

**New Approaches to
Common Mental Illnesses
A Brave New World for Psychiatry
is Just Around The Corner**

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*My brief was to comment on
developing biological treatments for
mental illness*

*A rapid review of some developing
biological treatments for
Affective Disorders*

Anti-inflammatories and depression

- NSAIDs
- TNF inhibitors and polymorphisms
- Anti-cytokine antibodies
- Minocycline: multiple effects

Glutamate (refresher summary)

- Amino acid, “Engine room transmitter”
- Excitatory effect; link to neurotoxicity
- Most common transmitter in brain
- Four receptor groups: **AMPA**, **NMDA**, Kainate, metabotropic group
- Lamotrigine, vortioxetine, memantine and minocycline
- Involved in large number of medical disorders

Ketamine

- Ketamine inhibits glutamate NMDAR’s but also provokes post-synaptic activation (etc)
- Promotes synaptic growth/connectivity in PFC and hippocampus
- Rapid/transient antidepressant in severe MDD
- Also helps: PTSD, OCD, GAD
- Brevity of benefit is major challenge
- Dose: circa 0.5mg/kg with slow administration

Cannabinoid receptors & ligands

- Cannabis receptors widely distributed; CB1 and CB2
- Synaptic modulators: retrograde and operated by endocannabinoids
- Affect mood, arousal, memory, pain, appetite, sleep, inflammation, etc.
- THC and cannabidiol of most interest (2 of 113 plant cannabinoids)
- Interact with orexin receptors

Cannabinoids and treatment

- Potential use in treating Post Traumatic Stress Disorders
- May be useful treating Generalized Anxiety Disorder and Social Anxiety Disorder
- Uncertain role in treating mood disorders; can be aggravating
- Cannabidiol is most promising
- Roles in bipolar disorders and psychosis uncertain
- Note negative cannabinoid effects

Suvorexant

- Second “true” hypnotic, after agomelatine
- Orexin 1 & 2 receptor antagonist
- Orexins (hypocretins) connected to cannabis 1 receptors and have many other connections
- Contribute to wakefulness, arousal, appetite and other functions
- Alter activity of acetylcholine, serotonin and noradrenaline
- Some morning somnolence; half life 12 hours

Transcranial Magnetic Stimulation

- rTMS already proven effective in severe depressive disorders (note melancholic)
- Not as effective as ECT but fewer side effects
- “Deep TMS” appears more promising
- Non-dominant hemisphere stimulus may be more effective in PTSD
- Obsessive Compulsive Disorder?
- Magnetic Stimulation Therapy (derivative) may be helpful

MDMA (Ecstasy)

- Enhances serotonin, noradrenaline, dopamine, oxytocin, cortisol, neurotrophic factors
- Reduced amygdala and insula activation
- Increased amygdala and hippocampus communication
- Increased activity in the prefrontal cortex
- Facilitates re-programming of memories
- Use concurrently with psychotherapies

Other similar medications

Psilocybin

- Serotonin 2a receptor agonist

Methylphenidate and dexamphetamine

- Inhibit noradrenaline/dopamine transporter in PFC
- Dexamphetamine also increases release of monoamines and inhibits MAO

Evidence of efficacy with psychotherapy in treatment of resistant depression for all above

Diet

- Balanced diet antidepressant
- Methyl-folate supplements
 - improved serotonin, dopamine and noradrenaline synthesis
 - plus homocysteine metabolism, nucleic acid synthesis
 - polymorphism of methyl-tetrahydrofolate reductase gene

Diet

- N-acetyl cysteine
 - component of glutathione
 - cysteine-glutamate antiporter
- Omega-3, SAME, probiotics, Vitamins C and D
 - Uncertain
- “Leaky gut” and blood brain barrier

Watch this space 😊