

## Medications for bipolar disorder

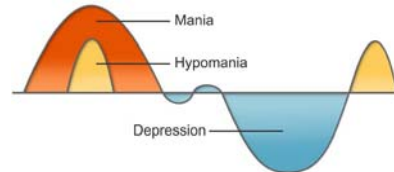
- Findings from Australian National Survey of Mental Health and Wellbeing (Mitchell et al, 2004)
- In 12 months, only one-third saw a mental health professional
- 40% received no medication for their bipolar disorder.



In this session we'll look at medications for bipolar disorder. It's clear in Australia that there's an under treatment for this condition which is a problem because we have many effective treatments that can make much difference to people's lives. In 2004, we reported on the findings relating to bipolar disorder from a large Australian survey called the National Survey of Mental Health and Wellbeing. In that study, we found that in the 12 months prior to interview, only one third of individuals with bipolar disorder had in fact seen a mental health professional on at least one occasion and 40% had received no medication for this condition over that 12 month period, indicating that many Australians with this condition aren't sufficiently treated. In the next series of slides we'll start to look at some of the specific treatments for the different phases and components of this illness.

## General issues for medications for bipolar disorder

- Need to consider both:
  - Treatment of acute phases of hypomania, mania and bipolar depression
  - Preventing relapse into these phases
- Virtually all the highest quality studies (double-blind randomised controlled trials) have been of bipolar I
  - uncertain if the findings are applicable to bipolar II.



When we look at the treatment of bipolar disorder we need to consider two issues. The first is the treatment of the acute presentations of the illness and here we'll be looking at hypomania and mania, in general we'll lump those together. And also bipolar depression the depressed phase of this condition. As well as looking at the acute treatments we'll be also looking at preventing relapse into these phases because in many ways prevention of future episodes is the biggest issue for people with this condition. Another point we need to make before we go into more detail is that I'll be focusing on bipolar I disorder. Virtually all the high quality studies, and by that we mean studies that have been double blind, people don't know what treatment they've been allocated to and randomised, this is the scientific standard for being certain about the information to come out of studies and the strong information is for bipolar I disorder. It's not clear whether these results are applicable to bipolar II disorder.



## Different types of medications used in bipolar disorder

- **Mood stabilisers:** medications that work in both acute phases of depression and 'highs' and in their prevention: Lithium is best known of these
- **Antidepressants:** mainly used in acute bipolar depression
- **Antipsychotics:** used during mania; some have also now been shown to have mood stabilising properties.

Now, there are a number of different types of medications we use for this condition. First, we use the term mood stabilisers and these are medications that work in these different phases that we've spoken about, both the depression and the elevated or 'high' episodes, and also preventing those, so they're effective in both acute episodes either for mania or depression or some for both, and in prevention. And the one that is most familiar to people is Lithium. There are others that we'll talk about. We'll also be talking about antidepressants and these are mainly used in the acute management of bipolar depression. And also, antipsychotics, these have been traditionally used just during manic episodes but it's becoming apparent that some of them also have mood stabilising properties, in other words some of them seem to prevent future episodes of illness.



## General issues for medications for bipolar disorder

- Medications are critical to managing bipolar disorder
- However, growing evidence suggests that the most effective treatment is the combination of medications and psychological treatment
- Recent research reports less depression being experienced by patients (on medications) randomised to a form of cognitive therapy compared to those on medication alone.

We need to put medications in their context. While they're a critical part, and a very important part of managing bipolar disorder, there is growing evidence, including some of our own, that for many patients the best or most effective treatment is combining these medications with psychological treatment. For example, one of our recent completed research projects at the Black Dog Institute that was led by our Research Clinical Psychologist, Jillian Ball, has recently reported that depressed episodes are less common for patients if they're exposed to a form of treatment called cognitive therapy, and this is in addition to medication so if you have cognitive therapy with your medication you're less likely to have a depressed relapse.

## Acute treatments for mania



- Mood Stabilisers:
  - Carbamazepine (Tegretol)
  - Lithium (Lithicarb, Quilonum)
  - Valproate (Epilim, Valpro)
- Atypical Antipsychotics:
  - Aripiprazole (Abilify)
  - Olanzapine (Zyprexa)
  - Quetiapine (Seroquel)
  - Risperidone (Risperdal).

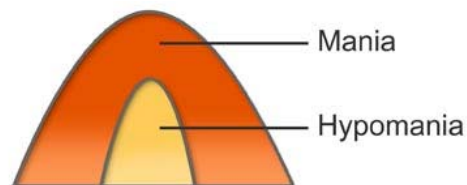
Now, there are several mood stabilisers and we'll just go through these. There are Carbamazepine, Tegretol is the most common brand name, Lithium, some of the common brands are Lithicarb, Quilonum. And Valproate, which you might know as Epilim or Valpro. And there are a number of what we call atypical antipsychotics, these are medications that were originally developed for schizophrenia but have now been shown to be very effective and many to have mood stabilising properties, for bipolar disorder.

