

Cannabinoids and Health

Module 10

Lecture 4: Treatment of Mood Disorders and
Psychosis

Treatments: Depression

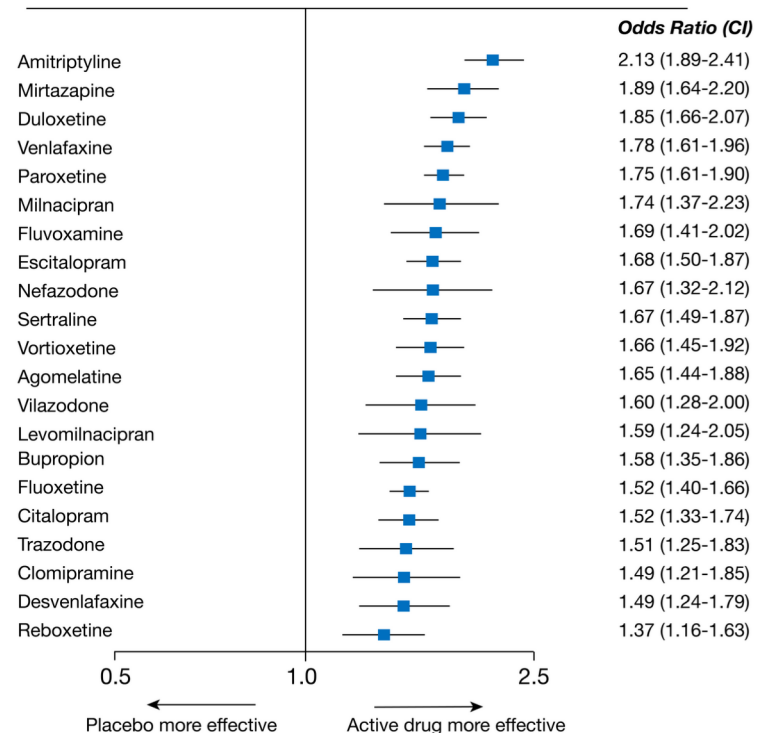
- Pharmacological Treatments (three basic medications)
 - **Monoamine Oxidase Inhibitors** – increase monoamine availability (serotonin, dopamine, norepinephrine) by decreasing enzymes that breakdown these neurotransmitters
 - **Selective Serotonin Reuptake Inhibitors** – increase serotonin availability by preventing the reuptake of serotonin into neurons
 - **Serotonin-Norepinephrine Reuptake Inhibitors** – increase both serotonin and norepinephrine availability by preventing reuptake
 - Tricyclics, an old school medication not really used anymore acted in this way (by blocking the transporters that led to their reuptake)

Treatments: Depression

- Effectiveness is modest overall
- Other countries have found them to be ineffective for mild to moderate depression

Are antidepressant drugs effective?

The effectiveness (here measured as the efficacy) of antidepressant drugs measured relative to placebos from meta-analysis of 522 trials comprising 116,477 participants. Effectiveness was measured as the odds-ratio (OR) of a $\geq 50\%$ reduction of the total score on a standardised observer-rating scale for depression, relative to a placebo. Values greater than 1.0 indicate the antidepressant drug was more effective than the placebo. All results were statistically significant.



Side effects of anti-depressants

- nausea
- increased appetite and weight gain
- loss of sexual desire and other sexual problems, such as erectile dysfunction and decreased orgasm
- fatigue and drowsiness
- blurred vision
- constipation
- dizziness
- agitation
- irritability
- anxiety
- insomnia
- dry mouth

Psychotherapy for depression

- The types of cognitive behavioral treatments discussed in previous modules (e.g., cognitive behavioral therapy, mindfulness based cognitive therapy, acceptance and commitment therapy, etc) are available for depression
- Psychotherapy is equally effective as compared to medications
- Psychotherapy does not have side effects
- But psychotherapy is expensive, requires numerous sessions, and takes time and commitment

Treatments: Bipolar

- The medication most supported for treating bipolar disorder is lithium – reduces risk of suicide, death, and self-harm.
 - The required dosage is slightly less than the toxic level.
 - Thus, patients need to have their blood levels of lithium closely monitored.
 - This harm potential raises concerns, in the event that patients are in a manic/impulsive state

Treatments: Bipolar

- Meta-analytic studies have examined the efficacy of lithium for bipolar disorder
 - Lithium reduces the risk of depressive episode relapse
 - Lithium reduces the risk of manic episode relapse

Reviews and Overviews

Long-Term Lithium Therapy for Bipolar Disorder: Systematic Review and Meta-Analysis of Randomized Controlled Trials

John R. Geddes, M.D.,
F.R.C.Psych.

Sally Burgess, M.R.C.Psych.

Keith Hawton, D.Sc., F.R.C.Psych.

Kay Jamison, Ph.D.

Guy M. Goodwin, D.Phil.,
F.R.C.Psych.

Objective: The authors sought to determine the efficacy and acceptability of lithium for relapse prevention in bipolar disorder.

