Your Pharmacist / Your Advocate

(New treatments and resolutions for your prescription problems)

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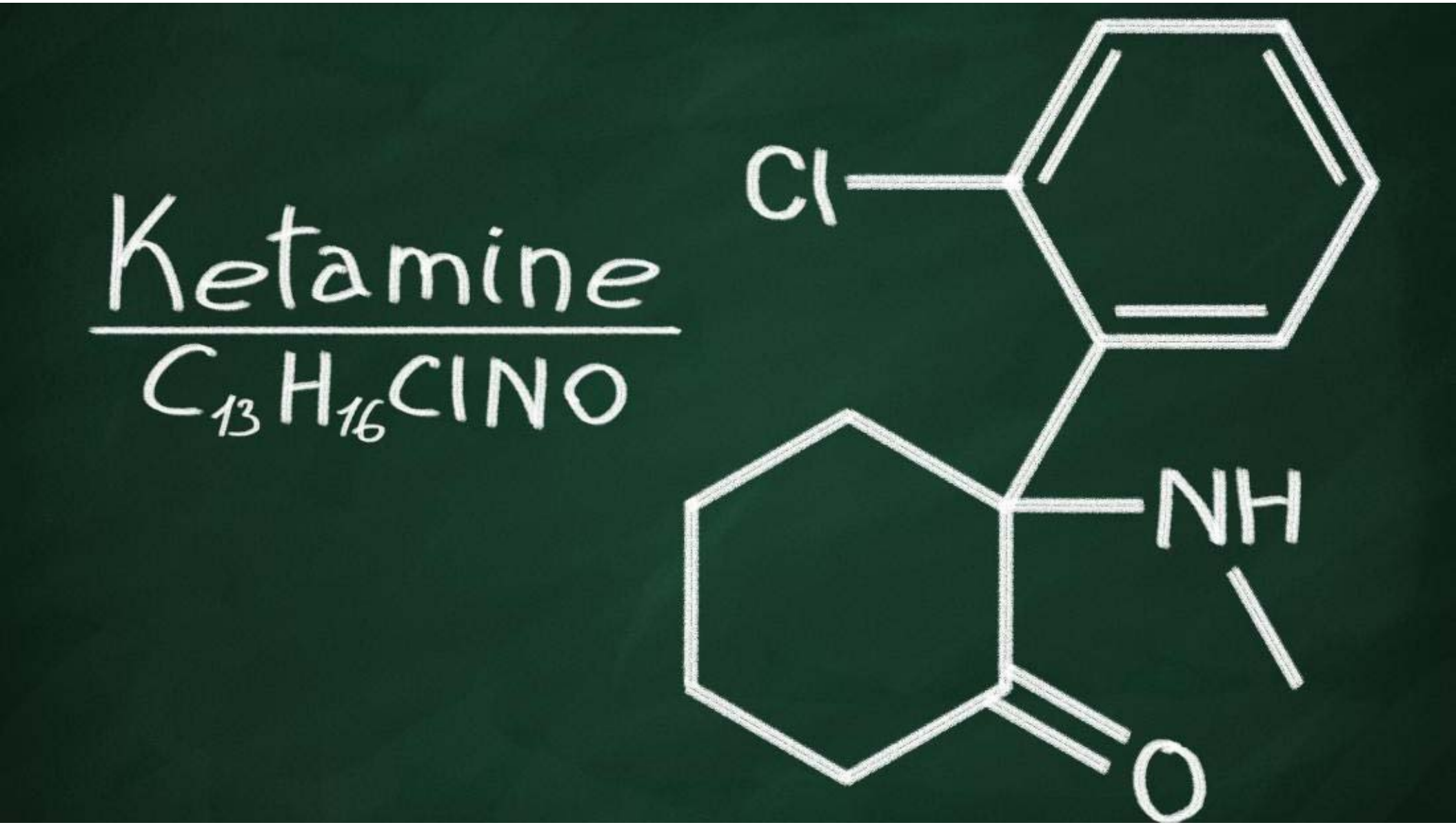
Novel Treatments

