



St. Vincent's Hospital, Melbourne  
Australia



ST VINCENT'S  
HEALTH AUSTRALIA

# Buprenorphine and mental health

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UNDER THE STEWARDSHIP OF MARY AIKENHEAD MINISTRIES

# Buprenorphine for mental health?

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“I have just spent 5 years in gaol. Every day I got 1 to 2 mg of Suboxone. It kept me sane. Since I have been out I have been going nuts. I can't think. I feel really down...”

Silvio, 37

# Opioids for depression

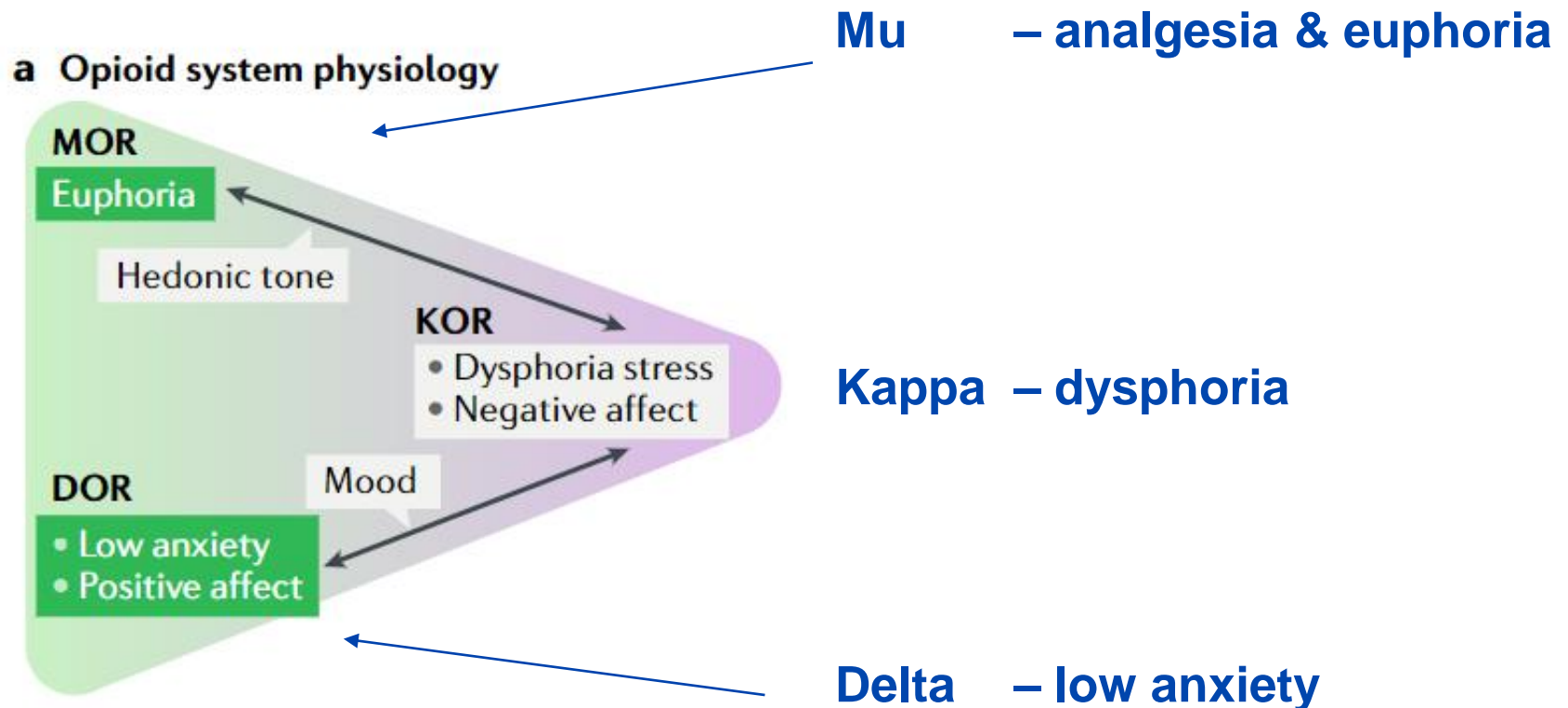
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- 1891 Kraepelin recommended opioid tinctures for depression
- 1977 Kline demonstrated that infusing  $\beta$ -endorphine had an anti-depressant effect
- 1980 Emrich noted possible antidepressant effect of buprenorphine
- 1990 Kosten noted depression improved in opioid addicts

