conversely, clozapine-topiramate cotreatment moderated greater efficacy, but less weight loss, compared to topiramate-nonclozapine antipsychotic combinations. All-cause discontinuation was similar between topiramate and control groups (trials = 7, RR = 1.24 [95% CI, 0.76 to 2.02], P = .39). Topiramate trended only toward more paresthesia than placebo (trials = 4, RR = 2.03 [95 % CI, 0.99 to 4.18], P = .05).

CONCLUSIONS: Topiramate-antipsychotic cotreatment significantly reduced total, positive, negative, and general psychopathology and weight/BMI in patients with schizophrenia spectrum disorder while being well tolerated. However, larger studies are needed to confirm and extend these findings.

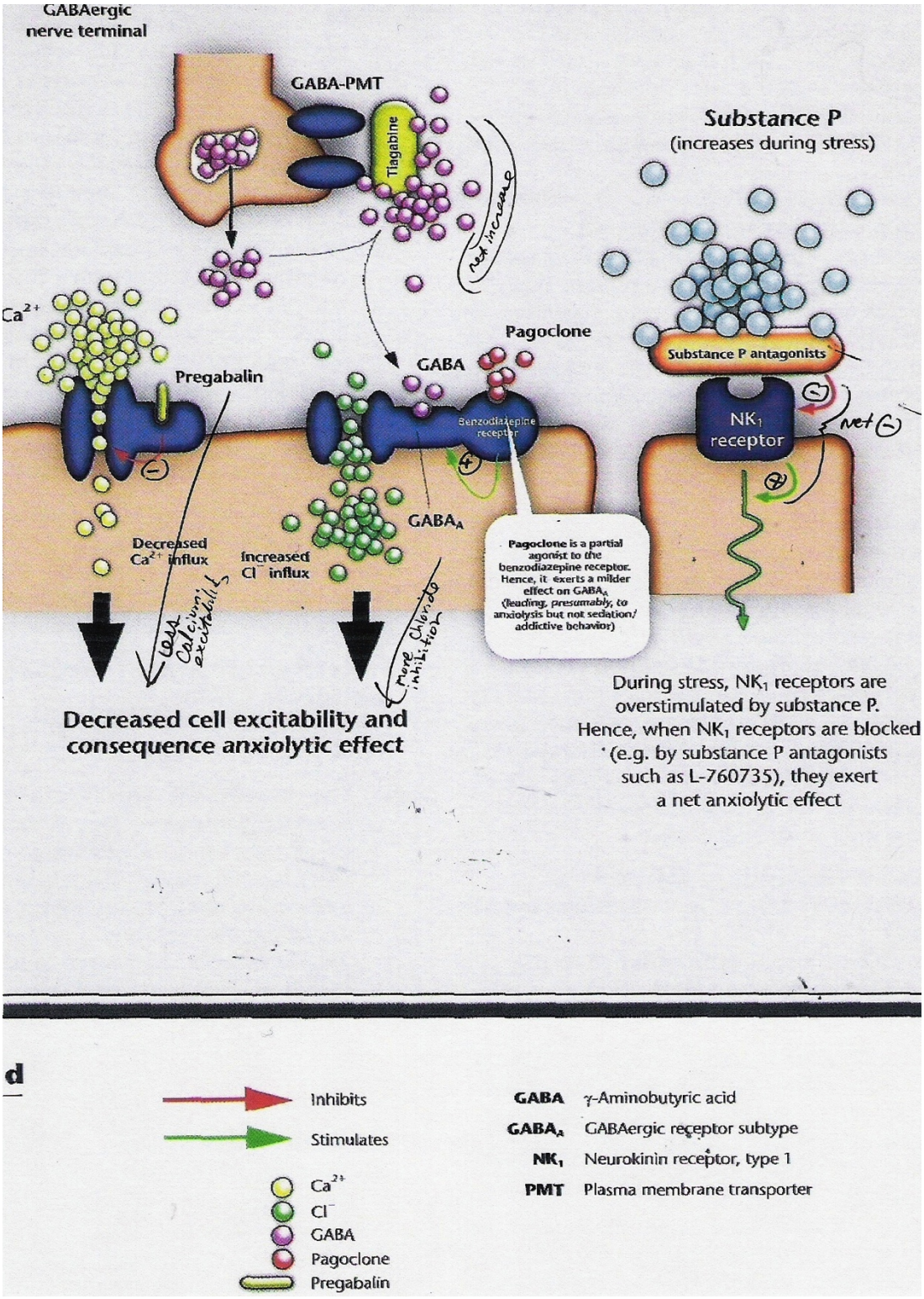
- **Neurontin (gabapentin; since 1993)**
  - Pharmacodynamics/metabolism
    - Dose range 900-4800 mg/day
    - Kidney, metabolism
    - Half-life 5-7 hours
    - Time to steady state is 1-2 days
    - Comes in 100, 300, and 400 mg ***caps*** and 600 and 800 mg ***tabs***. Also comes in solution (250 mg/5 ml; 470 ml bottle).
    - Antacids can reduce absorption (e.g., Maalox) reduces bioavailability by 20%)
    - Dosing: 900-3600+ mg/D, but bioavailability decreases as dose increases so that, when given in 3 divided doses, bioavailability is as follows:
      - 900 mg—60% bioavailable, which is 540 mg
      - 1200 mg—47% bioavailable, which is 564 mg
      - 2400 mg—34% bioavailable, which is 816 mg
      - 3600 mg—33% bioavailble, which is 1188 mg
      - 4800 mg—27% bioavailable, which is 1296 mg
  - Mechanism
    - It's a leucine analog that binds to the alpha-2-gamma subunit of voltage-gated calcium channels, closing N and P/Q presynaptic calcium channels, diminishing neuronal activity and glutamate levels
    - Increases GABAergic activity
    - What it doesn't do:
      - While structurally related to the natural amino acid neurotransmitter GABA (it's a leucine analog), it does not directly modify binding to the GABAa or GABAb receptos. It is not converted to GABA or a GABA agonist.
      - It is not an inhibitor of GABA reuptake or degradation.
      - Does not bind to any of the following receptors/channels: benzodiazepine, glutamate, NMDA, glycine, adrenergic, adenosine, cholinergic/nicotinic, dopamine1/2, histamine, serotonin, opiate, cannabinoid, sodium channels, voltage sensitive calcium channels
      - Does not alter uptake of serotonin, dopamine, or norepinephrine