- Ketamine and NMDA Receptor Modulators
  - **Dextromethorphan**
  - Memantine
  - Amantadine
- LDN (Low Dose Naltrexone)
- CBD (Cannabidiol)


Ketamine
$C_{13}H_{16}ClNO$
Cl
NH
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Ketamine
$C_{13}H_{16}ClNO$

- Ketamine, an NMDA receptor antagonist, is an anesthetic agent that has been used by some pain specialists for CRPS. There is a growing body of clinical evidence to support the use of ketamine in the treatment of neuropathic pain
- After its introduction in the 1970's, Ketamine immediately found a role in battlefield anaesthesia during the Vietnam conflict, where its safety (because of relative lack of cardiorespiratory depressant effects) and its analgesic properties were advantageous.

Ketamine

Ketamine acts by a distinct, synergistic route to opioids and has also been suggested to attenuate the development of opioid tolerance (Ketamine: new uses for an old drug?*Hirota K, Lambert DG, Br J Anaesth. 2011 Aug; 107(2):123-6.)*

studies suggest that the prolonged infusions can produce reductions in pain that persist for weeks. There would appear to be evidence of a substantial (>50%) analgesic effect that could be worthwhile in refractory cases of CRPS if its duration could be prolonged.

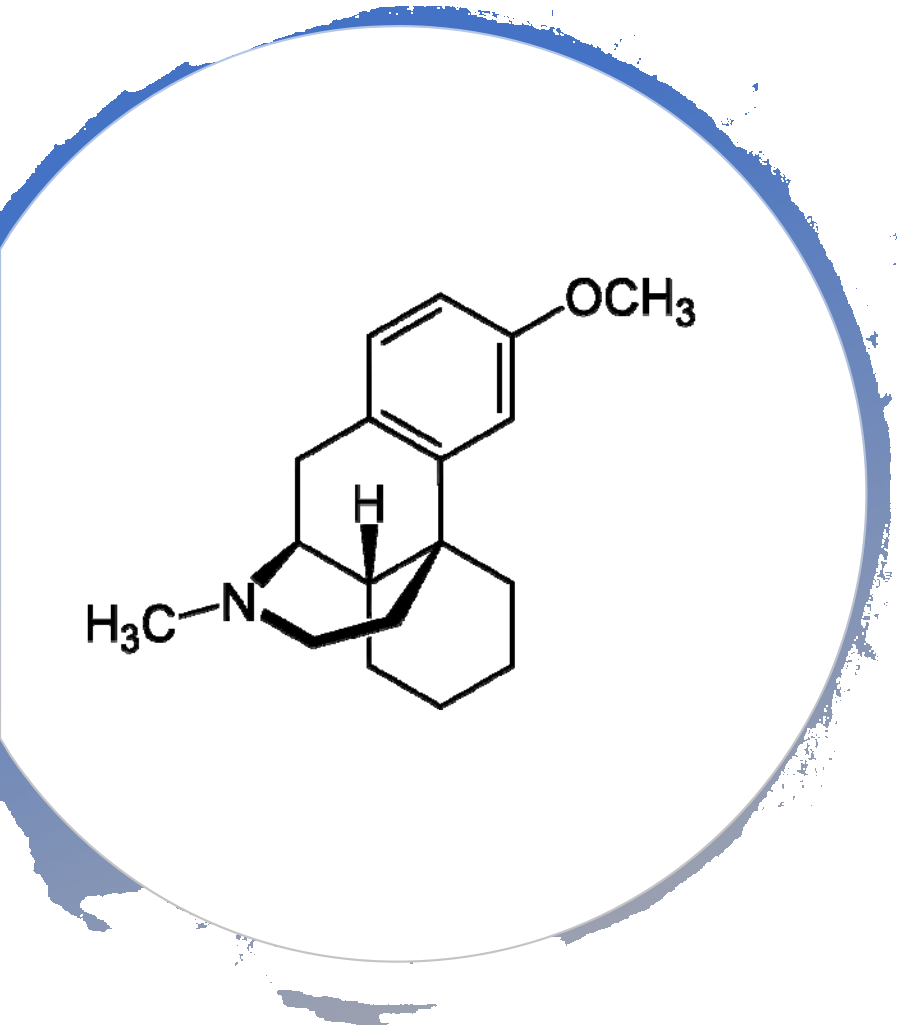
Ketamine

Prolonged ketamine infusion has been included in the list of potential therapeutic options for the management of CRPS in the UK and Dutch guidelines.

