

# Micro-induction technique

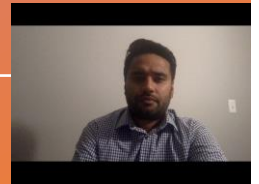
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Disclosures: None

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# Micro-induction technique



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- The United States is facing devastating consequences of the opioid epidemic, with an increase in opioid misuse and related overdoses, causing more than 130 deaths per day
- FDA has approved buprenorphine, methadone and naltrexone as treatment for opioid use disorder.

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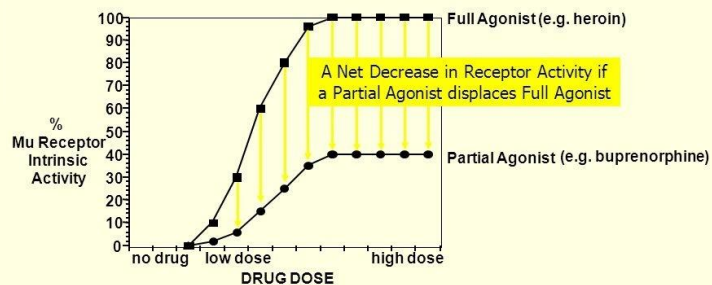
- Buprenorphine's high-binding affinity as a partial  $\mu$ -opioid agonist displaces preexisting full agonists causing precipitated withdrawal, which requires most individuals starting buprenorphine to endure moderate withdrawal prior to induction to avoid precipitated withdrawal



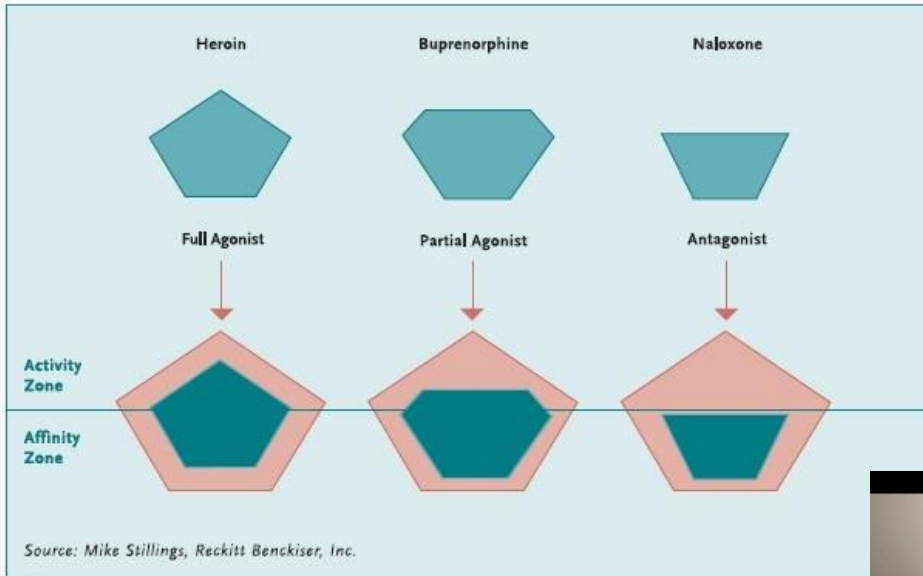
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## Buprenorphine Precipitated Withdrawal

- Displaces a full agonist off the mu receptors
- Buprenorphine only partially activates receptors
- Net decrease in activation occurs and withdrawal develops (must be in withdrawal to start)

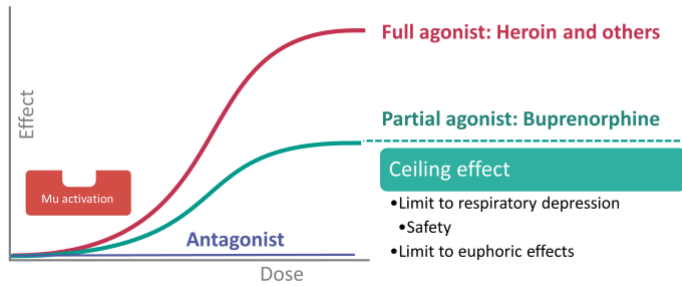


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### Buprenorphine MOA



Lutty, K., & Cowen, A. (2004). Buprenorphine: a unique drug with complex pharmacology. Current neuropharmacology, 2(4), 399-402.



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- Buprenorphine, a partial opioid agonist, binds to the  $\mu$ -receptor with significantly higher affinity than most full-agonist opioids. When buprenorphine displaces preexisting opioids from their receptors through competitive inhibition, the result is the precipitation of opioid withdrawal.



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To avoid this outcome, patients are instructed to abstain from all full opioid agonists and to wait for the emergence of mild to moderate withdrawal symptoms prior to initiating buprenorphine.

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This is very cumbersome and challenging for the patient and quite hard to explain from provider prespective.

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Complicated inductions may be associated with poorer long-term treatment outcomes and greater risk of relapse

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What to do then?  
Is there any  
alternative ?



