Low Dose Naltrexone in Treatment of Obesity and Weight Loss

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OBJECTIVES

- LDN success story as immunomodulator
- Learning from clinical practice with the use of low-toxicity pharmaceuticals that have wide range of applications
- Discuss neurobiologic significance of endorphins in homeostasis of weight
  Discuss metabolic syndrome as proinflammatory state
- Discuss possible application of LDN in management of obesity from above two perspectives
- Provide a practical approach to using LDN using clinical vignettes

BASIC TENETS OF LDN:

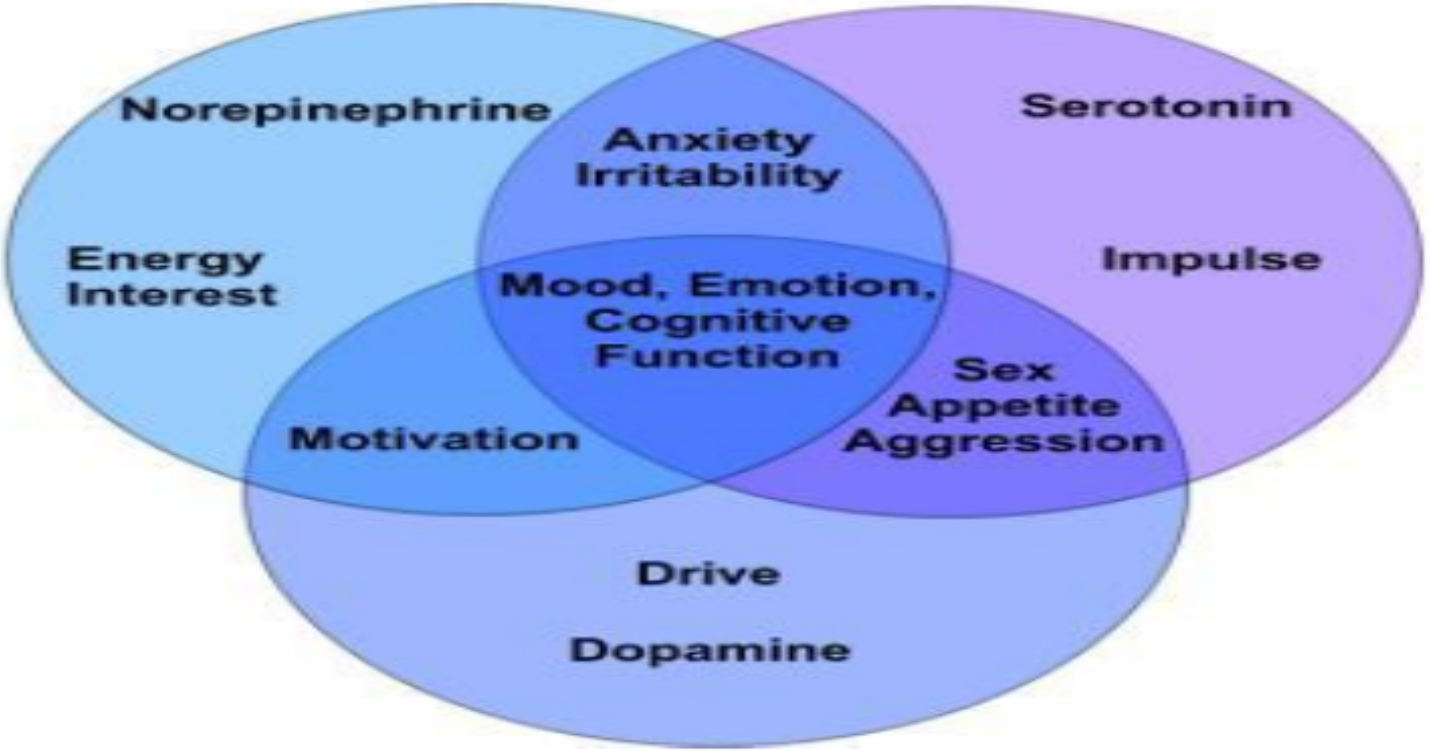
- LDN increases natural endorphins from pituitary
- Likely increases dopamine
- Interaction between endorphins and dopamine is complex.
- It is likely that LDN modulates natural activity and produces “healthy” levels
- Low-Dose effect can have a “tonic” influence
- Cellular effects are produced by dopamine and endorphins