  - ***Evidence***
    - ***Emerging evidence of lack of efficacy in the treatment of mania/bipolar disorder (either alone or in combination with other mood stabilizers) or in schizophrenia***
      - Case series and open-studies were positive, but controlled studies were negative
      - Hamrin and Bailey, 2001: 12 y.o. boy with ADHD and bipolar II on Neurontin 200 mg/day and methylphenidate 30 mg/day
      - Soutullo et al, 1998: case series in youth
    - Anxiety
      - Pande, 1999: Neurontin 900-3600 mg somewhat effective in social phobia
      - Some efficacy in other anxiety disorders, including bsessive compulsive disorder
      - Most common dose range for anxiety 900-2400 mg/day
    - ?Efficacy in depression as adjuvant
    - Migraine prevention
    - Chronic pain; as high as 3600 mg.day
    - Alcohol dependence
    - Cannabis dependence at 1200 mg/day divided tid (Mason et al, 2012)
    - Tardive dyskinesia at 900 mg/day
    - Movement dyskinesias at 900 mg/day
    - Cannabis use disorder at 1200 mg/day (Levin et al, 2011)
  - Some of the side effects/risks (in studies of epilepsy and, separately, chronic pain
    - sedation/lethargy/fatigue 38.4% vs. 23.8%
    - balance/coordination problems 18.8% vs. 5.6 placebo
    - dizziness 17-28% vs. 6.9-7.5% placebo
    - double or blurred vision 14% vs. 3.9% placebo
    - nausea, stomach upset or vomiting 9.4% vs. 5.4% placebo
    - tremor 6.8% vs. 3.2% placebo
    - diarrhea 5.1% vs. 3.1% placebo
    - slurred speech 2.4% vs. 0.5% placebo
    - memory problems 2.2% vs. 0 placebo
    - weight gain 1.8-2.9% (one report 15%) vs. 0-1.6% placebo
    - dry mouth 1.7-4.8% vs. 0.5-1.3% placebo
    - swelling in extremities 1.7-8.3% vs. 0.5-2.2% placebo
    - constipation 1.5-3.9% vs. 0.8-1.8% placebo
    - flatulence
    - decreased libido
    - little to no cognitive impairment. Little to no EEG slowing
    - in pre-marketing development for the use of Neurontin in seizure disorders,
      - incidence of sudden and unexplained death was 8 of 2203 patients
      - this is 8 deaths out of 2103 patient-years of exposure
      - this amounts to **0.004** (more specifically 0.0038) deaths per patient-year
      - exceeds the rate expected in a healthy population matched for age and sex, which is **0.0005**
      - it is within the range of estimates for the incidence of sudden and unexplained deaths in patients within epilepsy not receiving Neurontin, which is **0.005**