Studies has shown that the acute analgesic effects of ketamine can outlast the expected half-life of the drug, suggesting that there may indeed be some suppression of neural sensitization in pain circuits.

The beneficial effects of the ketamine infusion on pain scores are lost by 12 weeks, which must be set against the chronicity of the disease. Thus, repeated dosing would be needed for patients with CRPS. **(watch for Liver Function)**

An oral lozenge preparation of ketamine has been shown to have adequate pharmacokinetics



Dextromethorphan | C18H25NO

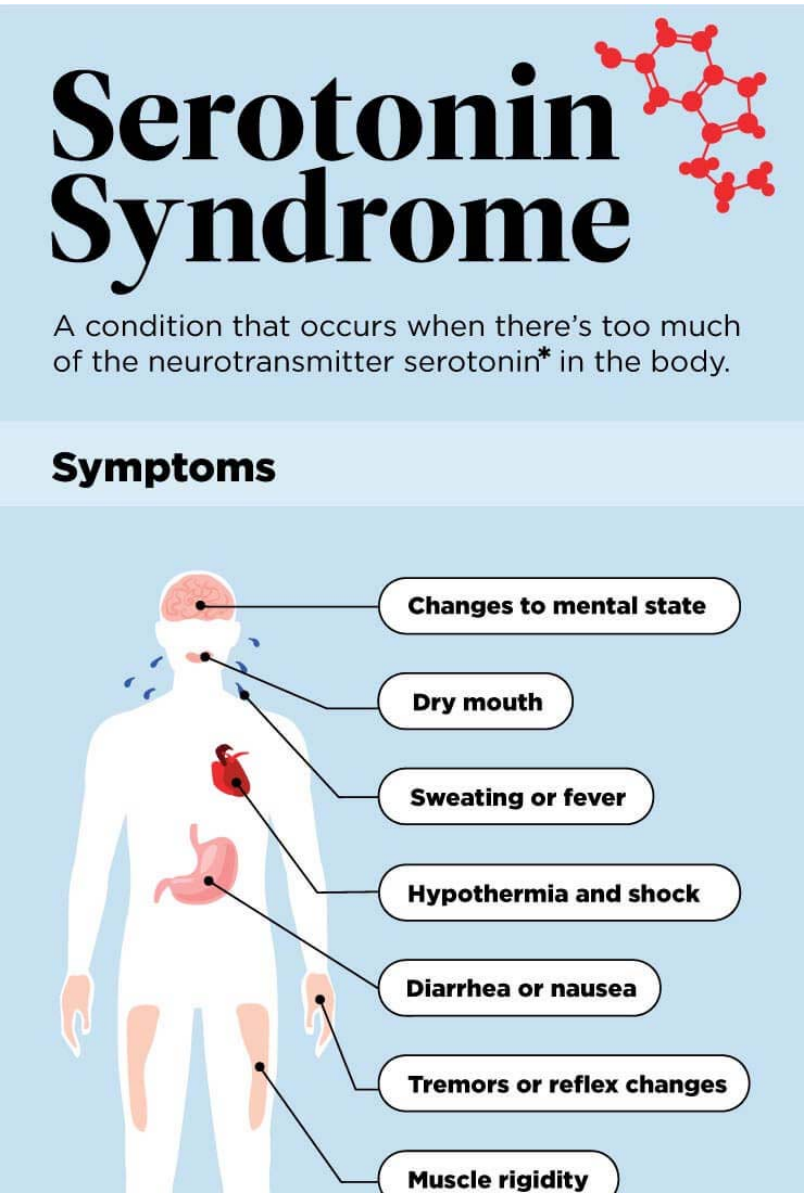
- Dextromethorphan, memantine, and amantadine are weaker NMDA receptor blockers, and consequently, are also thought to have fewer central nervous system side effects.
- For the sake of this presentation we want to focus on dextromethorphan because we have very good results from it in our Pharmacy with our patients