And those where there is the best evidence for this condition are Aripiprazole or Abilify,

Olanzapine or Zyprexa, Quetiapine or Seroquel, and Risperidone with Risperdal being the brand name.

## Acute treatments for mania

- During the acute treatment of mania, it is often necessary to use a calming medication such as an antipsychotic or a benzodiazepine until the behaviour and thoughts start to settle.



During the acute treatment of mania, as well as being on a mood stabiliser that we looked at previously, it's often necessary also to have a calming medication such as an antipsychotic or a benzodiazepine, some benzodiazepines you might have heard of are Valium or Seropax and these can be helpful short term until the behaviour and thoughts of mania start to settle with the mood stabiliser.



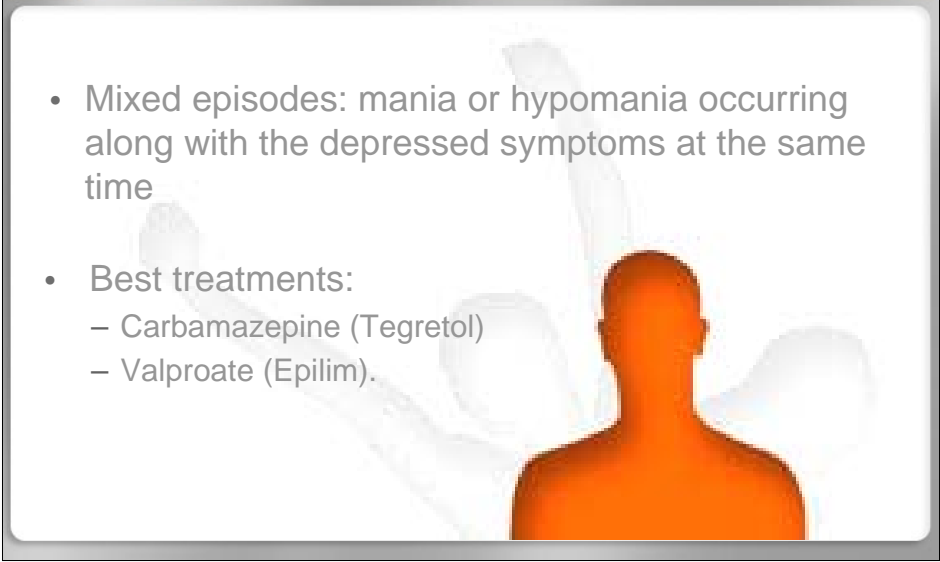
## What if the mania does not settle?

- Change mood stabilisers
- Add a second mood stabiliser (e.g. Epilim to the Lithium)
- Rarely: ECT may be the most effective treatment in a small number of people for whom medications are not effective.

What do we do in the situation where the manic episode or hypomanic episode doesn't respond to our first choice of medication? There are a number of options that we have here. The first is that we can change to a different mood stabiliser; the second is to add a second mood stabiliser for example if you're on Lithium, adding Epilim to that. In the rare circumstance where someone has a very severe and protracted mania that isn't responding to medications, ECT or Electro Convulsive Therapy, may be the most effective management for this very small number of individuals.



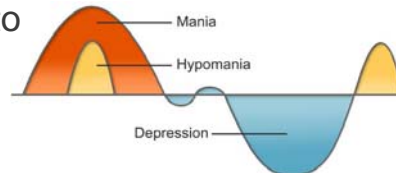
## Treatments for mixed episodes

- Mixed episodes: mania or hypomania occurring along with the depressed symptoms at the same time
  - Best treatments:
    - Carbamazepine (Tegretol)
    - Valproate (Epilim).
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We now look at the treatment of mixed episodes. And to remind you, mixed episodes is where there's a combination of mania or hypomania along with depression and most commonly the mania or hypomania is the most prominent part of this picture. Here we know that the best treatments are Carbamazepine and Valproate, some of those that were originally developed as anti-epileptic agents a number of years ago.

## Options for acute treatment of bipolar depression

- Optimisation of mood stabiliser
- Addition of antidepressant to the mood stabiliser
- Addition of second mood stabiliser
- Addition of an atypical antipsychotic drug.



For the patient who's in a depressed episode and you're looking for the best way of managing that acutely, we have a number of options again. The first is to optimise the mood stabiliser, that means getting the dose and the blood level to a point where we can be sure that the patient is getting potentially the maximum benefit. Probably in Australia a more common treatment is to add an antidepressant to the mood stabiliser. So for example you might be on one of the newer SSRI antidepressants as well as being on one of the mood stabilisers that we've spoken about. Sometimes patients benefit from adding a second mood stabiliser, a bit like when we looked at the management of mania, for example adding Epilim to Lithium. And the last option is adding an atypical antipsychotic drug to the mood stabiliser.