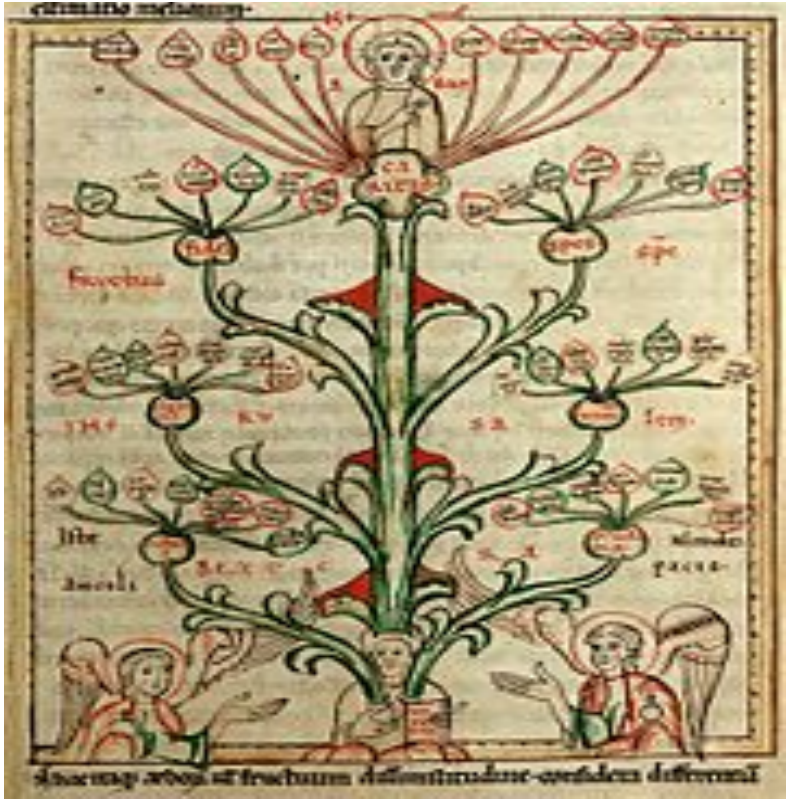
LDN and sleep

“usual doses” of naltrexone:

- sleep time and sleep latency - unchanged
- increased time in stage 2
- decreased time in stage 3
- REM time decreased (~50%)
- REM latency increased
- WASO (wake time after 1st sleep onset) - increased

ALL OF NEUROPHARMACOLOGY ON ONE SLIDE





Cellular Level

- Involved in satiety
- Dopamine and reward behaviors
- Opiates and pleasure behaviors
- Dopamine and Endorphins have immunomudolator effects on T cells
- Effects on sleep
- Effects on mood, well-being

LDN is a successful approach

- Low incidence of side effects
- Physiologic approach, takes into account natural sleep wake cycle
- Restores the natural state of affairs, targets the mastergland

Opiate Delta Receptor

Delta receptor (DOP)

- named after vas deferens tissue
- located in the brain
- mediates
    - analgesia
    - antidepressant
    - convulsant
    - physical dependence

Nociceptin Receptor: OLR-1

Nociceptin

- Endogenous antagonist of dopamine transport that may act either directly on dopamine or by inhibiting GABA to affect dopamine levels.
- Within the central nervous system its action can be either similar or opposite to those of opioids depending on their location.
- Controls a wide range of biological functions
    - Nociception
    - Food intake
    - Memory processes
    - Cardiovascular and renal functions
    - Locomotor activity to gastrointestinal motility
    - Anxiety to the control of
    - Neurotransmitter release at peripheral and central sites.[5

Kappa Receptor

- Locations:
  - Brain
    - hypothalamus
    - periaqueductal gray
    - claustrum
  - spinal cord
    - substantia gelatinosa
  - peripheral sensory neurons

LDN in weight loss

59 yo woman with history of morbid obesity, lymphedema, HTN, hyperlipidemia, chronic cough due to pneumonitis

- diagnosed with inflammatory arthritis
- decided to seek weight loss counseling
- treated with behavioral modification, dietary plan, LDN

Case #1:

- 3 months into treatment sustained 35 lb weight loss
- Reported feeling adherent with dietary plan
- Reduction of inflammatory markers, decreased need for corticosteroids
- Improvement in depression

Case #2:

50 yo woman with history of HTN, hypothyroidism, GAD, depression presented frustrated that she was unable to lose weight in the weight loss clinic. She wanted surgery

- Treated with diet and LDN only
- Was initially unable to exercise due to bilateral knee pain due to OA
- Lost 20 lb in 1 month and started to exercise

Endogenous Opiates and Dopamine

Opiates

- Leukenkephalins
- Metenkephalins
- Dynorphins
- Endorphins
- Morphine

Dopamine

OTHER DRUGS FOR WEIGHT LOSS

FDA Approved

- Lorcaserin (Belviq)
- QSymia (Topamax/Phentermine)

Non-FDA Approved

- Buproprion Wellbutrin
- Naltrexone
- GLP-1 agonists

Low Toxicity Pharmaceuticals in Clinical Practice

- LDN research trust as a repository for observational findings
  - Individual case-reports
  - Clinical case series
  - Case-control studies
  - RCTs

SOURCES

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