- a number of other side effects and risks in multiple organ systems
- Some case reports of abuse and dependence

- **Lyrica (Pregabilin)**
  - Analog of GABA/leucine and derivative of Neurontin
  - Decreases the release of norepinephrine, glutamate and substance P; decreases flux of calcium; may enhance GABAergic transmission. More selectively binds to the alpha2-gamma subunit of calcium channels in the brain than Neurontin
  - FDA-approved for the management of neuropathic pain associated with diabetic peripheral neuropathy and post-herpetic neuralgia; 9000 patients studied; recently approved for the treatment of fibromyalgia—1800 additional patients studied.
  - Approved for the treatment of generalized anxiety disorder in Europe
  - Evidence
    - Bipolar disorder:
      - Schaffer et al, 2013, adjunctive use in treatment-resistant bipolar disorder in adults and adolescents
        - Uncontrolled study
        - 41% response rate
        - ~90 mg/day
        - Side effects: overactivation, weight gain
    - Anxiety
      - Some evidence of efficacy in the treatment of anxiety in adults; 5 placebo-controlled trials suggesting it is at least as effective as Xanax and Effexor and more effective than placebo in generalized anxiety disorder, including:
        - Pfizer: 1-year open-label study, 265 patients (68 completing the year and 140 completing 36 weeks); good effect and well-tolerated except for dizziness and tiredness
        - Rickels, 2005: 4-week, multicenter, double-blind, placebo-controlled trial of pregabilin and alprazolam; both treatments equally effective.
        - Pande, 2004: 600 mg/day effective
        - More rapidly acting than Effexor
    - Some evidence of efficacy in the treatment of pain due to nerve damage in diabetes and shingles.
    - Evidence of efficacy in treating pain and fatigue in fibromyalgia
    - Evidence of efficacy for widespread pain, sleep disruption, and fatigue due to fibromyalgia.
    - May reduce anger dysregulation (and amygdala hyperactivation) (Aupperle et al, 2012)
  - Side effects
    - dizziness (30%)
    - sedation (22%)
    - imbalance
    - tremor
    - speech slurring
    - tingling sensations
    - memory problems
    - coordination problems
    - mood changes
    - nausea
    - weight gain
    - blurred or double vision
    - ? no sexual dysfunction.
  - Better tolerated than Neurontin.
  - Improves slow wave sleep
  - Recommended supplements to take while on Depakote
    - Vitamins B12, B6, A, D, E, K
    - Folic acid
    - Carnitine
    - Zinc
    - Copper
    - Selenium
    - Biotin
    - Calcium
  - Pharmacodynamics
    - Dose range 150-600 mg/day in 2-3 divided doses; give 1/3-1/6 the dose of Neurontin
    - Starting dose in adults 50 mg three times-a-day or 100 mg twice-a-day, with the dose increasing to 300 mg, a common and effective dose; can raise dose 150 mg every few days to maximum of 600 mg
    - Elimination half-life is 5-7 hours; steady state in 1-2 days
    - Excreted unchanged by the kidney.
    - Caps: 25, 50, 75, 100, 150, 200, 225, 300 mg

- Minimal drug-drug interactions.

