

BIPOLAR NEUROSCIENCE

Lee Hale

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INTRODUCING...

- PhD in Structural Biology from Imperial Collage London.
- Research Scientist at LifeArc – biophysics, microbiology, cancer and neuroscience.
- Consultant for IDBS – scientific software.





BIPOLAR DISORDER

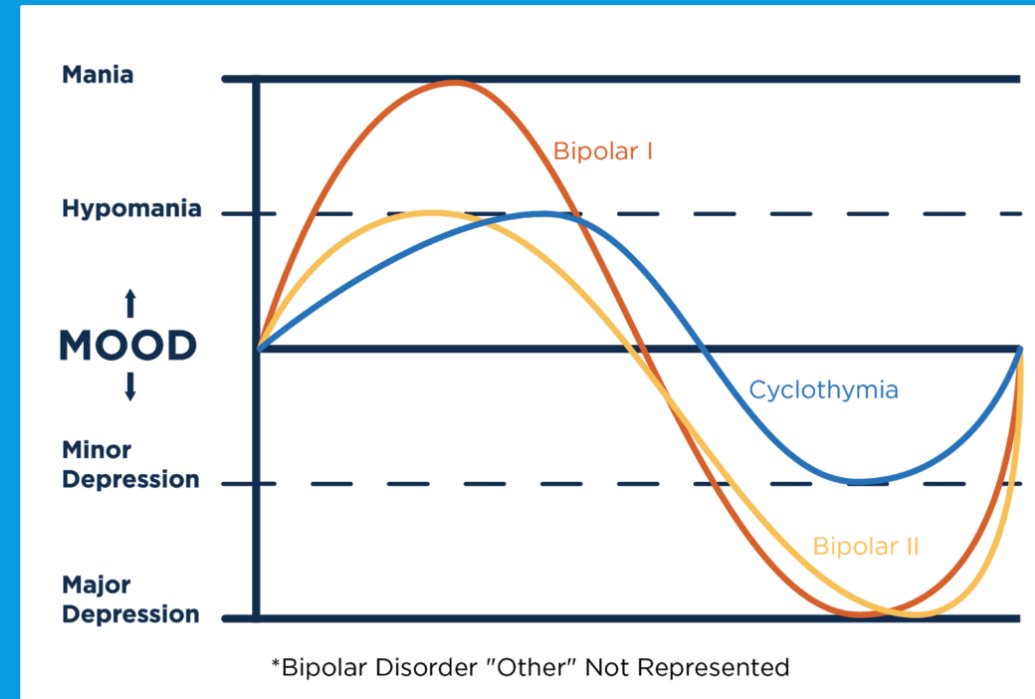
BIPOLAR DISORDER

- Used to be called manic depression until 1980
- A severe mental health condition that affects moods.
- People with bipolar disorder have depressive and manic episodes.
- Manic episodes can veer into psychosis – deluded thinking in which you see or hear things that are not there or become convinced of things that are not true.
- 1-2% of the population have bipolar.
- As many as 5% are on the bipolar spectrum.

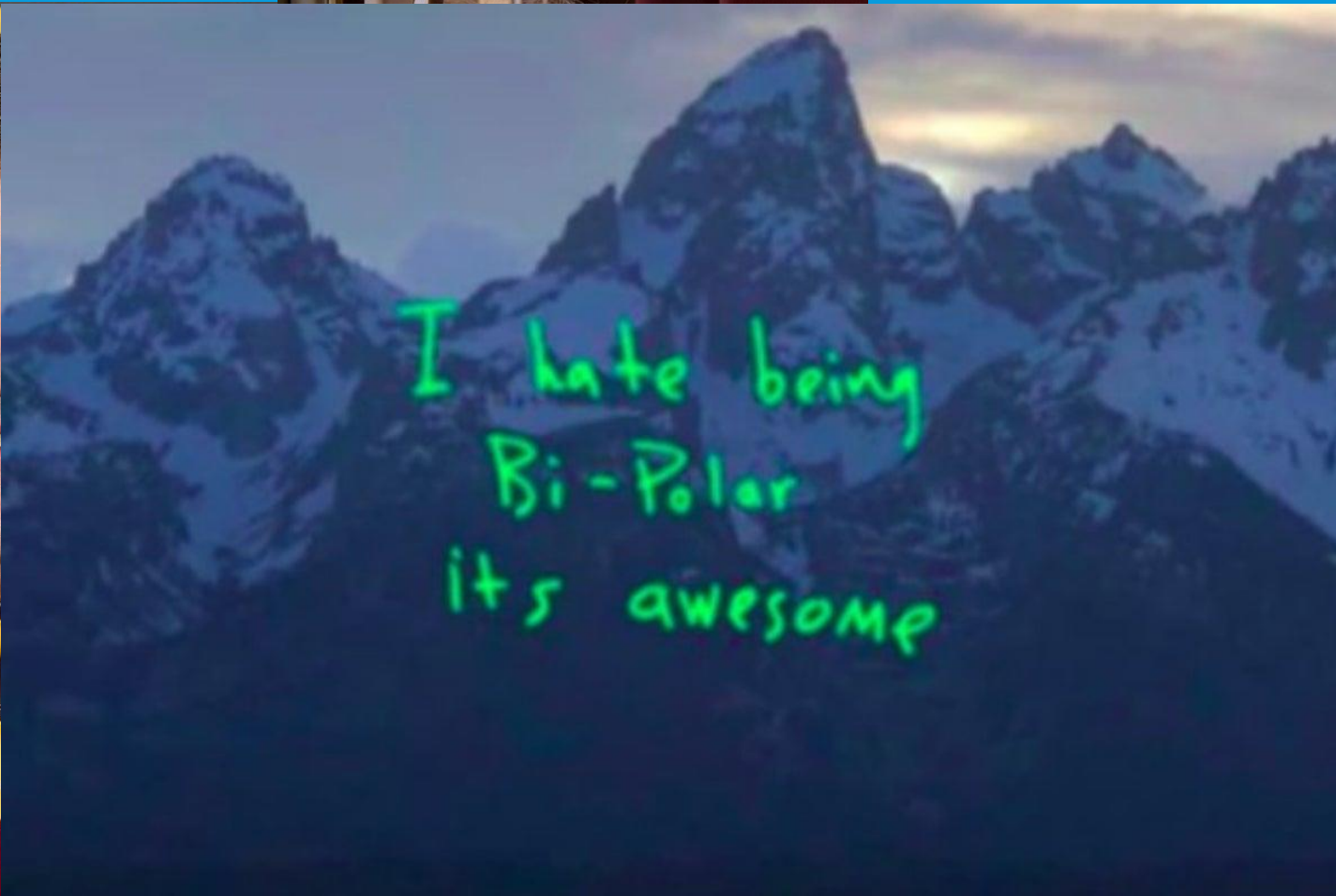


THE BIPOLAR SPECTRUM

- **Bipolar I** – or 'Classic Bipolar' – Most intense type. Involves episodes of mania and depression that last 1-2 weeks or longer. Often require hospitalisation.
- **Bipolar II** - Involves major depression that can last for weeks as well as bouts of hypomania that can last several days or more.
- **Cyclothymic disorder** – Causes lower grade of hypomania and depression that can last for weeks. May involve emotional dysregulation and anxious, impulsive, reactive behaviour.