Dextromethorphan

- Dextromethorphan (d-3-methoxy-N-methylmorphinan) is the d-isomer of the codeine analogue methorphan
- unlike the L-isomer, it does not act through opioid receptors. Instead, dextromethorphan binds with high affinity to sites associated with sigma ligands and low affinity to the phencyclidine (PCP) channel of the N-methyl-D-aspartate (NMDA) receptor

Dextromethorphan

- Dextromethorphan (DXM) is an antitussive drug. It is one of the active ingredients in many overthe-counter cold and cough medicines, including generic labels. It is sold in syrup, tablet, spray, and lozenge forms. In its pure form, dextromethorphan occurs as a white powder.
- Clinical trials in postoperative cancer patients have demonstrated that dextromethorphan may reduce pain intensity, sedation, and analgesic requirements (Weinbroum, 2005; Weinbroum et al., 2003)



Dextromethorphan (SEROTONIN SYNDROME WARNING)

- Dextromethorphan (DXM) is a moderate serotonin reuptake inhibitor that simultaneously promotes serotonin release.
  - **Thus it is imperative that you monitor patients that are on SSRIs to avoid Serotonin Syndrome**

Dextromethorphan Side effects

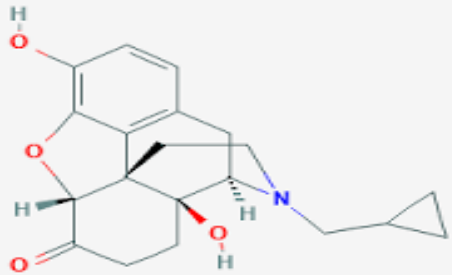
- nausea.
- vomiting.
- constipation.
- drowsiness.
- dizziness.
- sedation.
- confusion.
- nervousness.