- **Dilantin (phenytoin; since 1938)**
  - Some evidence of efficacy in adult mania, depression, and anxiety; no evidence of safety and efficacy in the treatment of pediatric psychiatric disorders.
  - Bersudsky, 2005: 5 week, double-blind controlled study of augmentation with Haldol in mania and schizoaffective disorder, manic type. Also a 6 month maintenance phase study. Also compared with Prozac for unipolar depression. Safe and effective.
- **Gabatril (tiagabine; since 1998)**
  - GABA-reuptake (GAT-1) inhibitor (SGRI) with actions on both presynaptic neurons and glia; modulates spread of GABA from synapse to extrasynaptic sites
  - Interacts with voltage-gated calcium channels (the alpha2-gamma subunit) to increase GABA.
  - Does not appear to be associated with dependence liability or withdrawal.
  - Evidence
    - Anxiety
      - Some evidence (case reports) of safety and efficacy in the treatment of generalized anxiety disorder (GAD)
      - Recent randomized study comparing Gabatril and Paxil in the treatment of GAD demonstrated significant efficacy
      - Pollack, 2005: GAD; 8-week, RCT, multicenter, 266 patients; some improvement but not statistically significant
    - Some evidence of safety and efficacy in the treatment of primary insomnia at doses of 2-12 mg/day. Increases slow wave sleep.
    - Case reports of efficacy in adults with bipolar disorder (but an open-label study of eight adults with acute mania patients demonstrated no improvement)
    - No evidence of safety and efficacy in the treatment of pediatric psychiatric disorders.
  - Take with food.
  - FDA-approved for the adjunctive treatment of partial onset seizures in patients aged 12 years or older.
  - Side effects
    - Dizziness 45% (vs. 11% placebo)
    - Headache 40% (vs. 36% placebo)
    - Nausea 30% (vs.26% placebo)
    - Fatigue 23% (vs. 12% placebo)
    - Somnolence OR sedation OR asthenia 34% (vs. 14% placebo)
    - Worse attention 8% (vs. 2% placebo)
    - Irritability 8% (vs. 8% placebo)
    - Anxiety 7% (vs. 1% placebo)
    - Unsteadiness
    - Grand mal seizures, even in the absence of seizure disorder; from 1997 through 12/31/04, there have been 59 postmarketing reports of seizures in patients without a history of epilepsy.
    - Severe nausea
    - Worsening of mania or depression
    - Associated with decline in verbal memory and a decrease in energy.
  - Recommended supplements to take while on Depakote
    - Vitamins B12, B6, A, D, E, K
    - Folic acid
    - Carnitine
    - Zinc
    - Copper
    - Selenium
    - Biotin
    - Calcium
  - Pharmacodynamics
    - Liver metabolism
    - No induction of liver enzymes
    - Half-life 7-9 hours (4-7 hours if given with enzyme inducers)
    - Dosing
- in children, 0.1-2 mg/kg/d; 4-32 mg/day; split 2-4 times-a-day
  - start at 2-4 mg/D
  - increase by 2-8 mg every week
- in adults, 4-56 mg/day, split 2-4 times-a-day, in adults
  - Comes in 2, 4, 12, 16, and 20 mg tabs



- **Keppra (levetiracetam; FDA-approved for adult epilepsy in 1999)**

Pharmacodynamics

- dose 500-3000 mg/D
- In children with seizures, begin with 20 mg/kg split twice-a-day, increase every two weeks by 20 mg/kg to target dose of 60 mg/kg.
- 65% renal metabolism; half-life 6-8 hours
- Comes in 250, 500 and 750 mg tabs and 100 mg/mL oral solution
- Steady state in 2 days

Evidence

- Some evidence of safety and efficacy in adults with psychiatric disorders, including bipolar disorder and aggression.
- Anxiety disorders

- Kinrys et al, 2007: 40 adults with anxiety disorders deemed partial responders or nonresponders to antianxiety medication, received Keppra as an adjunct; average dose was 2000 mg day (range 1000-3000 mg/day); duration averaged 9.3 weeks (range 4-14.4 weeks); significant improvement; well-tolerated
- Papp, 2006: Keppra safe and effective in an open-label study of 18 patients with panic disorder
- Kinrys, 2006: 1500-2500 mg/day helpful in in 23 clients with PTSD; side effects: sedation/tiredness 30%, lightheadedness 4%, dry mouth 4%, stomach upset 4%, no side effects 56%.
- Simon et al, 2004, open-label study of Keppra 250-3000 mg for the treatment of social anxiety disorder in 20 adults; evidence of efficacy and safety

- In autism, had beneficial effects on attention, hyperactivity, and mood instability.
- FDA-approved for add-on for partial seizures in adults (1999)
- FDA-approved for use in pediatric partial-onset seizures (4 years of age and up)

Side effects

- Drowsiness
- Fatigue
- Headache
- Nausea
- Dry mouth
- Dizziness
- Nervousness,
- Emotional lability
- Suicidal ideation
- Aggression
- Depression
- Irritability
- Psychosis
- Weight neutral
- Idiosyncratic leucopenia, neutropenia, pancytopenia, thrombocytopenia
- No sexual side effects
- Favorable cognitive side effect profile. Not associated with changes in EEG.
- A number of other side effects and risks in multiple organ systems