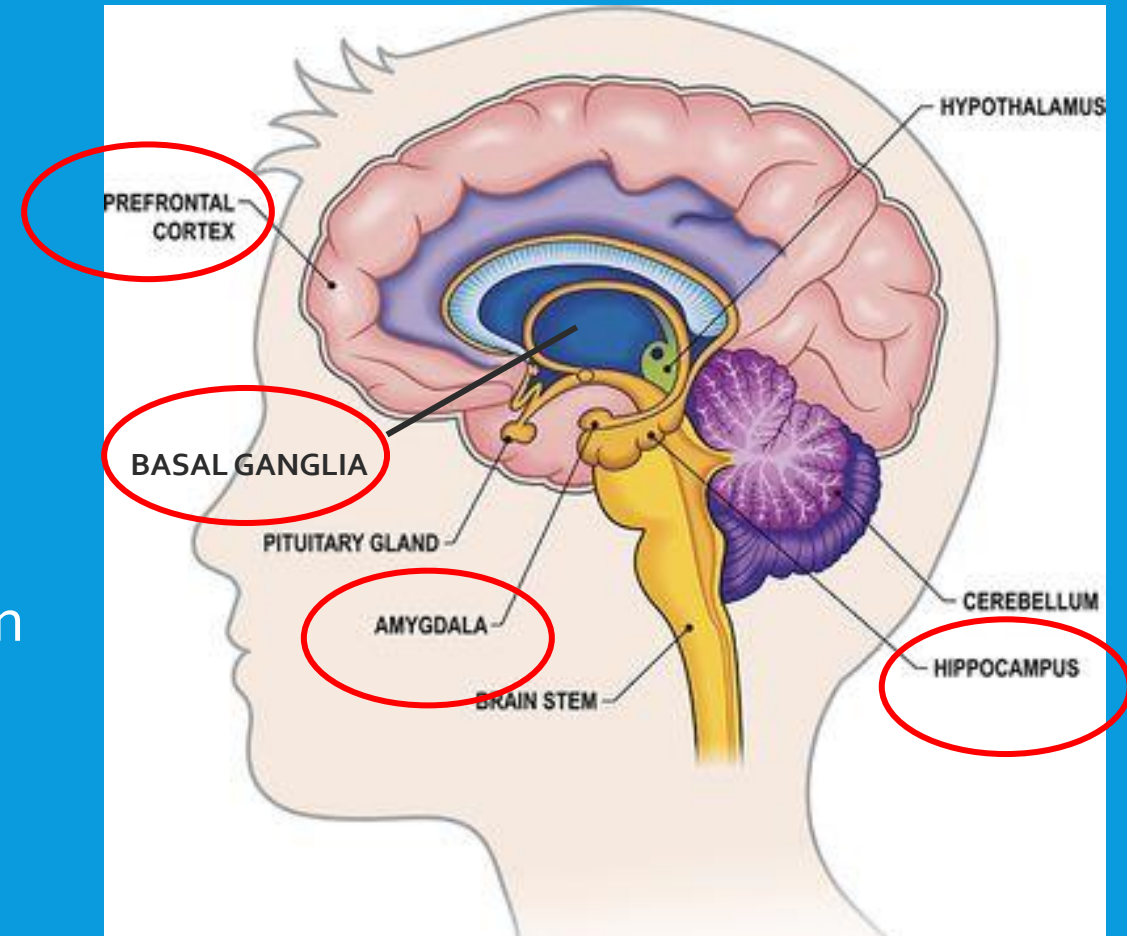
NOTABLE PEOPLE WITH BIPOLAR



THE BRAIN AND NEUROTRANSMITTERS

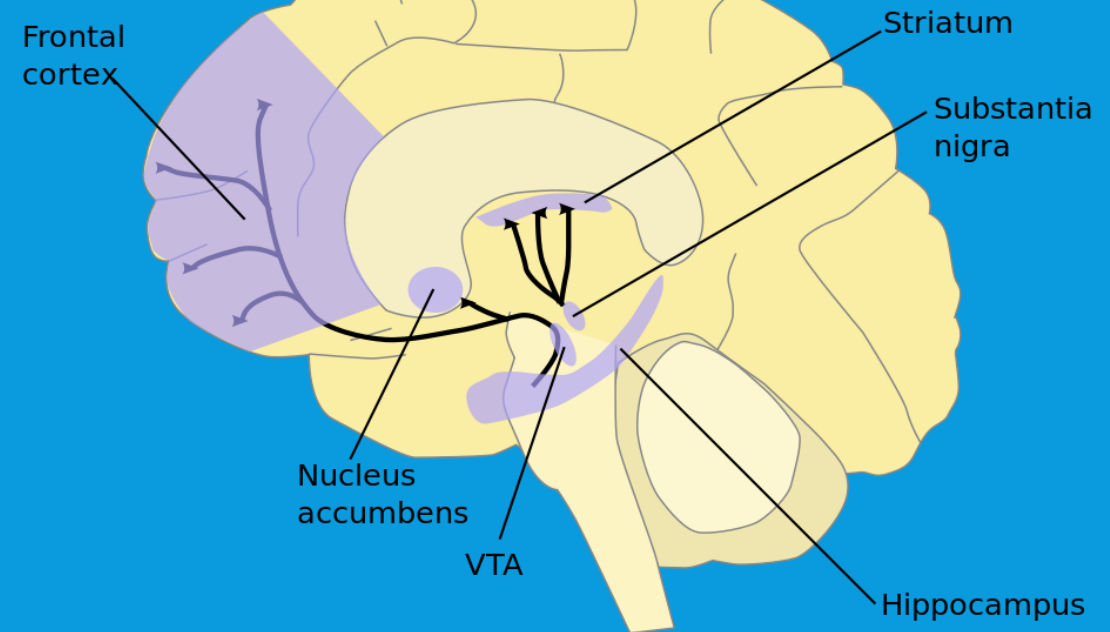
THE BRAIN

- Prefrontal cortex is the cerebral cortex covering the front part of the frontal lobe – planning complex cognitive behaviour, personality, decision making and social behaviour.
- The amygdala is responsible for emotional behaviour and motivation (part of the limbic system).
- The basal ganglia is associated with control of voluntary motor movements, learning, cognition and emotion.
- Hippocampus plays a major role in learning and memory