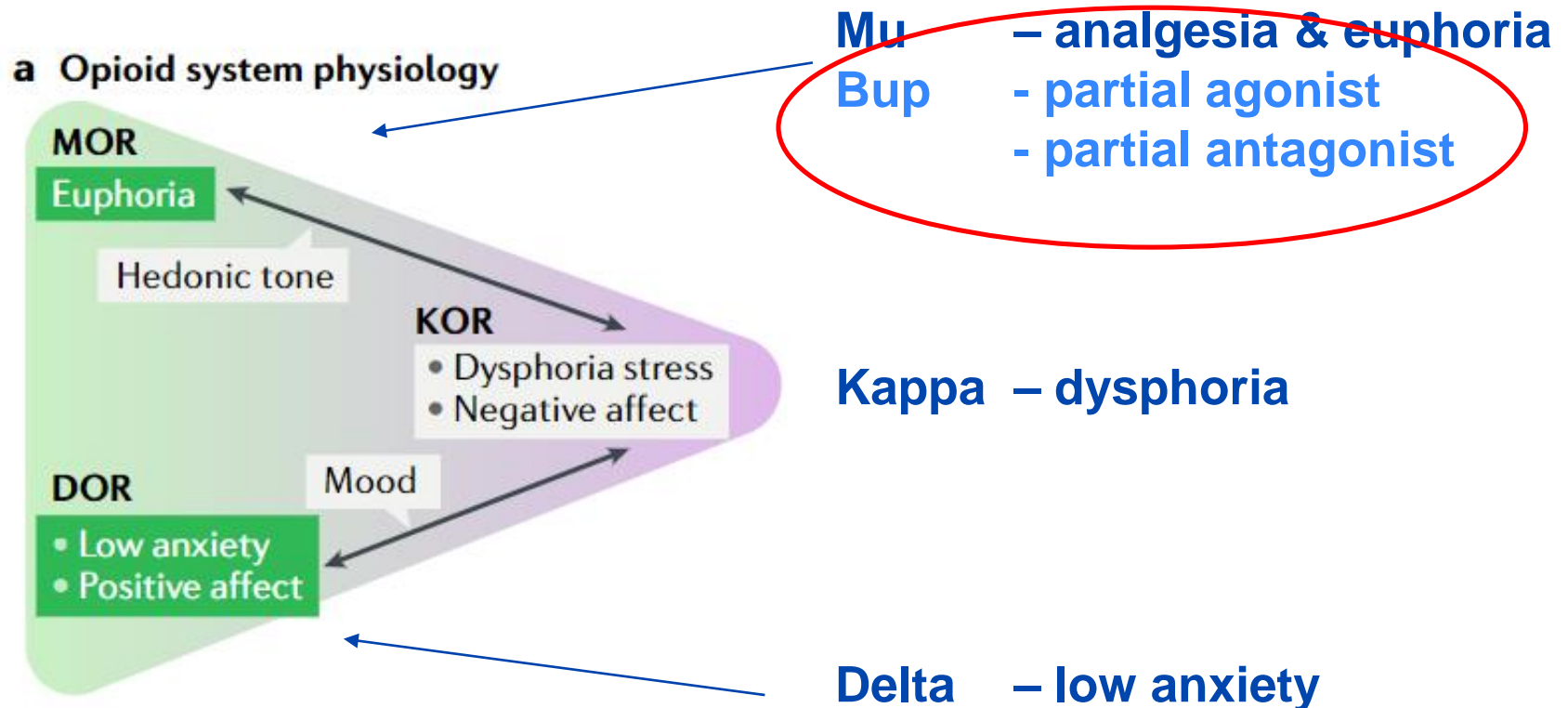
Emrich, H. M., Vogt, P., & Herz, A. (1982). Possible antidepressive effects of opioids: action of buprenorphine. *Annals of the new York Academy of Sciences*, 398(1), 108-112.

