

Opioid Review and MAT Clinic

February 27, 2019

Announcements

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- CME evaluation forms are due to Katie Stangl by Friday, March 1st at 4:00pm.

Upcoming Presentations

- **March 6th**: Dr. Charlie Reznikoff, How to Think About “Pain” as a Symptom
- **March 13th**: NO ECHO
- **March 20th**: Dr. Charlie Reznikoff, Pattern of Use and Risk of Stimulant Addicts
- **March 27th**: Dr. Cresta Jones, Using Naltrexone/Vivitrol in Pregnancy

Rx Drug Abuse & Heroin Summit

- April 22-25
- Atlanta, Georgia
- <https://www.rx-summit.com/>

You should all consider attending!

Opioid Induced Hyperalgesia

The Big Foot of Opioid Topics

Outcomes

- **Determine the difficulty in diagnosing opioid induced hyperalgesia**
- **Formulate an understanding of what leads to opioid induced hyperalgesia**

Opioid Induced Hyperalgesia (OIH)

- **Definition:** State of nociceptive sensation caused by exposure to opioids
- **Allodynia:** pain from stimuli, not generally considered painful
- **Paradoxical response:** actually have more pain with use of analgesic
- **Nociceptive** : pain arising from the stimulation of nerve cells (distinct from arising from damage or disease)

OIH

- **First described by Albutt in 1870**
- “Does morphia tend to encourage the very pain it pretends to relieve. I have much reason to suspect that a reliance upon hypodermic morphia only ended in that curious state of perpetuated pain.”



OIH

- **History Continued...**
- **Flash forward to 2005**

General Review OIH

- **“Clinical experiment” with high dose continuous opioids- with results as we know include**
 - **Overdose death**
 - **Falls and fractures**
 - **Care accidents**
 - **Endocrinopathies**
 - **Constipation**
 - **Decrease disease resistance**
 - **NAS**
 - **Refractory tolerance**
 - **Addiction**

General Review OIH

- **Evidence that neuroadaptation interferes with long term analgesia from opioids**

General Review OIH

- Evidence that opioids increase pain which may improve through taper



General Review OIH

- **Studies have shown patients taking intermittent moderate doses have equal pain scores of patients on high dose continuous opioids (with less harm)**