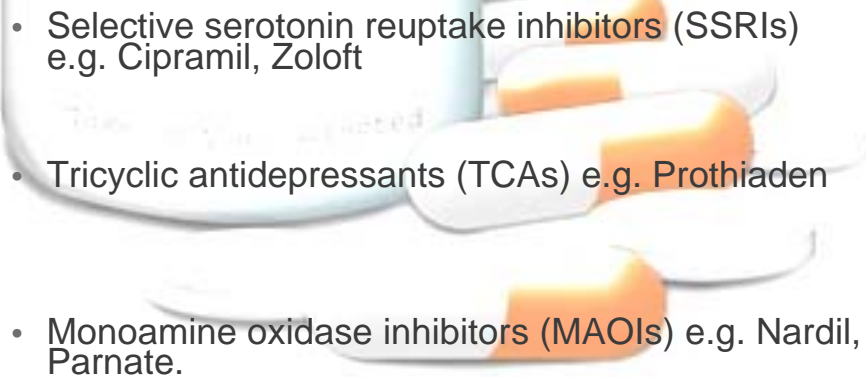
## Mood stabilisers for acute treatment of bipolar depression

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- Lithium
    - Most effective at blood levels of at least 0.8 mmol/L
  - Lamotrigine (Lamictal)
    - Most effective at doses of at least 200 mg.


We'll just go into a little bit of detail about some of the specific choices that we have. So let's look at the mood stabilisers that are effective in the acute treatment of bipolar depression. Those for which there's the best evidence are Lithium and Lamotrigine. Lithium appears to be most effective if you have blood levels of at least 0.8 mmol per litre and for this medication doctors will be normally regularly looking at Lithium levels. The second is Lamotrigine, brand name Lamictal. This is a newer anti-epileptic medication that's been found to be very effective for bipolar depression and most people will need doses of at least 200mg a day to gain benefit from this.



## Effective antidepressants for bipolar depression (from controlled trials)

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- Selective serotonin reuptake inhibitors (SSRIs) e.g. Cipramil, Zoloft
  - Tricyclic antidepressants (TCAs) e.g. Prothiaden
  - Monoamine oxidase inhibitors (MAOIs) e.g. Nardil, Parnate.

What are some of the antidepressants that have been shown to be effective for bipolar depression in scientific or controlled trials or studies? The class of medications that will be used most commonly are what we call the selective serotonin reuptake inhibitors and the short term for that is SSRIs. And common examples of this would be Cipramil and Zoloft. There are a number of other antidepressants that have also been shown to be effective for this presentation and these include the tricyclic antidepressants or TCAs and a common brand name would be Prothiaden but there are many others than are also effective. In the uncommon circumstance where people aren't benefiting from these antidepressants there is an older class called the monoamine oxidase inhibitors or MAOIs and these are Nardil and Parnate.



Failure to respond to mood stabiliser  
± antidepressant

- Switch or substitute antidepressants
- Switch or substitute mood stabilisers
- Electroconvulsive therapy (ECT).

Again we look at the options if patients don't respond to some of the simple first steps and again we're focusing here on depression. So we had the situation where a person is being treated with a mood stabiliser with or without an antidepressant but they're not getting better, so what are the options? The first is to switch or substitute antidepressants so that might mean using one of the options on the previous page that wasn't the first choice or trying a new antidepressant. You can also switch or substitute mood stabilisers. Electroconvulsive therapy or ECT is often a very effective treatment for bipolar depression because quite a few people don't respond well to medications. It's simple, safe and often profoundly beneficial.



## Long-term treatment

- Lithium
  - best studied treatment
  - most effective at preventing manic episodes
  - weakly effective for preventing bipolar depression
- Lamotrigine
  - most effective at preventing bipolar depression
- Olanzapine
  - need to watch weight gain, diabetes, lipid levels
- Valproate
- Carbamazepine

We now move from the acute treatment of bipolar disorder to looking at long term treatment or prevention. Now, there are a number of options that we have here and we'll go through those. Lithium, although it's a very old medication, Australian discovery of the late 1940s, is still the best supported, so the strongest evidence is for Lithium, despite for some patients, it being a difficult drug to tolerate. It's most effective at preventing manic episodes, and that has held up well over the years, in terms of evidence. It's also weakly effective at preventing bipolar depression. Lamotrigine we looked at earlier in terms of the acute management of depression, and its strongest evidence is for preventing bipolar depression. Olanzapine also, the growing evidence is that it's effective for preventing, particularly manic but also depressed episodes, but you need to be aware that there are potential adverse effects with weight gain, and a small number of people develop diabetes or elevated lipid levels. Some of the other treatments that are effective are Valproate or Epilim, and Carbamazepine or Tegretol.



## Final thought

Psychological treatments in conjunction with medication are often the best and preferred treatment package.

Finally, although this session has been on medications for bipolar disorder, we just need to emphasise that psychological treatments in conjunction with medication are often the best and preferred treatment package.