Kosten, T. R., Morgan, C., & Kosten, T. A. (1990). Depressive symptoms during buprenorphine treatment of opioid abusers. *Journal of Substance Abuse Treatment*, 7(1), 51-54.

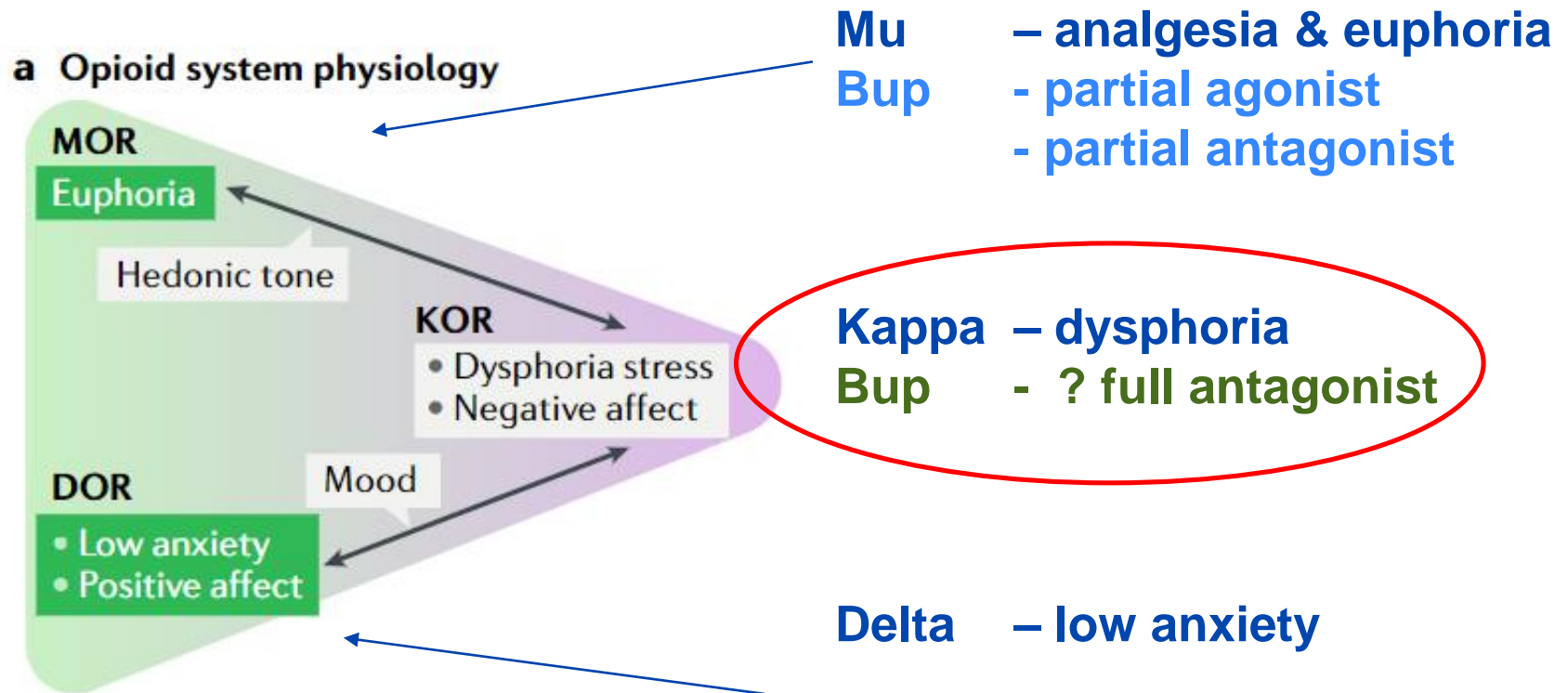
# Opioid receptors



# Opioid receptors

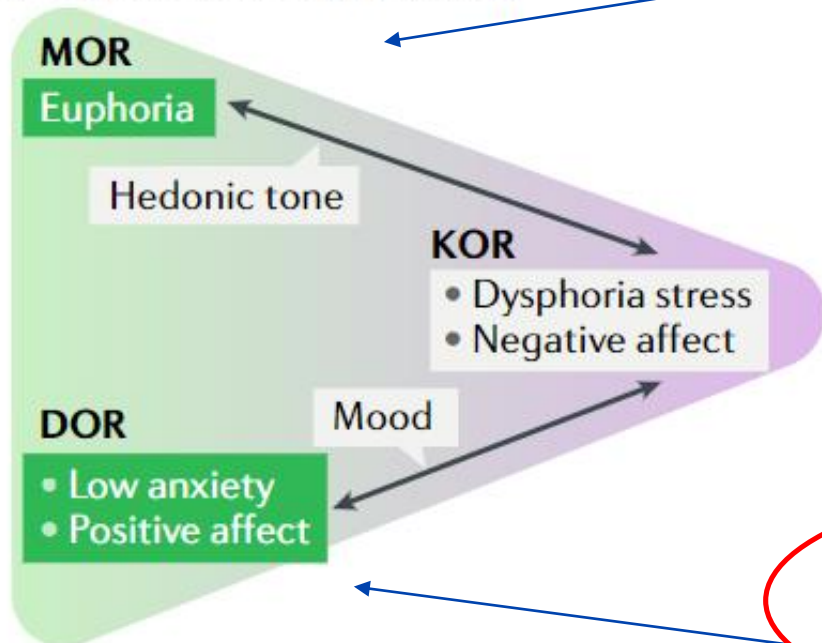


# Opioid receptors



# Opioid receptors

## a Opioid system physiology



**Mu** – analgesia & euphoria  
**Bup** - partial agonist  
 - partial antagonist