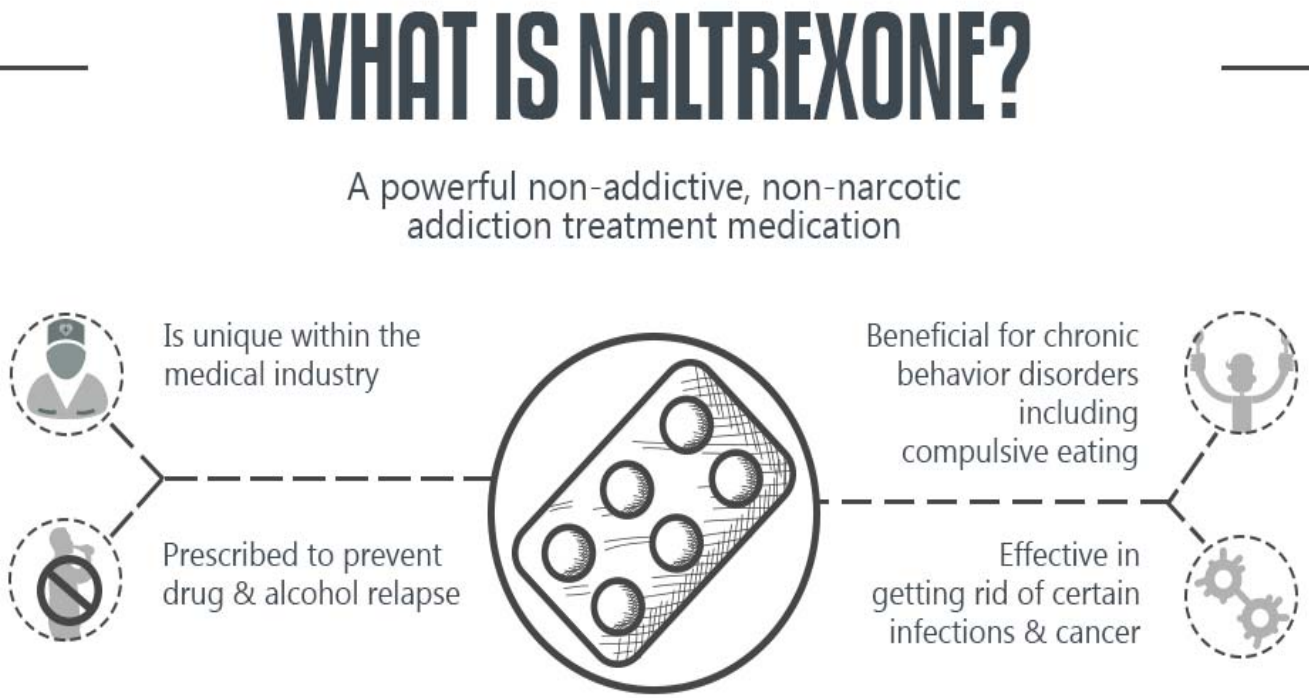
Dextromethorphan dosing

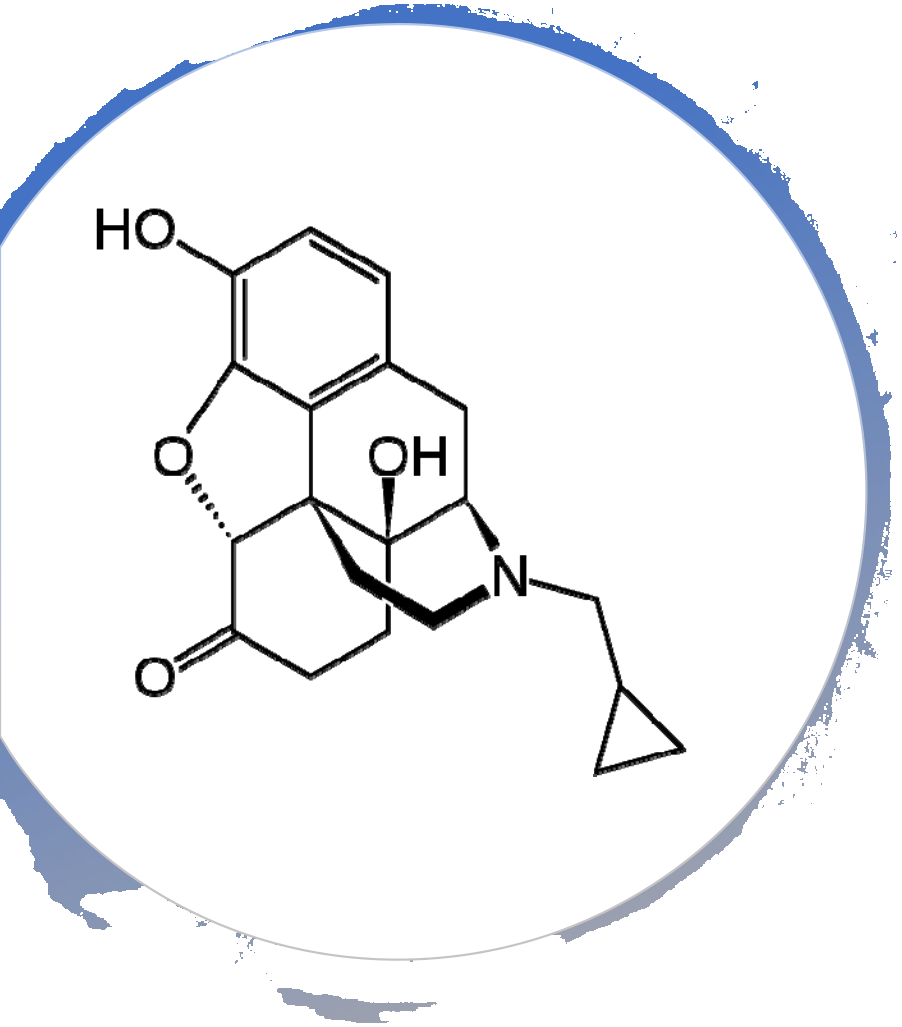
50, 100, 150 and 200mg Bid up to Tid

SR DOSING PLEASE

LDN (Low Dose Naltrexone)