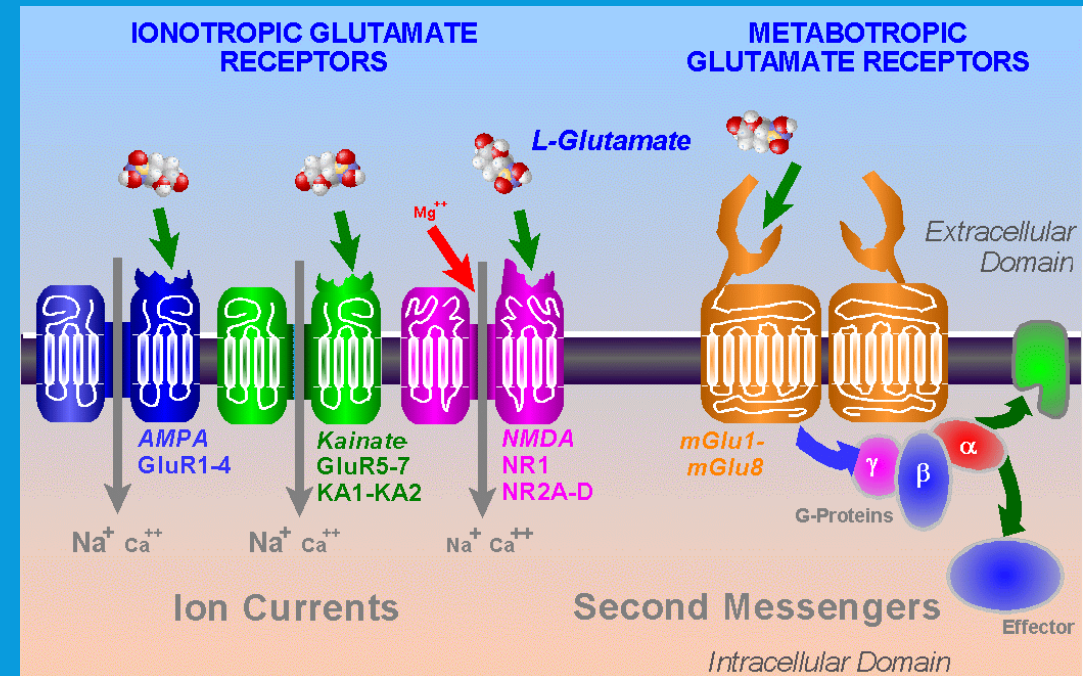
DOPAMINE

- Dopamine is a neurotransmitter that plays important role in executive functioning, motor control, motivation and reward.
- Dopamine is made in nerve cell bodies in the ventral tegmental area (VTA), substantia nigra and the hippocampus, and is released in the nucleus accumbens and prefrontal cortex.
- The nucleus accumbens plays a role in motivation, aversion, reward and reinforcement learning. It has a significant role in addiction.
- Dopamine dysfunction is implicated in bipolar mania and schizophrenia.



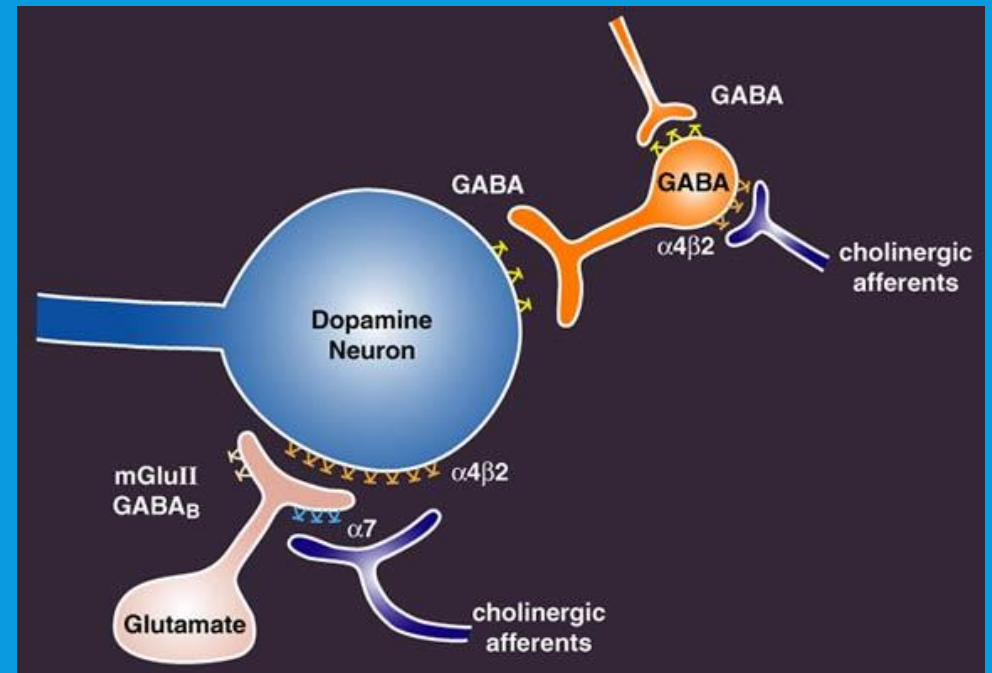
GLUTAMATE

- Glutamate is a non-essential amino acid and excitatory neurotransmitter, needed for keeping the brain functioning properly.
- It triggers neurons to release neurotransmitters to other receptors
- Glutamate plays a major role in learning and memory.
- Biochemical receptors for glutamate include AMPA, NMDA and metabotropic receptors.
- Tomatoes, cheese and mushrooms contain high amounts of glutamate. (Unrelated to MSG)



GABA

- Glutamate is used to make gamma-aminobutyric acid (GABA)
- GABA has the opposite effect of glutamate – it's the main inhibitory neurotransmitter.
- GABA exerts its inhibitory effect through GABA_A and GABA_B receptors
- Decreased GABA functioning is associated with mania in people with bipolar
- GABA exerts a strong inhibitory effect on dopaminergic neurons

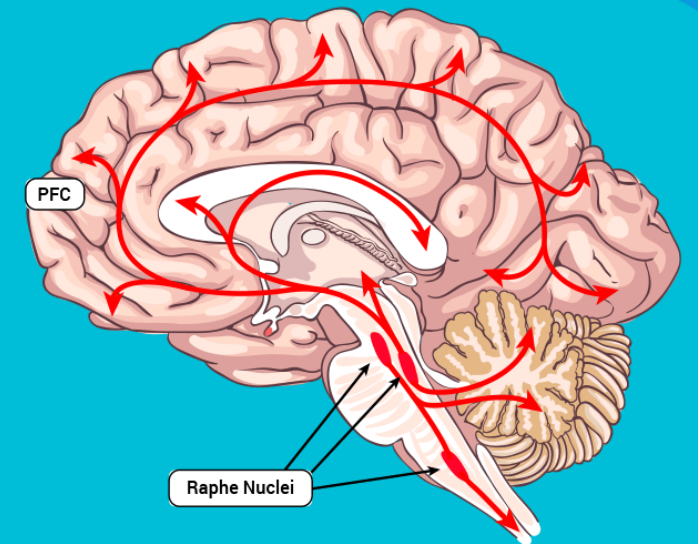


SEROTONIN

- Serotonin (5-hydroxytryptamine, 5HT) is a neurotransmitter involved in modulating mood, cognition, reward, learning and memory.
- Derived from the amino acid tryptophan, found in meat, cheeses and nuts.
- Produced by raphe nuclei and distributed to various areas of the brain, including the prefrontal cortex.
- Reduced levels of serotonin are implicated in depression, but increased levels are associated with bipolar mania.