**Kappa** – dysphoria  
**Bup** - ? full antagonist

**Delta** – low anxiety  
**Bup** - ? agonist

# Introducing the n-receptor

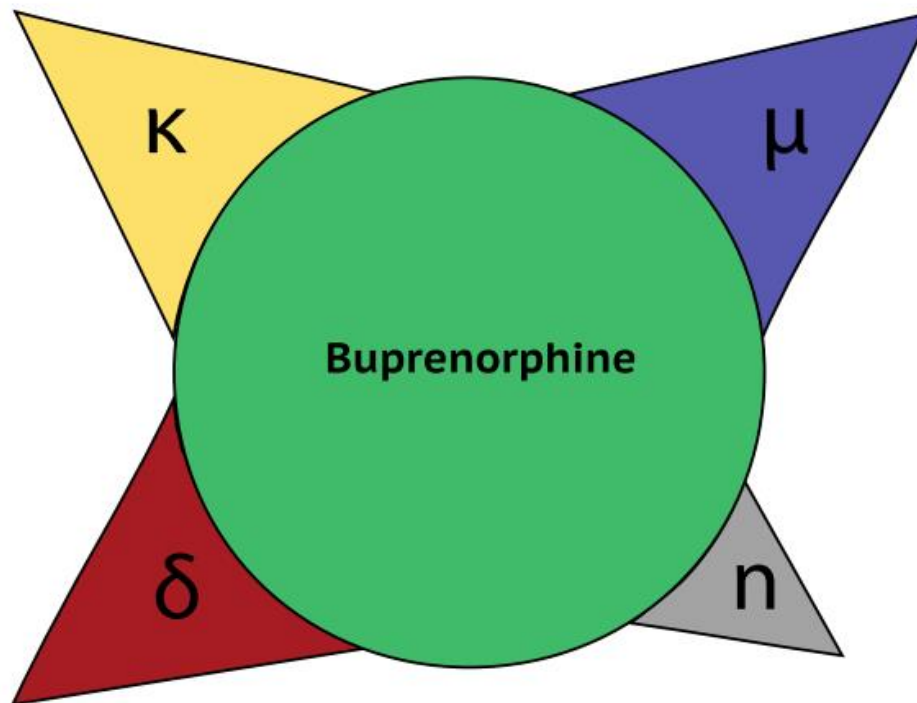
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- Receptor identified in 1994
- Initially an 'opioid receptor' except
  - Opioid agonists have no effect
  - Agonists dynorphin and nociceptin/orphanin
- Activation of the NOP receptor
  - Down regulation of dopamine
  - Down regulation of glutamate
  - Causes low mood and may worsen schizophrenia
- Antagonism may be a treatment for depression and psychosis



