

Treatments for Major Depression

Drug Treatments

The two (2) classes of drugs that are "typical" antidepressants are:

1. _____
2. _____

These 2 classes of drugs increase the amount of monoamine neurotransmitters through two distinct mechanisms of action.

- compared to placebo treatment (30-35% rate of spontaneous recovery), both of these drug classes improve all the symptoms of major depression in approximately 70-75% of patients.

- the other 25-30% of patients are nonresponsive due to:
 - a. inadequate dosage of drug (i.e., oral dose does not necessarily correlate with blood levels);
 - b. inaccurate initial diagnosis (not major depression);
 - c. simply nonresponsive to drug treatment.
- when diagnosis and drug dosage are accurately determined, effectiveness rate of drug therapy climbs to _____.

- these drugs are NOT general stimulants; they produce mostly _____ individuals (e.g., sleepiness, difficulty in processing sensory information, decreased motor coordination and cognitive skills).

- antidepressant drugs alone can _____ bipolar disorder, particularly manic episodes.

- antidepressants do not produce addiction or tolerance.

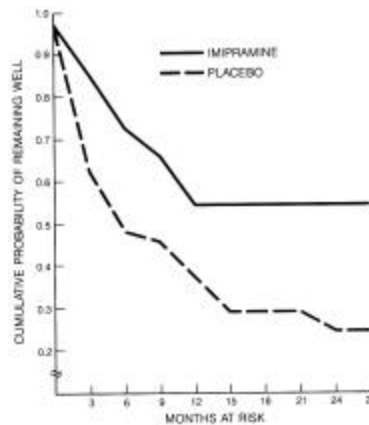
- antidepressants are NOT a cure for depression. 1

Treatments for Major Depression (continued)

Relapse and antidepressant drugs: maintenance drug therapy helps _____, when compared to placebo drug treatment.

- generally agreed that drug therapy should be continued for _____.

- might require chronic drug treatment in severe cases.



- MAOIs may be more effective at treating _____ of depression (often accompanied by hyperphasia - overeating and hypersomnia - sleepiness). 2

Treatments for Major Depression (continued)

Second generation antidepressant drugs importantly include more specific monoamine neurotransmitter reuptake blockers:

- first generation tricyclic antidepressants often blocked, to various extent, the transporters for _____.
- an important second generation class of antidepressants specifically target the _____, therefore named _____.
- recent clinical studies suggest _____ between SSRIs, TCAs, and MAOIs.
- significant advantages of SSRIs include a _____, which explains their widespread and favored prescription.
- examples of SSRIs: _____.

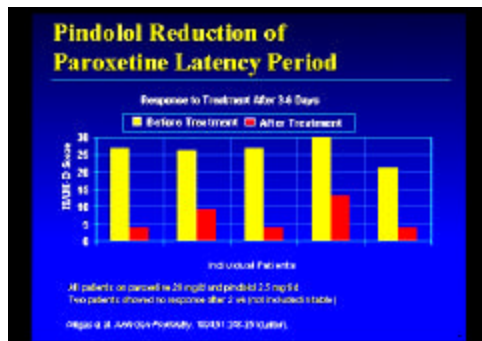
All drug classes (TCAs, MAOIs, SSRIs) have a delayed onset for clinical improvement that normally varies from no less than one week, and up to 3-4 weeks.

Recently, combination (also termed augmentation) therapy of two drugs, an SSRI (paroxetine) together with a serotonin receptor antagonist (5-HT_{1A}) has shown a much quicker response time (3-6 days) instead of the 1-4 weeks period normally required for clinical effectiveness.

- 5-HT_{1A} is an _____.
- SSRI elevates levels of 5-HT which activate _____ of dorsal raphe neurons, as well as a _____.
- pindolol or buspirone (5-HT_{1A} antagonist), block this effect, allowing more 5-HT to be released in synapse.

Treatments for Major Depression (continued)

Reduction of latency for clinical efficacy of SSRIs by 5-HT_{1A} antagonist pindolol (same result with buspirone - BuSpar - another 5-HT_{1A} antagonist).