SEROTONIN PATHWAYS

Distribution of serotonin from **raphe nuclei** through cortex and into the cerebellum.



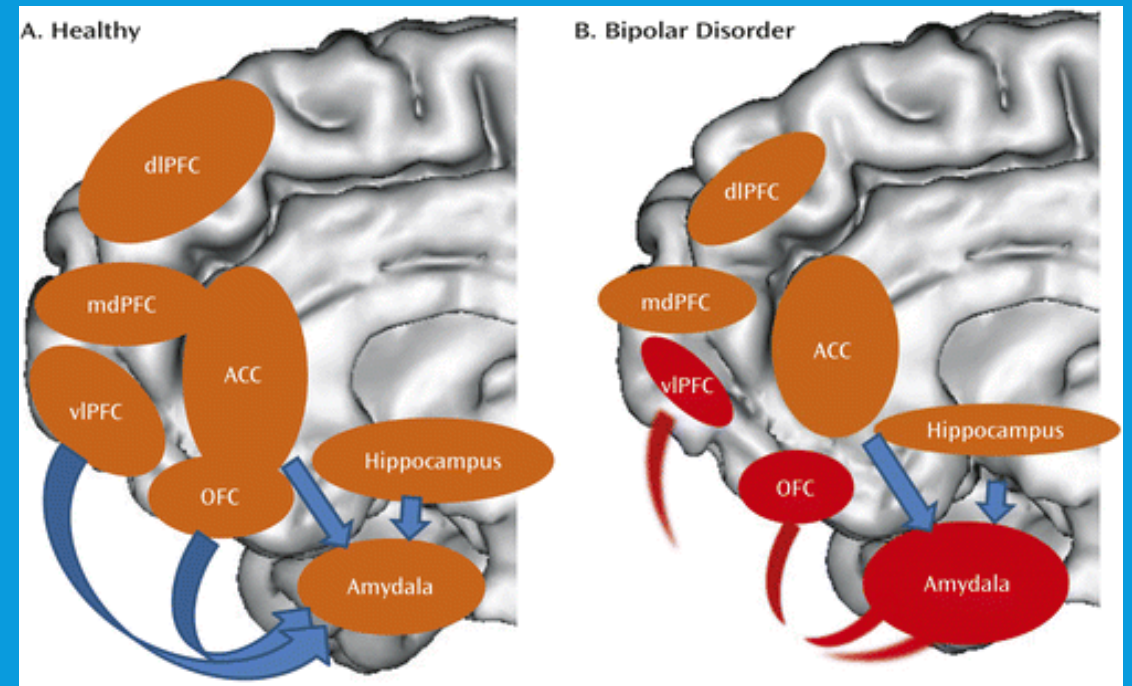
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BIPOLAR NEUROSCIENCE

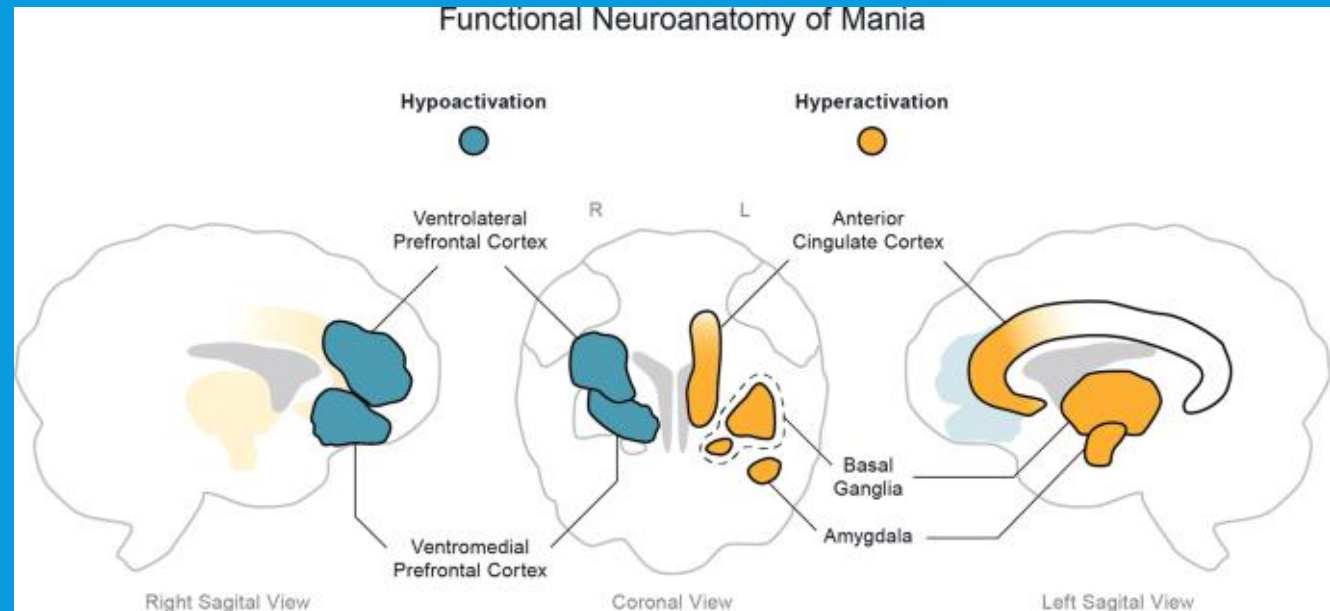
BIPOLAR NEUROSCIENCE

- MRI scans of 6,503 people, including 2,447 adults with bipolar disorder and 4,056 healthy controls showed thinning of grey matter in the brains of patients with bipolar disorder.
- Grey matter volume decreases are seen in the prefrontal cortex, amygdala and hippocampus.
- Abnormalities in neural circuits supporting emotion processing, emotion regulation and reward processing.