# Binds to all the opioid receptors

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# Trials of BUP in depression?

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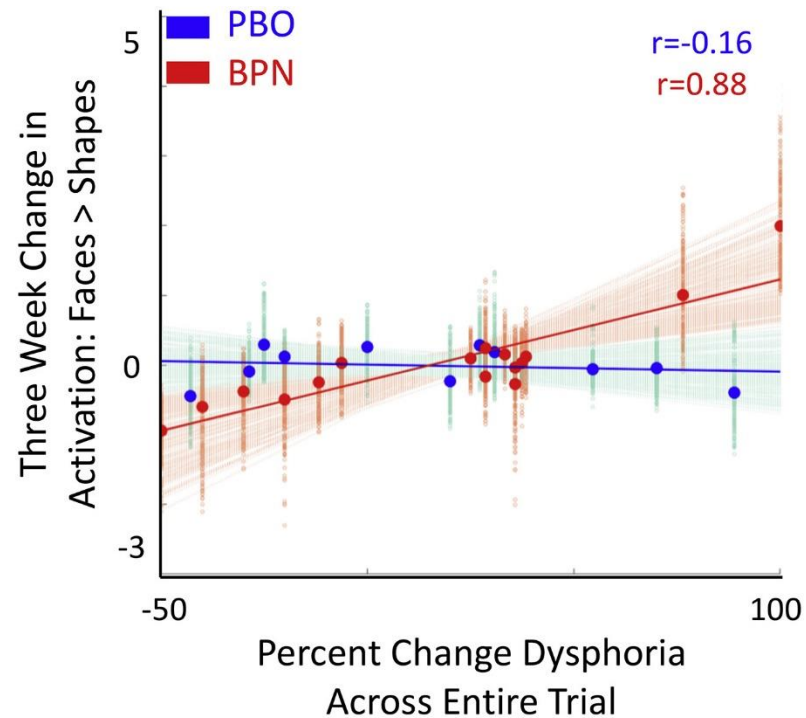
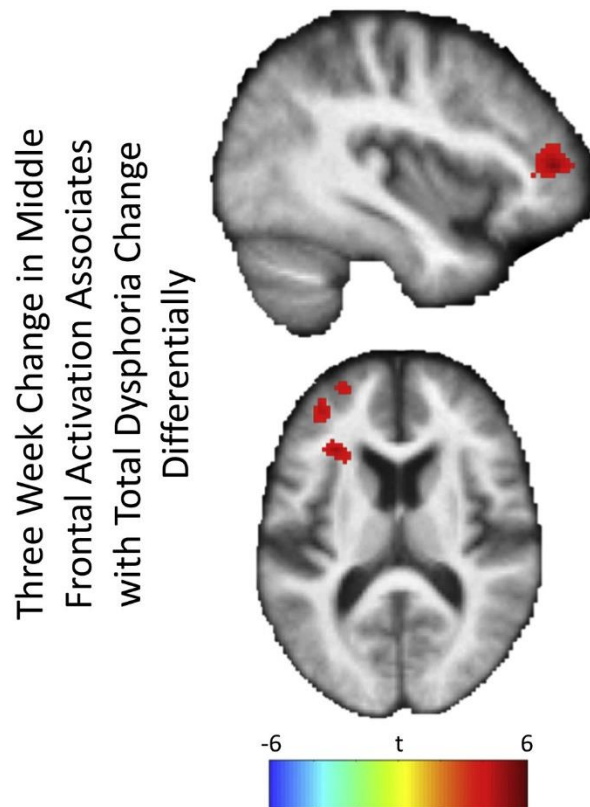
- 1995 Bodkin noted patients with refractory depression responded to buprenorphine
- 2008 Nyhuis demonstrated effectiveness in patients not responding to ECT
- 2014 Karp demonstrated safety and tolerability (0.2 to 1.4 mg/Day)
- 2016 Yovell demonstrated the 'anti-suicidal' potential (0.1 to 0.4 mg/day)