Method: A systematic review and meta-analysis of randomized controlled trials comparing lithium with placebo in the long-term treatment of bipolar disorders was conducted. Data were obtained from searching the registers of the Cochrane Collaboration; reviewing reference lists,

adverse effects and total withdrawal rates.

Results: Five randomized controlled trials (770 participants) were included. Lithium was more effective than placebo in preventing all relapses (random effects relative risk=0.65, 95% CI=0.50 to 0.84) and manic relapses (relative risk=0.62, 95% CI=0.40 to 0.95). The protective effect of lithium on depressive relapses was smaller and was less robust (relative risk=0.72, 95% CI=0.49 to 1.07).

Side Effects of Lithium

- Hand tremor
- Increased thirst
- Increased urination
- Diarrhea
- Vomiting
- Weight gain
- Impaired memory
- Poor concentration
- Drowsiness
- Muscle weakness
- Hair loss
- Acne
- Decreased

Other medications

- Mood "stabilizers"
 - Carbamazepine (Carbatrol, Epitol, Equetro, Tegretol)
 - Divalproex sodium (Depakote)
 - Lamotrigine (Lamictal)
 - Valproic acid (Depakene)
- Carbamazepine, lamotrigine, and valproic acid originally developed as anticonvulsants
- What cannabinoid is an anticonvulsant?
- Antipsychotics also used in Bipolar Disorder
- These meds also have undesirable side effects

Treatments: Schizophrenia

- The first-line psychiatric treatment for schizophrenia is antipsychotic medication.
 - Most effective for reducing positive symptoms
 - Antipsychotics fail to significantly improve the negative symptoms and cognitive dysfunction.
 - Antipsychotics also have serious side effects, including weight gain and perturbations in motor systems
 - Antipsychotics have a moderate response rate (40-50%)
 - Patients need to take the medication long term to avoid relapse

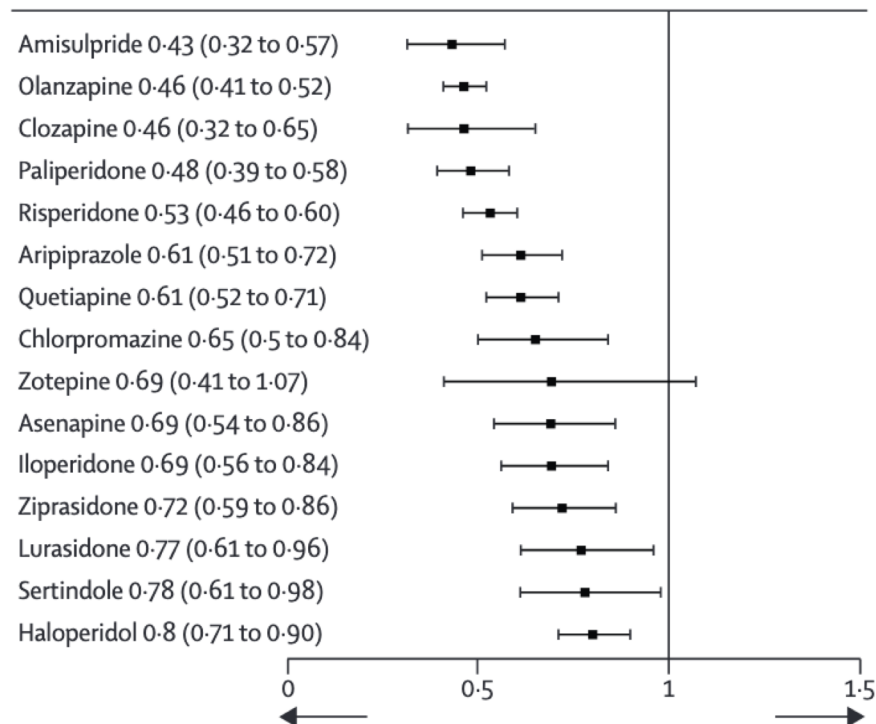
Antipsychotic Side Effects

- Stiffness and shakiness – can be quite severe with older drugs
- Uncomfortable restlessness (akathisia)
- Uncontrollable movements of the jaw, lips and tongue (tardive dyskinesia)
- Sleepiness and slowness
- Weight gain
- A higher risk of getting diabetes
- Sexual problems due to hormonal changes
- Constipation
- Dry mouth
- Blurred vision

Treatments: Schizophrenia

- Antipsychotics all come with a wide range of adverse, unintended effects, which make many patients hesitant to comply with the medication.

A All-cause discontinuation OR (95% CrI)



Conclusions

- There are a number of anti-depressant medications on the market
 - The side effects are mostly tolerable but undesirable
 - The effectiveness is modest and/or questionable for moderate depression
- Bipolar disorder is treated with lithium or mood stabilizers (i.e., antiseizure medications)
 - Also undesirable side effects
- Schizophrenia treated with antipsychotics
 - Also serious and undesirable side effects