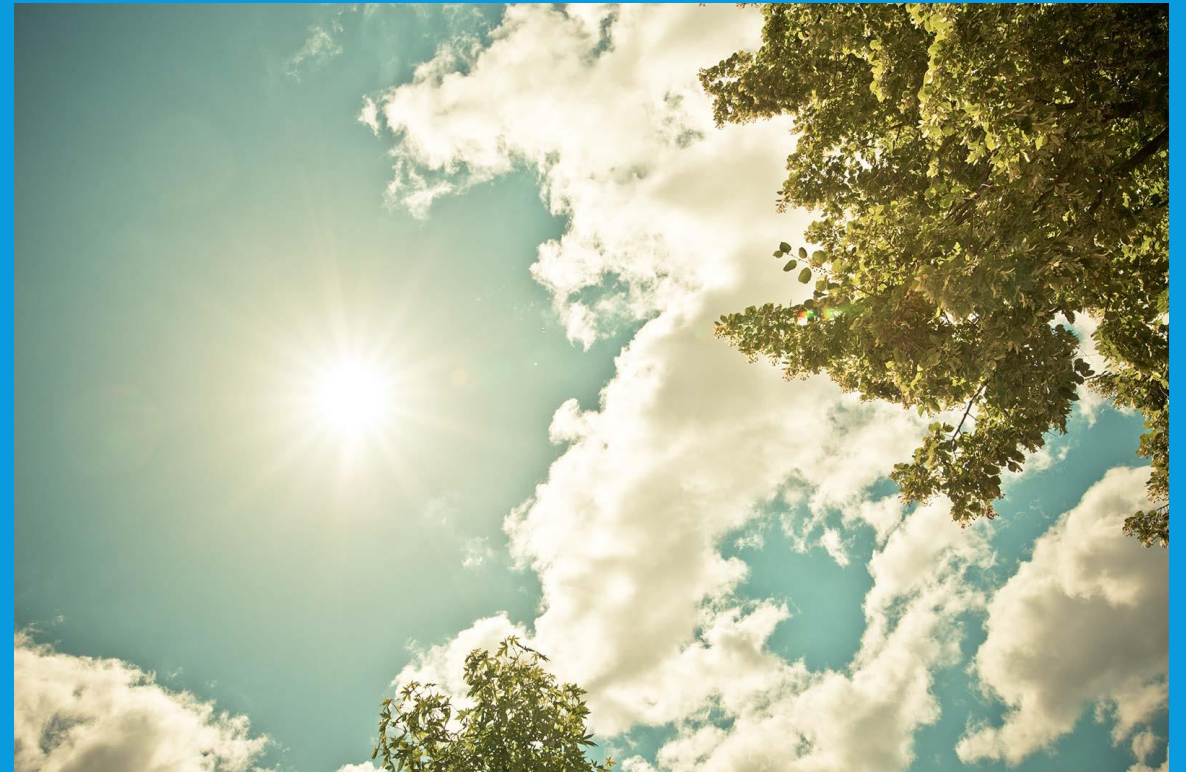
MANIA NEUROSCIENCE

- Mania is characterised by increased energy, elated and/irritable mood, grandiosity, lack of sleep, impaired thinking and poor judgement.
- The exact mechanism for mania is unknown, but is thought to be due to excessive dopamine in the right prefrontal cortex.
- Hyperactivity of the amygdala, basal ganglia and anterior cingulate cortex in the left hemisphere of the brain.



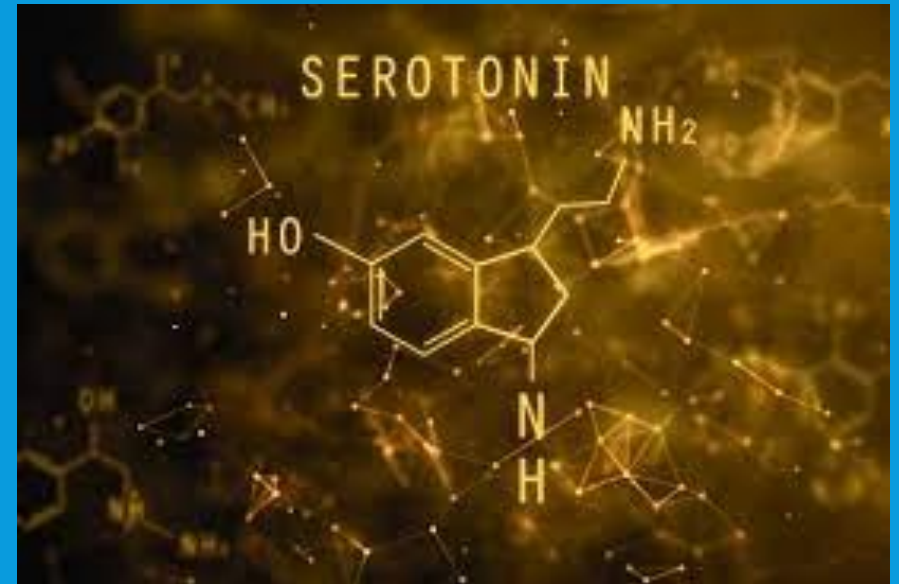
MANIA TRIGGERS

- High levels of stress
- Changes in sleep patterns or a lack of sleep
- Use of recreational drugs or alcohol
- A significant life change
- Childbirth
- Seasonal changes – some people are more likely to experience mania in spring



DEPRESSION NEUROSCIENCE

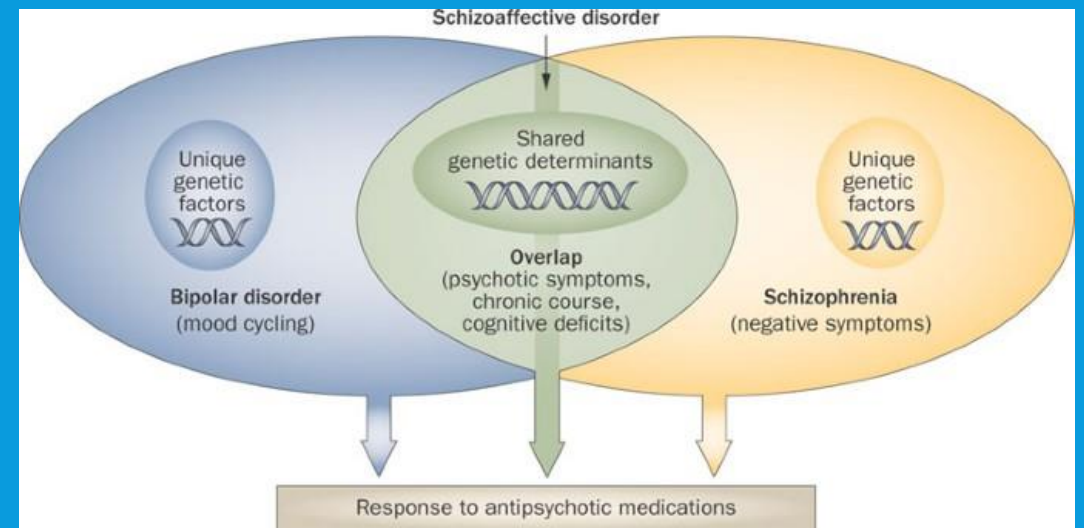
- Bipolar depression is characterised by sadness, psychomotor difficulties and anhedonia (a reduced ability to experience pleasure).
- Bipolar depression is clinically indistinguishable from major depressive disorder.
- Lower binding of serotonin to serotonin transporters may have a role in bipolar depression.
- Lower amounts of the serotonin transporter (BP₁) in the midbrain, amygdala and hippocampus.
- Traditional SSRIs (e.g. sertraline) can cause mania