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Microinduction  
technique

- A microdosing technique also commonly known as micro-induction method first introduced and trialed in 2010 by Hamming et al. in Bern, Switzerland which was then referred to as Bernese method.
- What is Bernese Method ?
- a novel approach to induction was introduced for patients who were unable to tolerate the emergence of opioid withdrawal symptoms



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- In this method of microinduction, repeated small doses of BPN are administered to the patient in an increasing fashion, while the patient continues the use of the opioid at the same dose. BPN tends to accumulate at the receptor because of slow dissociation from the receptor and long receptor binding time. By doing this, BPN will finally displace the full opioid agonists.

Hamming



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- there is no consensus regarding a singular microdosing approach, possibly suggesting that the method may be employed as long as the basic principles of small incremental doses are used
- SL buprenorphine appears to be the most common formulation used for such purpose, but transdermal buprenorphine may also be a viable option. However, in the United States, transdermal buprenorphine is not permitted for OUD treatment. Based on the available data, microinduction may be a safe and effective alternative to standard induction procedures



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## Our experience and outcome

- We present two cases of successful microinduction from methadone to buprenorphine (BPN) in an outpatient setting without discontinuation of methadone.
- The unsuccessful attempts to taper methadone below a certain dose in both patients prompted them to transition to BPN.



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## Patient A

- A 56-year-old Caucasian male with past psychiatric history (PPH) of opioid use disorder (OUD) on methadone therapy, for the last 23 years (currently at 50 mg), was induced to BPN using microinduction technique.
- Patient had osteoarthritis of the left hip requiring support for ambulation. He was unemployed and had financial concerns. Patient desired a switch to BPN but feared withdrawal symptoms using traditional BPN induction method.



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- He was initially on 140 mg and had successfully tapered to 50 mg. However, he could not be brought down further due to unrelenting withdrawal symptoms and cravings.
- Microinduction was performed over 6 days. On day 1, the patient was induced with 0.5 mg of BPN/ naloxone (NLX) film under supervision.
- At the end of 2 hours, 50 mg of methadone was administered with no any withdrawal signs and symptoms.



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- On day 2, 1 mg of SL (sublingual) BPN was administered, and on day 3, 2 mg of SL BPN was administered, followed by same dose of methadone on both days with no withdrawal sign and symptoms.
- COWS scale was frequently performed with score constantly less than 5.
- On day 4, we repeated the same dosage of 2 mg of buprenorphine with unchanged methadone dosage under supervision.
- On day 5, 4 mg of BPN was given and on day 6 we administered 10 mg of BPN with continued dosage of 50 mg of methadone.
- On day 7, we increased the BPN dose to 12 mg and discontinued methadone.



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## Results



- No withdrawal symptoms were noted during the entire process of microinduction. He was then provided a 7 days script for BPN at 8-2 mg twice a day, with follow-up to the clinic in 7 days. Patient tolerated the medication with no cravings and no withdrawal symptoms. Patient was maintained at BPN .



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Patient B

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A 38-year-old female with a PPH of OUD and was on methadone 42 mg for the last 2 years.

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Due to her financial issues, she was unable to pay for her methadone carry on doses and, hence, was on daily dosing through the methadone program.

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Other challenge she was facing to come daily for methadone dosing

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Due to her financial issues and pandemic related transportation difficulties, she desired to be switched to BPN–naloxone therapy.

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We completed the prelim analysis including a drug screen. she was an appropriate fit for transition to buprenorphine.



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- She was initially on 70 mg of methadone and was tapered to 42 mg. The dose could not be decreased further due to the onset of withdrawal symptoms including severe anxiety and cravings. Patient was educated about the microinduction technique, and she consented for the process.



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## Microinduction schedule

Day	BPN dose	Methadone dose	Cows score before induction	Cows score after BPN induction	Any withdrawal symptoms
1	0.5 mg S/L	42 mg	4	1	No
2	1 mg S/L	42 mg	8	8	No
3	2 mg S/L	42 mg	3	2	No
4	2 mg S/L	42 mg	N/A	N/A	No
5	6 mg S/L	42 mg	1	1	No
6	12 mg S/L	Discontinued	2	2	No



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- On day 7, the SL BPN dose was increased to 16 mg in two divided doses of 8 mg BD. The patient was given a 7-day prescription. No adverse effects were noted on further follow-ups. She tolerated the medication well and continued the same dose thereafter.



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## Follow up

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Both patients successfully transitioned to buprenorphine without facing any withdrawal.

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Urine drug screens performed during follow up revealed no illicit drugs.

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Both of our patients reached a therapeutic dose of 12 mg of BPN/NLX without requiring a period of opioid withdrawal prior to initiation.



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## Discussion

- Advantages

1. Certainly, there are advantages of buprenorphine microinduction namely the avoidance of prerequisite withdrawal.

2. There is a growing body of evidence that suggests buprenorphine microinduction is a feasible alternative to traditional induction with the potential for greater tolerability and acceptability.

3. Microdosing may also bridge the gap in treatment retention between buprenorphine and methadone and may attract the subset of individuals with OUD who see the prerequisite of mild to moderate withdrawal as a barrier to treatment with buprenorphine.

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- This data also shows promise for the transition from higher dose methadone, which again may increase accessibility to buprenorphine treatment and allow individuals to engage in the less restrictive office-based treatment, which may allow for greater quality of life.
- Decreases the drop out from treatment

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# However

Despite the initial promise, more rigorous studies are needed to clarify microinduction protocols.

More studies required to further clarify the most efficient and optimal protocols in various settings and populations.



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