Recommended supplements to take while on Depakote

- Vitamins B12, B6, A, D, E, K
- Folic acid
- Carnitine
- Zinc
- Copper
- Selenium
- Biotin
- Calcium

Mechanism

- May be GABAergic (appears to inhibit the actions of zinc and beta-carbolines which themselves inhibit the GABA receptor)
- Partial blockade of excitatory neurotransmitter release
- Reduces neuronal transmission through high-voltage-activated calcium channels
- Selectively binds to SV2A protein which modulates calcium-dependent synaptic vesicle release (exocytosis); may enhance SV2A functioning to inhibit abnormal neuronal activity in epileptic neurons

- **Vigabatrin (since 1989)**

Inhibits GABA transaminase

No current evidence of safety and efficacy in the treatment of psychiatric disorders; a recent small uncontrolled study (Brodie, 2003) demonstrated safety and efficacy in the treatment of cocaine addiction.

Side effects include visual field defects, daytime sleepiness, and headaches. Good cognitive profile.

- **Zonegran (zonisamide)**

Mechanism:

- Pro-GABAergic
- Anti-glutaminergic
- Blocks voltage-sensitive sodium and T-type calcium channels
- May increase dopamine and serotonin release/functioning
- Inhibits MAO-B
- Inhibits carbonic anhydrase
- Structurally similar to sulfonamide

Evidence:

- McElroy, 2006: RCT, DB, binge eating disorder; effective but not well tolerated (often discontinued due to accidental injury, psychological complaints, cognitive complaints
- 2006 open prospective trial of add-on Zonegram in bipolar I, II, and NOS depression; safe and effective; side effectives included sedation and nausea/

- Open label trial of 24 patients with mania and acute psychotic conditions: 71% responded
- Kanba, 1994: open-label, 4 week augmentation study in bipolar mania (15), schizoaffective mania (6), schizophrenic "excitement" (3); 80% response rate; no drop outs.
- McElroy (2005) demonstrated in an open-label prospective trial of adjunctive zonisamide in 62 outpatients with bipolar disorder over 48 weeks; while many patients experienced positive efficacy, 32% discontinued the medication due to worsening mood symptoms.
- No evidence in children;

Side effects/risks

- Dry mouth 43% vs. 33% placebo
- Somnolence 40% vs. 23% placebo
- Headache 37% vs. 30% placebo
- Nausea 37% vs. 17% placebo
- Nervousness 27% vs. 10% placebo
- Taste change 23% vs. 7% placebo
- Stomach upset 20% vs. 3% placebo
- Thinking abnormality 17% vs. 10% placebo
- Amnesia 17% vs. 10% placebo
- Dizziness 13% vs. 7% placebo
- Insomnia 13% vs. 7% placebo
- Back pain 13% vs. 3% placebo
- Libido decrease 10% vs. 3% placebo
- allergic reaction (it is a sulfonamide), Stevens-Johnson Syndrome, toxic epidermal necrolysis
- fulminant hepatic necrosis
- agranulocytosis--rare
- aplastic anemia--rare
- other blood dyscrasias
- drug interactions
- serum creatinine increase (average increase 8%); not clear if significant
- kidney stone 4%
- hyperthermia, less sweating—especially in kids--rare
- weight loss

Recommended supplements to take while on Depakote

- Vitamins B12, B6, A, D, E, K
- Folic acid
- Carnitine
- Zinc
- Copper
- Selenium
- Biotin
- Calcium

Pharmacodynamics

- Dosing
  - Adults
    - Range 100-600 mg/d in 1-2 doses/day
    - Start 100 mg/D
    - Increase every 2 weeks by 100 mg to maximal dose 600 mg (in adults)
    - Weight loss: 200-400 mg/day (no evidence of increased benefit over 400 mg/day)
  - Youth:
    - Initial 2-4 mg/kg/d
    - Maintenance 4-8 mg/kg/day
- Half-life 63 hours (50-70 hours) but 25-40 hours if given with enzyme inducers
- Steady state in 7-14 days
- Level 10-40 mcg/mL
- Comes in 25, 50, and 100 mg caps
- Comparative neurocognitive effects of lithium and AED mood stabilizers (Gualtieri and Johnson, 2006): from least detrimental to most: Lamictal>Trileptal>lithium>topamax>Depakote>Tegretol.