BIPOLAR VS SCHIZOPHRENIA & ADHD

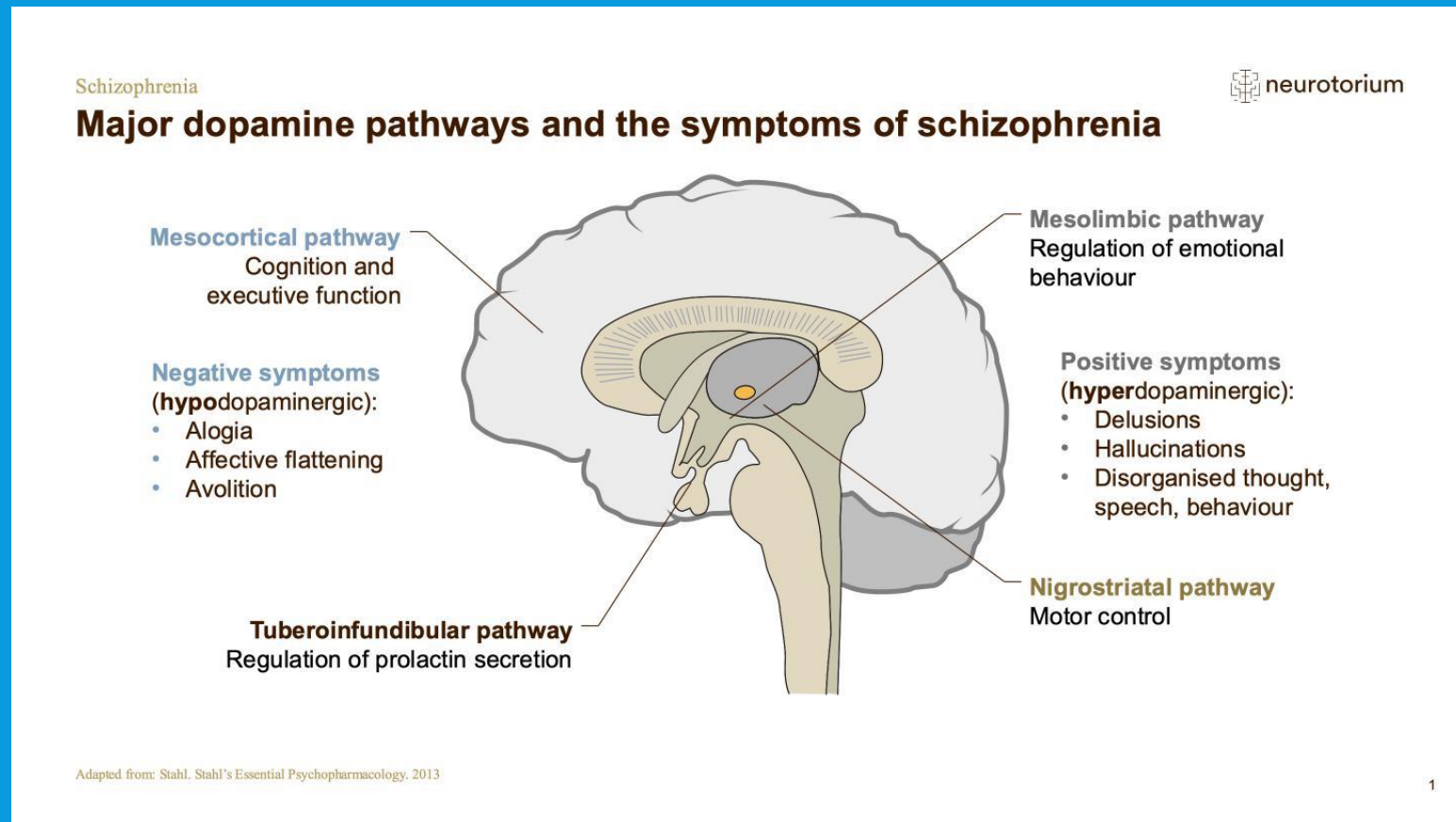
BIPOLAR VS SCHIZOPHRENIA

- People with schizophrenia experience psychosis, such as hallucinations or delusions.
- People with bipolar can also experience psychosis, especially during manic episodes.
- Some people have schizoaffective disorder, which involves a combination of schizophrenia symptoms and mood disorder symptoms.
- The CACNA1C gene is associated with schizophrenia as well as major depression and bipolar.



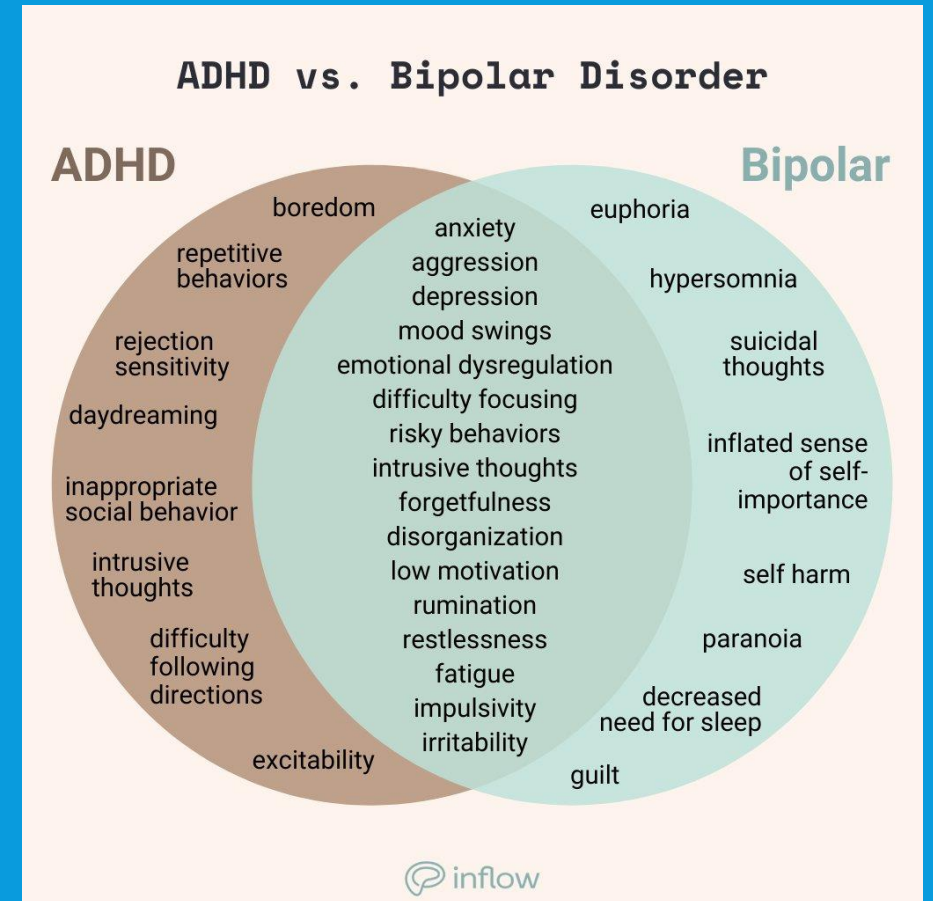
BIPOLAR VS SCHIZOPHRENIA

- Hallucinations and delusions in schizophrenia are caused by dopamine dysfunction in the mesolimbic and mesocortical pathways.
- Excessive glutamate signalling has also been implicated for schizophrenia.
- Dopamine dysfunction is also present in bipolar patients, particularly during mania.