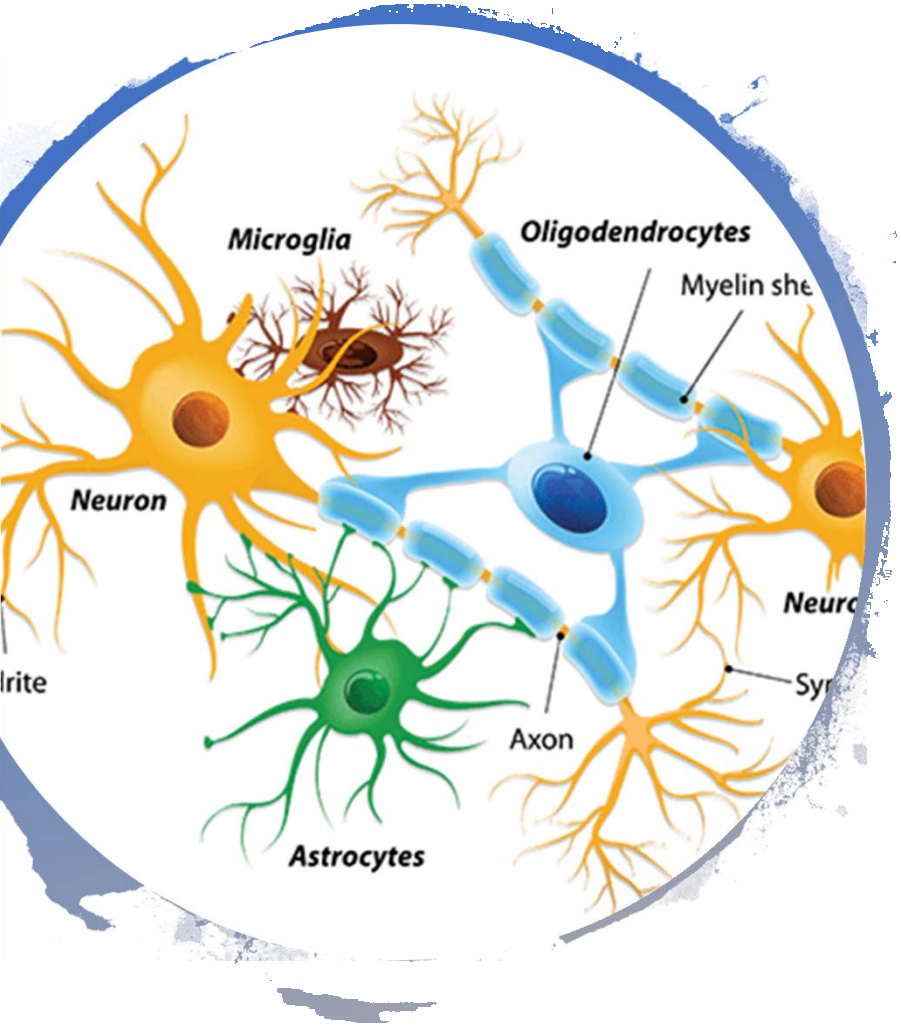


Naltrexone

- Naltrexone is a reversible competitive antagonist at μ and κ receptors
- A regular dose of Naltrexone starts at 50mg
- Low Dose Naltrexone (LDN) is 0.5mg to 4.5mg
- Low Dose Naltrexone blocks the opioid receptor briefly thus the body floods the system with its endogenous opioids (endorphins) and Opiod growth factor (OGF) [Met(5)]-enkephalin, while also increasing the density of the OGF-receptors to respond to the increase in production.
  - This is called the Positive feedback Mechanism