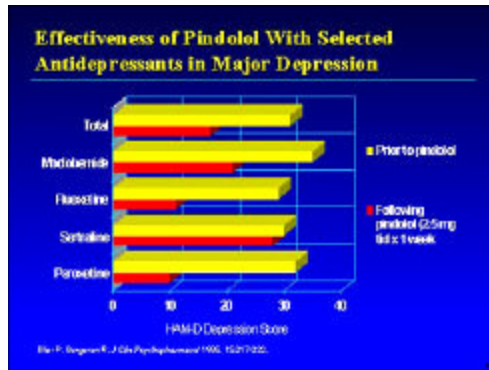


HAM-D score = _____; widely used index of depressive symptoms

- higher scores (in the 20s) are usually associated with _____
- lower scores = symptomatic relief.

Treatments for Major Depression (continued)

This more recent combination treatment with paroxetine and pindolol can also _____.



5

Drug Treatment Side-effects

1. Anticholinergic side effects: peripheral anticholinergic blockade is also a side-effect of antidepressant drugs, particularly the tricyclic antidepressants, and less so for the MOAIs (very little with SSRIs).
- these include _____.

2. Cardiovascular side effects: independent from their autonomic peripheral side-effects, tricyclic antidepressants can cause _____.
- they are also responsible for orthostatic hypotension and dizziness due to low blood pressure in the brain.

3. Cognitive side effects: some of the tricyclic antidepressant (imipramine, amitriptyline) are accompanied by _____ that may impair performance of cognitive (memory) and psychomotor (driving) tasks.
- these side-effects are particularly apparent in non-depressed individuals taking antidepressants.
- patients will usually not become tolerant to these side-effects, and the best action is to switch to a drug with lesser or no sedative effects.

4. Miscellaneous side effects: there are small incidences of antidepressants induced _____.

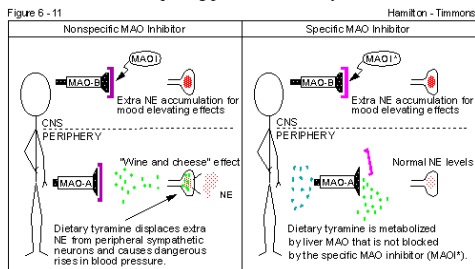
6

Drug Treatment Side-effects (continued)

5. The _____ side effect of MAOIs: inhibitors of monoamine oxidase interferes with the normal functioning of several liver enzymes.

- a monoamine oxidase in the liver (_____) is responsible for the metabolism of _____, an amino acid found in several types of food and drinks (_____).
- tyramine accumulation in the circulation produces the release of _____.

- MAO-A is found predominantly in the liver, whereas MAO-B type is found in the brain.
- unfortunately, most MAOIs are _____, requiring patients to be very careful with their diets.



6. **SSRIs side effects:** this class of antidepressants has become popular because of their low incidence of serious side-effects. Some side-effects include _____.

Electroconvulsive Therapy (ECT) for the Treatment of Depression

Use of electric currents passed through the scalp and brain, which evoke "grand-mal" seizures.

- performed under _____ to avoid fractures.
- _____ is provided to minimize possibility of cell damage by oxy gen deprivation to the brain.
- ECT therapy normally involves inpatient care with 3 sessions weekly for a total of 6-12 treatments, depending on response.
- indicated in the treatment of drug non-responsive depressed patients, and for patients showing depressed symptoms with psychotic features.
- in these refractory and often severely depressed patients, ECT is _____.
- also indicated in patients who cannot tolerate the side effects of antidepressant drugs, or in which cardiovascular disorders would risk serious complications.
- indicated in pregnant women with depression, because ECT is much safer than antidepressant drugs for the fetus.
- indicated if probability of suicide is high because it provides quicker clinical results.