BIPOLAR VS ADHD

- ~20% of people with ADHD also have bipolar disorder.
- 3-4% of adults have ADHD
- The ADHD brain produces an insufficient amount of dopamine.
- The ADHD brain craves dopamine, so can lead to addictions.
- Like during bipolar mania, people with ADHD often have sleep disturbances due to a racing brain.
- People with ADHD can hyperfocus on something of great personal interest for an extended period of time, at times mentally drowning out the world around.



BIPOLAR TREATMENTS

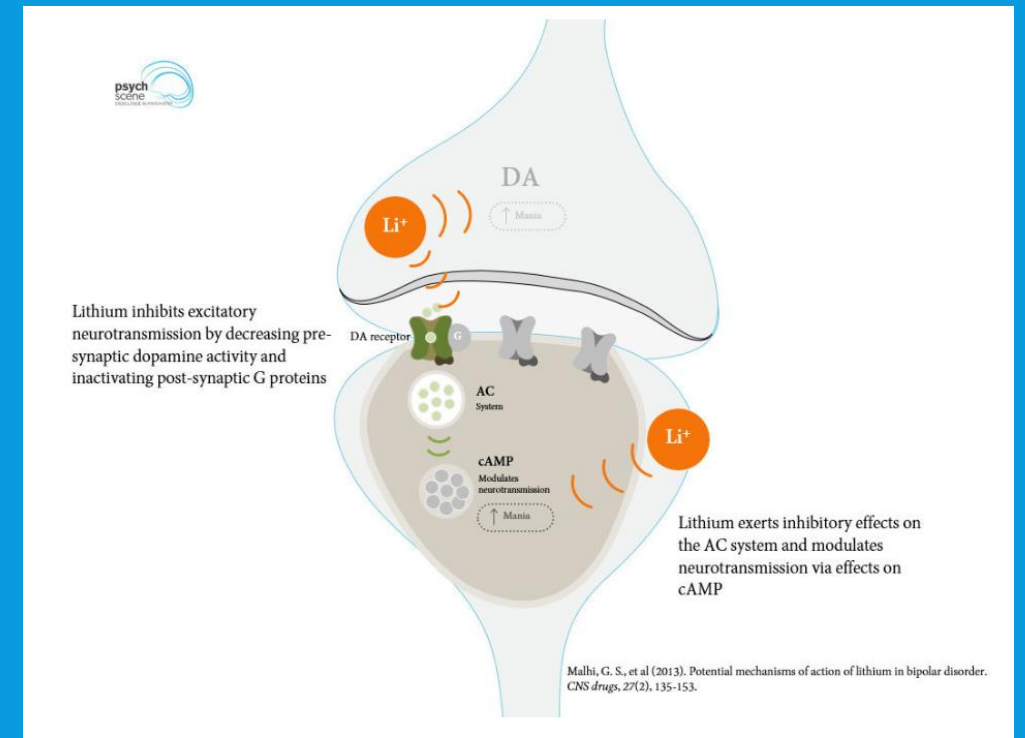
HISTORY OF BIPOLAR TREATMENTS

- The ancient Greeks and Romans discovered that using lithium salts in baths calmed manic people and helped depressive people.
- People could be executed for having bipolar disorder.
- Strict religious dogma stated that people with bipolar disorder were possessed by demons and put to death.



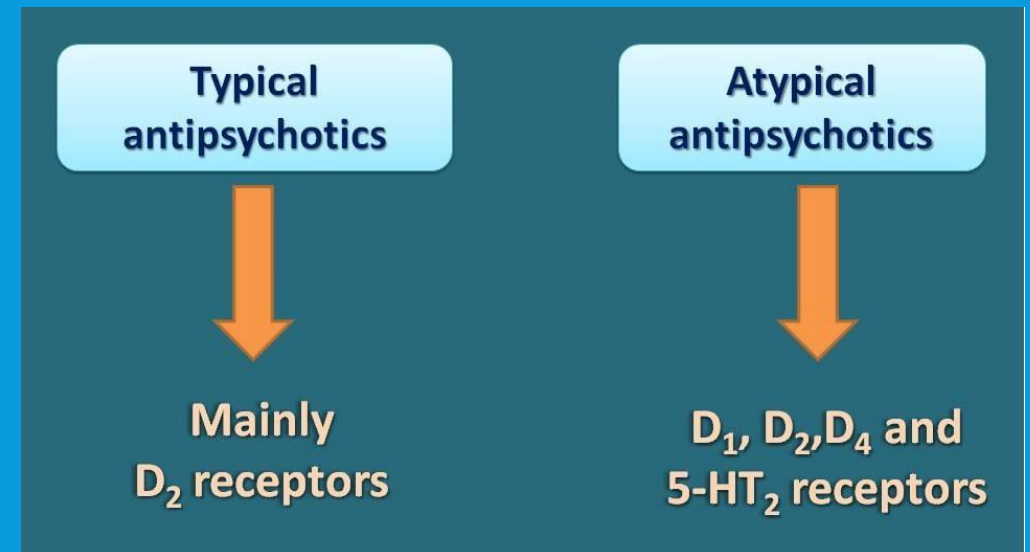
THE SCIENCE OF LITHIUM

- Lithium carbonate has been used to treat mania since 1949 and affects many aspects of neurotransmission.
- Lithium decreases presynaptic dopamine activity
- Lithium inactivates postsynaptic G proteins, which reduces excitatory neurotransmission in the brain.
- It reduces glutamate activity.
- Increases the levels of inhibitory neurotransmitter GABA and activates the GABA receptor



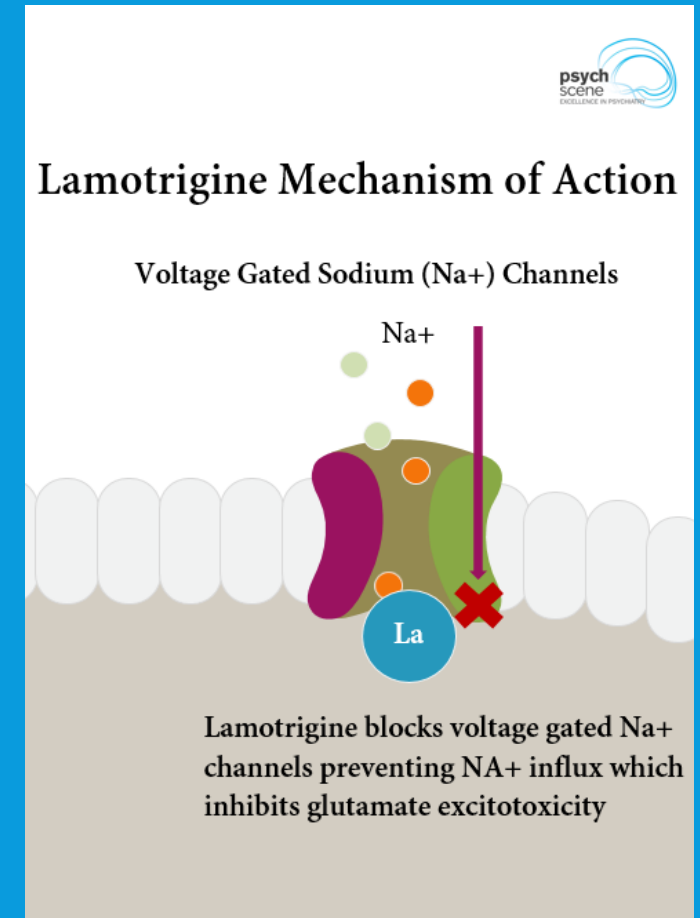
ANTI-PSYCHOTICS

- Antipsychotics can be typical or atypical
- Typical antipsychotics include chlorpromazine and haloperidol. These act on the dopaminergic system, blocking the dopamine type 2 (D₂) receptors.
- Typical antipsychotics can cause uncontrollable body movements.
- Atypical antipsychotics include clozapine, olanzapine, quetiapine and risperidone.
- Atypical antipsychotics have lower affinity and occupancy for dopaminergic receptors and also bind to serotonin receptors 5-HT_{2A}