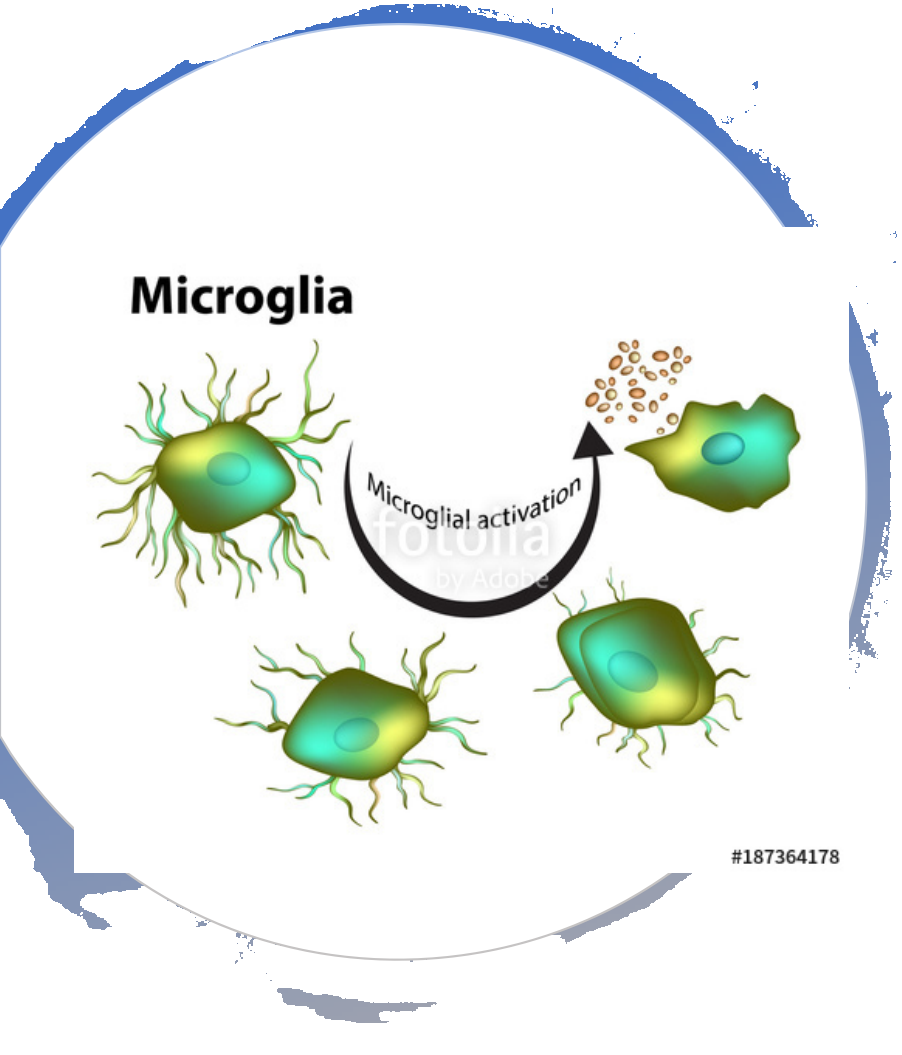
Low Dose Naltrexone Advantages

- A promising alternative for autoimmune diseases, chronic pain, and inflammation
- Increases natural opioids
- Balances the immune system
- Side effects are rare and mild
- Very few known drug interactions