Yovell, Y., Bar, G., Mashiah, M., Baruch, Y., Briskman, I., Asherov, J., Lotan, A., Rigbi, A., Panksepp, J., 2016. Ultra-Low-Dose Buprenorphine as a Time-Limited Treatment for Severe Suicidal Ideation: A Randomized Controlled Trial. *American Journal of Psychiatry* 173, 491–498

Karp, J.F., Butters, M.A., Begley, A.E., Miller, M.D., Lenze, E.J., Blumberger, D.M., Mulsant, B.H., Reynolds, C.F., 2014. Safety, Tolerability, and Clinical Effect of Low-Dose Buprenorphine for Treatment-Resistant Depression in Midlife and Older Adults. *The Journal of Clinical Psychiatry* 75, e785–e793.

Saxena, P. P., & Bodkin, J. A. (2019). Opioidergic agents as antidepressants: rationale and promise. *CNS drugs*, 33(1), 9-16.

# Frontal activation



Lin, C., Karim, H. T., Pecina, M., Aizenstein, H. J., Lenze, E. J., Blumberger, D. M., ... & Karp, J. F. (2019). Low-dose augmentation with buprenorphine increases emotional reactivity but not reward activity in treatment resistant mid-and late-life depression. *NeuroImage: Clinical*, 21, 101679.

# BUP for other disorders

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- **Augmentation of therapy in OCD**
- **Psychosis**
  - Precipitated by withdrawal
  - Relieved by reinstatement
- **Bipolar Disorder**
  - Effective augmentation of treatment

Liddell, M.B., Aziz, V., Briggs, P., Kanakkehewa, N., Rawi, O., 2013. Buprenorphine augmentation in the treatment of refractory obsessive-compulsive disorder. *Therapeutic Advances in Psychopharmacology* 3, 15–19.

Salehi, M., Emadossadat, A., Kheirabadi, G. R., Maracy, M. R., & Sharbafchi, M. R. (2015). The effect of buprenorphine on methamphetamine cravings. *Journal of clinical psychopharmacology*, 35(6), 724-727.

Ahmadi, J., Sahraian, A., & Biuseh, M. (2019). A randomized clinical trial on the effects of bupropion and buprenorphine on the reduction of methamphetamine craving. *Trials*, 20(1), 1-7.

Weibel, S., Mallaret, M., Bennouna-Greene, M., & Bertschy, G. (2012). A case of acute psychosis after buprenorphine withdrawal: abrupt versus progressive discontinuation could make a difference. *The Journal of clinical psychiatry*, 73(6), 0-0.

Bizzarri, J. V., Conca, A., & Maremmi, I. (2014). Does a buprenorphine augmentation control manic symptoms in bipolar disorder with a past history of heroin addiction? A case report. *A New Era. Provide Quality Patient Care*, 49.

# Should we rethink BUP?



The reasons given for the restrictions placed on opiate use are based on prejudice rather than scientific evidence.

Buprenorphine, with its unique pharmacological profile, has proved to possess antidepressant, anti-dysphoric and antipsychotic properties in psychiatric patients.

Maremmani, I., Pacini, M., & Pani, P. P. (2006). Effectiveness of buprenorphine in double diagnosed patients. Buprenorphine as psychotherapeutic drug. *Heroin Addiction & Related Clinical Problems*, 8(1), 31-48.