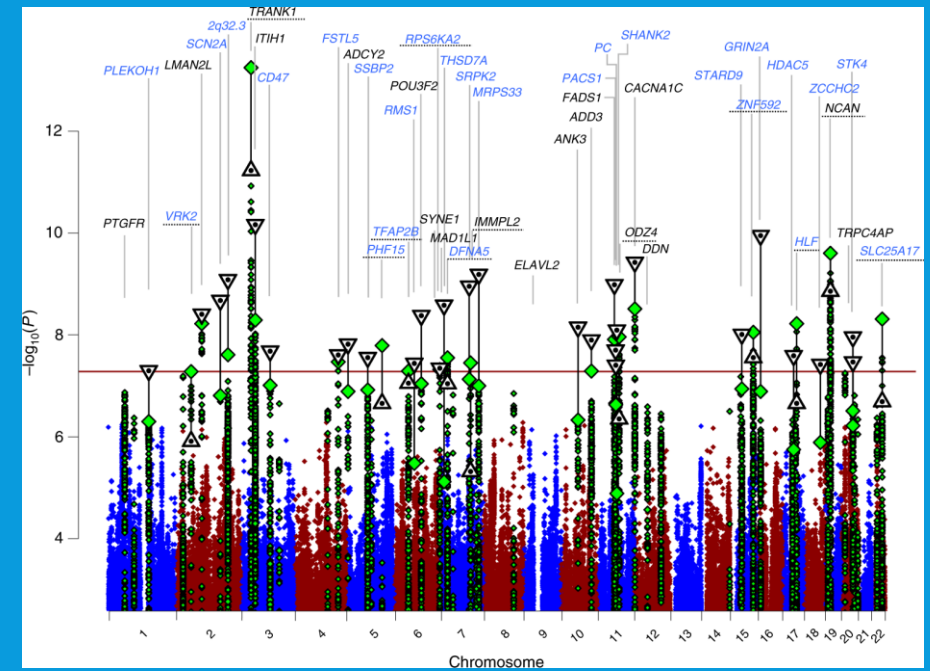
LAMOTRIGINE

- Lamotrigine is an anti-epileptic drug which enhances sodium channel inactivation and possible inhibition of synaptic glutamate release.
- Lamotrigine also inhibits uptake of serotonin, dopamine and noradrenaline and is effective against bipolar depressive episodes.
- Lamotrigine doesn't have efficacy against bipolar mania.



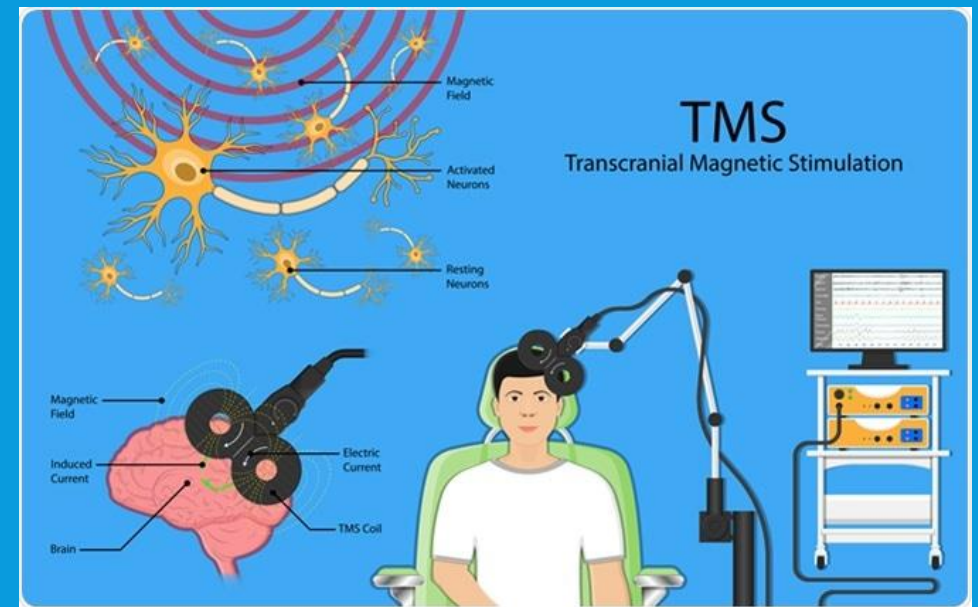
BIPOLAR GENETICS

- The risk of a parent passing on bipolar disorder is ~10-25%.
- Genome-wide association studies (GWAS) revealed that bipolar disorder seems to be influenced by ~266 genes
- One of the most consistently identified genes is *CACNA1C*, which codes for a calcium channel subunit that affects amygdala processing of emotional events
- Another gene of interest is *ANKK3*, which encodes ankyrin G. This couples axonal voltage-gated sodium channels to the cytoskeleton and has roles in dendrites and glia.



THE FUTURE OF BIPOLAR MEDICINE

- Gene therapy – with the hope of providing precision medicine for bipolar
- Electro-convulsant therapy – when an electric current is sent through the brain to cause a controlled seizure, has been used when patients don't respond to medications.
- Researchers are studying transcranial magnetic stimulation – a non-invasive procedure that uses magnetic fields to stimulate brain cells. This could be promising for bipolar depression.



TO ANYONE RECENTLY DIAGNOSED...

- Bipolar is a rough ride for the individual and for friends and family
- Medication is nothing to be ashamed about
- It may take a long time to figure out what medication is best
- There's less stigma than there was before
- Bipolar is another aspect of neurodiversity
- There are support groups available – e.g. Depression Xpression

MENTAL HOSPITAL EXPERIENCES

MENTAL HOSPITAL EXPERIENCES

- Delusions – thinking I was an alien from outer space
- Hallucinations – seeing faces everywhere, especially in garden foliage
- Paranoid thinking
- Believing I was present during historical events, and could predict the future.
- Lack of freedom in mental hospital – once you're 'sane', you still have to be present in the hospital and often are forced to take medication
- In my experience, mental health hospitals aren't all that safe
- It's hard work for Mental Health Nurses



<https://www.amazon.co.uk/Aqua-Maddas-Lisa-Hale/dp/Bo8L2HYRNW>

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THANK YOU!