LDN Effect on Glial (Glue) Cells

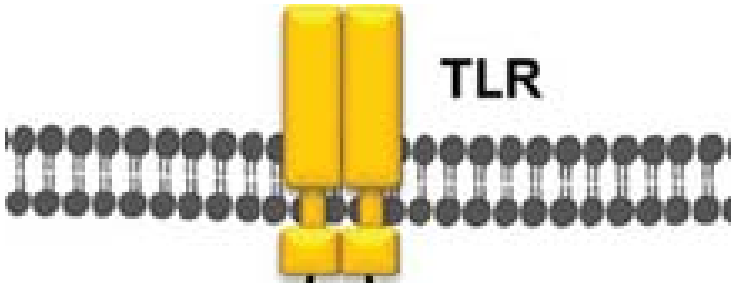
- Glial Cells are supportive cells in the central nervous system.
- Unlike neurons, glial cells do not conduct electrical impulses.
- The glial cells surround neurons and provide support for and insulation between them.
- Glial cells are the most abundant cell types in the central nervous system.
- Microglia normally stay in a resting state and are awoken during damage or infection
- Glial cells activation underlies common symptoms in autoimmune and other diseases fatigue, fever, inflammation, and pain.



LDN Effect on Glial (Glue) Cells

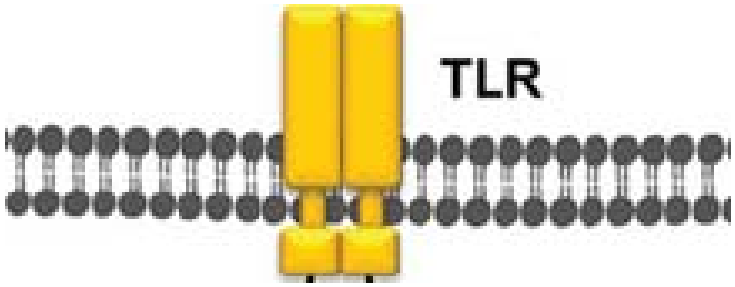
- When activated – glia release a variety of substances (proinflammatory cytokines, chemokines, etc.)
- These substances in turn increase the excitability of nearby neurons

LDN Blockade of TLR-4



- Toll Like Receptors are a class of proteins that play a key role in the innate immune system.
- Usually expressed in sentinel cells like macrophages and dendritic cells
- In the face of an infection, the microbes are recognized by TLR which activate the immune system.
- TLR4 is predominantly expressed by microglia

LDN Blockade of TLR-4



- Opioids cause glial cell activation by acting on the TLR4 receptors leading to a cascade of pro-inflammatory cytokines
- Opioid antagonists (naloxone, naltrexone) block TLR4 signaling
- By keeping the microglia in a resting state and increasing endorphins, **low-dose naltrexone reduces the pain and inflammation** in CRPS

CBD

(Cannabidiol)

Over the counter Vs Medical Card Requirement

- OTC:
  - 1)Has to be derived from some other source than Marijuana (Usually Hemp)
  - 2)THC concentration can not exceed 0.3% of the total cannabanoids
    - Ie: a 100mg product can not contain mofre than 0.3mg of THC
- Medical Card:
  - Can be derived from Marijuana and can contain more than 0.3% THC

CBD Products Over the counter:

- Whole plant extract: no certain saturation of CBD vs other Cannabanoids. Contains traces of THC and other Phyto Canabanoids / Terpenes)
- Broad Spectrum Whole Plant extract: THC is removed
- Isolate products: CBD Isolated VIA CO2 extraction and saturated into a different oil(Grape Seed, Olive Oil, Coconut Oil)
- Full Spectrum Products: CBD Isolate infused back into whole plant extract to contain the remainder of the Phytocananbanoids/terpenes. Containes trace THC
- CBD Broad Spectrum Products: Same as full Spectrum with THC removed

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CBD FULL SPECTRUM PRODUCTS

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CBD BROAD SPECTRUM PRODUCTS

- CBD Broad Spectrum Products: CBD Isolate infused back into whole plant extract to contain the remainder of the Phytocananbanoids/terpenes. Same as full Spectrum with THC removed

COMMON CBD DRUG INTERACTIONS

- CYP450 3A4 AND 2C19 INHIBITOR
- DO NOT USE WITH Triliptal, Tegretol and Keppra
- Monitor INR in warfarin Patients


Thank
you