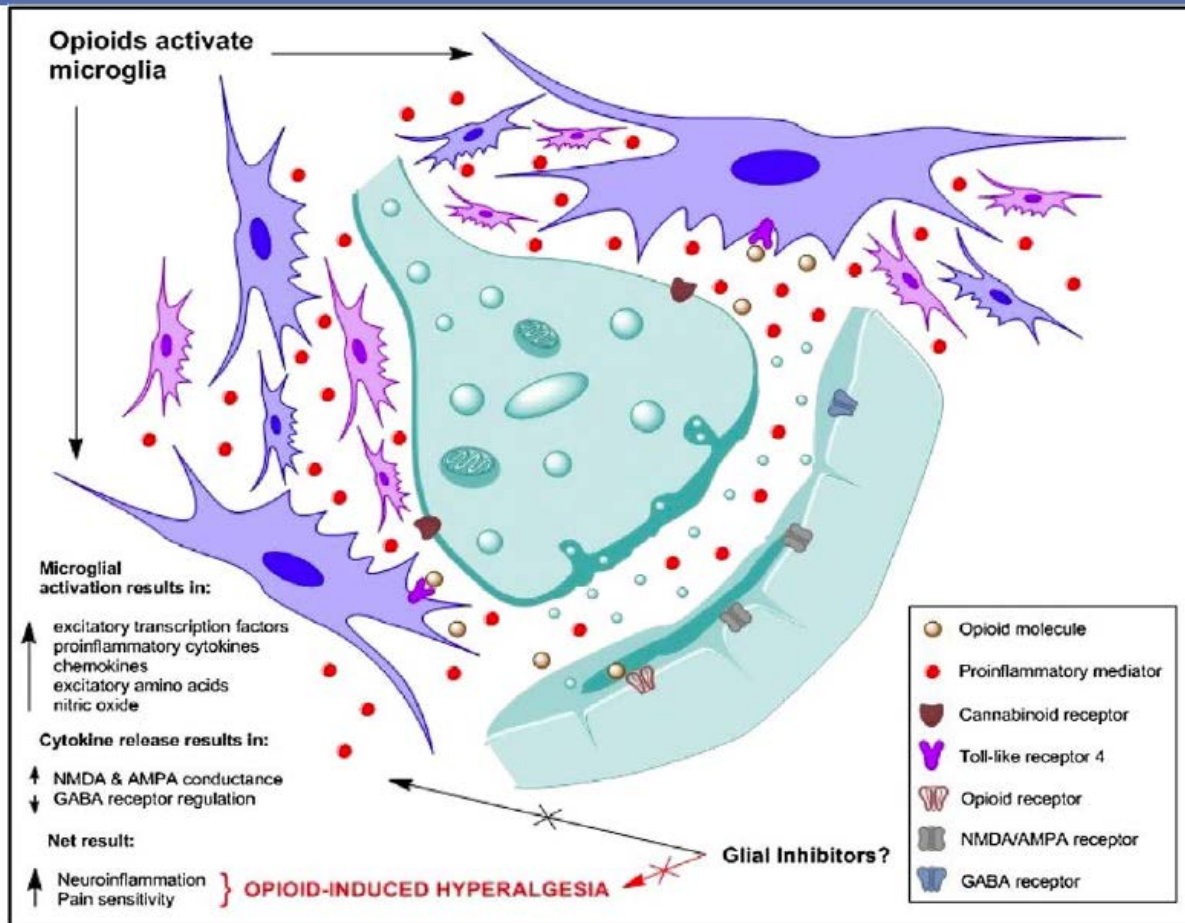
General Review OIH

- **Hyperalgesia mechanism- not completely understood**
- **Likely multiple pathways**



OIH

OIH Mechanisms - Microglia



OIH



OIH Mechanism

- **Descending pathways modulate pain sensitivity in spinal cord**
 - **Normally opioids enhance inhibitory signals and diminish facilitating signals along these tracts**
 - **Opioid exposure has been theorized to shift the balance favoring facilitation**

OIH Mechanism

- **Opioid exposure is thought to increase spinal dynorphins (pain transmission chemicals)**
 - **Paradoxically may increase pain sensitization**

OIH Mechanism

- **NMDA (N-methyl-D-aspartate) relationship with pain process is complex**
 - **Opioid effect on this system is poorly understood**
 - **Upregulation of intracellular proteins causes increased activity of NMDA receptors leading to increase pain sensation**

OIH Mechanism

- **Inflammatory process after exposure to opioids causes increase in cox expression and prostaglandins**

OIH Mechanism

- **Consequences of chronic opioid exposure**
 - **Neuronal programmed cell death**
 - **Possibly mediated through NMDA receptors**
 - **Resulting in disinhibition, which leads to tolerance and pain hypersensitivity**

OIH Mechanism

- **Exogenous opioids suppress production of endogenous opioids**
 - **Do endogenous opioids work to decrease pain through a mechanism that exogenous opioids do not**

Opioid Induced Hyperalgesia

**f FUN
FACTS**

OIH Fun Fact

- **Can develop early and at low dosages and after first doses**

OIH Fun Fact

- **Intraoperative opioids have been shown to cause increased opioid requirements for the same level of analgesia (tolerance)**
- **Increase sensitivity to pressure, heat, and cold**

OIH Fun Fact

- **If patients are on opioid preoperatively**
 - **Poorest hospital outcomes**
 - **Greater pain intensity**
 - **Higher hospital costs**

OIH Fun Fact

- **Hyperalgesia has some relationship to opioid dose and strength**
- **All opioids can cause hyperalgesia event as low doses, by any routes**
- **Tramadol can be a cause**

OIH Fun Fact

- **Duration**
 - **Resolution of symptoms can take days, months, or in some cases years**



Diagnosing OIH

- **Development of allodynia to cold and heat**



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Diagnosing OIH

- **DIH is a diagnosis of exclusion**
- **NO TEST**



Diagnosing OIH

- **Presumptive diagnosis based on:**
 - **Opioid use history**
 - **Response to opioids- paradoxical**
 - **Physiologic signs**
 - **Subjective complaints**
 - **Exclusion of other causes**
 - **Generalization of pain**

Treatment



Treatment

- **No treatments for OIH have been validated to date**



Treatment

- **Gabapentin has shown some efficacy in animal models but only a few case studies have suggested efficacy**
- **More studies needed**

Treatment

- **Ketamine- NMDA receptor antagonist produces analgesia, sedation, and amnesia thought to block calcium channels that start the phenomenon leading to central sensitization**

Treatment

- **Thus treatments have included**
 - **Opioid dose reductions**
 - **Opioid switching**
 - **Adjunctive analgesics like ketamine**

Treatment

- **Methadone**
 - **Weak NMDA antagonist**
 - **May need elevated doses to treat OIH**

Treatment

- **Cox inhibitors**
- **To address a possible inflammatory component**

Treatment

- **Efficacy of all of these are not well supported**

Clinical Implications of Opioid Induced Hyperalgesia

Clinical Implications

- **Pain inducing effects of opioids and their clinical importance can not be denied**

Clinical Implications

- **Once hyperalgesia occurs, reversal may not quickly resolve with taper**

Clinical Implications

- **Common mechanisms are involved including NMDA receptor activation**

Clinical Implications

- **Clinician always needs to decide if pain generator is responsible for worsening pain, or is it the opioid**

Clinical Implications

- **Opioid induced tolerance and hyperalgesia must be seen as a potentially irreversible phenomenon that should make us look closely at our prescribing practices**

Clinical Implications

- **Tolerance and OIH can sometimes overlap but can at times be distinguished by response to increase in opioid dosing**