Risks and side-effects of ECT

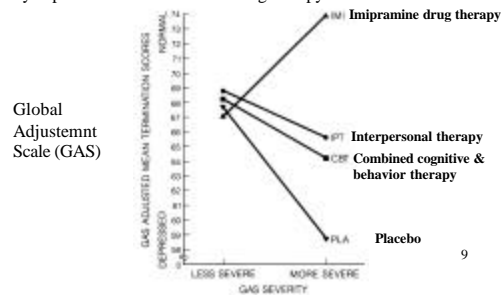
- as with other treatments, _____; without maintenance therapy, half the patients relapse within a year.
- among the risks associated with ECT, _____ has been estimated at approximately 0.01 - 0.8 %.
- evidence of brain damage by ECT is _____.
- memory loss for the time surrounding ECT (2 weeks before and after treatment) is a common side-effect, which normally subside within six months following treatment.
- bilateral ECT might be more prone to memory loss than unilateral ECT, but also more effective.

Psychotherapy in the Treatment of Depression

Different types of psychotherapy have been found to ameliorate the symptoms of depression, with an effectiveness comparable to that of antidepressant therapy.

- at least 3 types of psychotherapies have been shown to help depression: interpersonal, cognitive, and behavioral therapies.
- interpersonal therapy focuses primarily on assisting patients to _____, so that family and social interactions become more adaptive and positive.
- cognitive therapy focuses on a patient's _____, and the therapist then assigns tasks to counteract these negative cognitive attitudes.
- behavioral therapy focuses on the fact that depressed people do not receive _____; they teach depressed individuals skills to increase such positive reinforcements.

However, recent evidence suggest that more severely depressed patients may experience more relief with drug therapy.



Psychotherapy in the Treatment of Depression (continued)

The long-term effects of psychotherapy and drug therapy have not been found to be significantly different in terms of ameliorated symptoms (physiological symptoms such as sleep disturbances or cognitive symptoms such as worthlessness) or incidence of relapse.

- maintenance therapy with _____ - this might be important for individuals who do not want to keep taking medication (side-effects or others).

Treatment of Bipolar Disorder

A very successful treatment for bipolar disorder is with the salt _____.

- lithium ameliorates the symptoms of _____ of patients.
- patients normally experience the mood "normalizing" effects of lithium within two weeks from the beginning of treatment.
- as with other treatments, lithium does NOT cure bipolar disorder; maintenance therapy on lithium is required and very effective in preventing relapses.
- relapse rate for patients on lithium maintenance is approximately every _____ and _____, on average. In comparison, manic-depressive episodes every _____ are observed on placebo maintenance.
- antidepressant treatments are ineffective in treating mania, and if given during a depressive episode, they can trigger a manic episode.
- antipsychotics are sometimes used to calm agitated manic episodes initially, given their sedative effects, but lithium needs to be initiated simultaneously.
- likewise, lithium does not treat major depression very effectively.

Treatment of Bipolar Disorder (continued)

The mechanisms of action of lithium are VERY different from those of antidepressants.

- there are _____.
- instead, lithium acts by limiting the production of an intracellular second-messenger cascade precursor called _____.
- this precursor is involved in the production of the second-messenger inositol tris-phosphate (IP₃), one of the functions of which is to _____.
- intracellular calcium is involved in a variety of functions, including but not limited to, monoamine neurotransmitter release and reuptake, and monoamine receptor regulation.

Lithium's Side Effects

Lithium being a naturally occurring molecule, its side-effects are produced by the _____.

- some unpleasant side-effects of lithium include _____.
- most of these effects are reduced after about _____ of treatment, but tremors can be a pervasive problems for individuals performing fine motor skills.
- lithium poisoning can occur if blood concentration is too high, which primarily affects the brain and produces confusion, slurred speech, drowsiness, loss of balance, vomiting, and eventually coma and death, if not discontinued.
- some slowing of cognition can be observed with chronic lithium.
- kidney failure has not been demonstrated clinically with long-term lithium treatment.

11

Other Treatments for Bipolar Disorder

Some _____ drugs have shown effectiveness in ameliorating the symptoms of manic-depression.

- drugs such as _____, have shown a comparable effectiveness as lithium in the treatment of bipolar disorder and reduction in relapse rate.
- these drugs mainly act in the brain by generally _____.

Other treatments such as psychotherapy have traditionally not been favored in the treatment of bipolar disorder given the high rate of success of drug treatment for bipolar disorder.

- thus, the effectiveness of psychotherapy in treating bipolar disorder is not clearly established.

12