To eat, or not to eat: nutraceutical correction of essential fatty acid ratio for weight restoration and maintenance in anorexia nervosa

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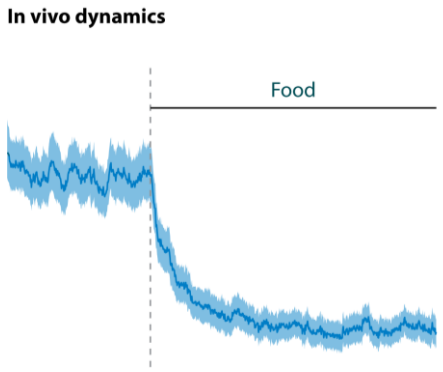
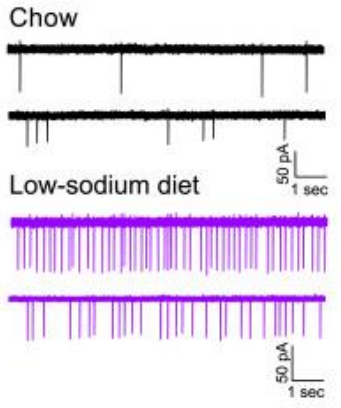
Neural encoding of **overall energy deficit**



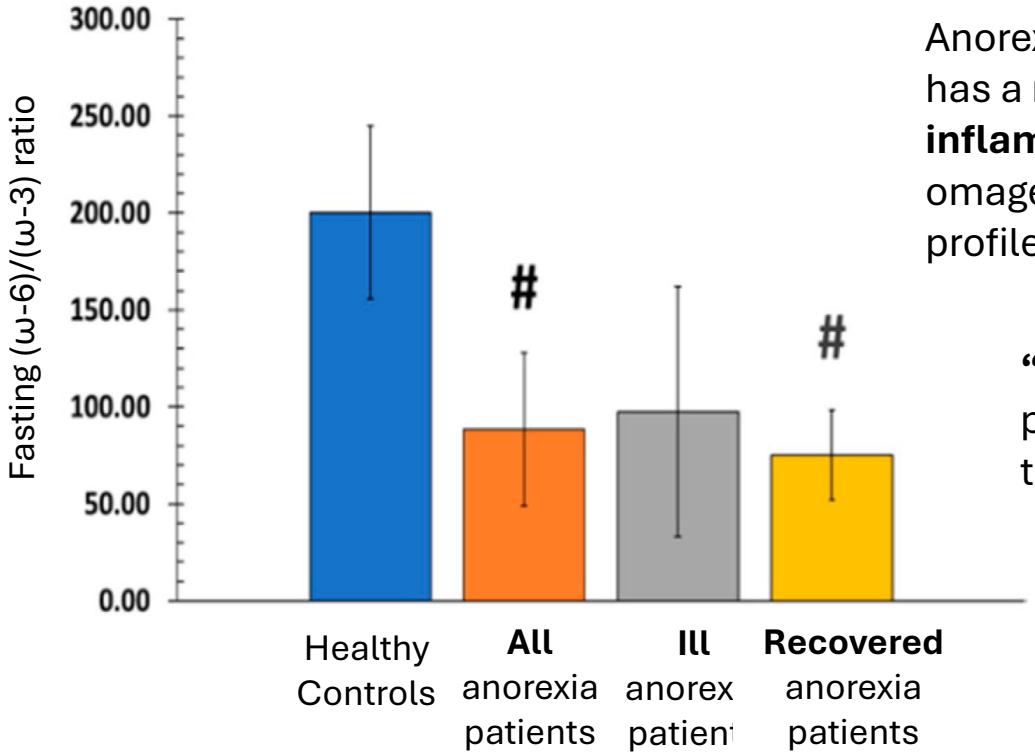
Betley *et al*. Nature 2015

Neural encoding of **sodium deficiency**



Resch *et al*. Neuron 2017

Anorexia patients have **lower omega-6/omega-3 ratio** than healthy controls



Anorexia patient has a **more "anti-inflammatory"** omage-6/omrga-3 profile

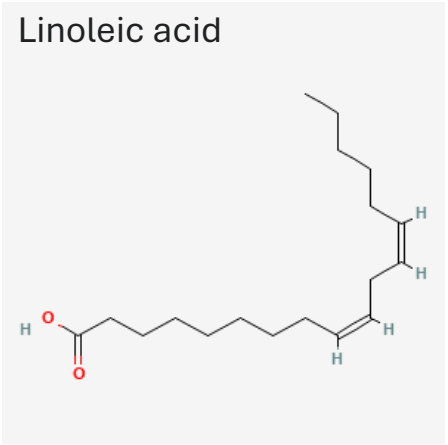
↓

"healthier" physiology than HC

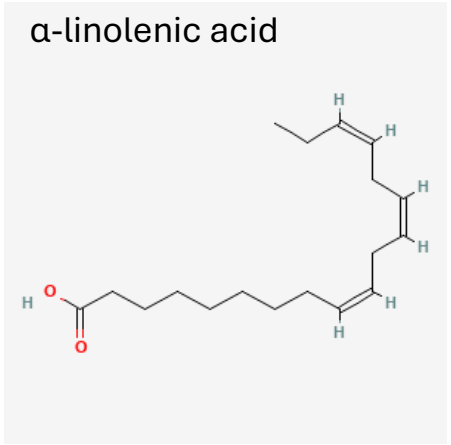
How could this be?

Two essential nutrients we do not report "craving" for

Omega-6 (ω-6)
Pro-inflammatory



Omega-3 (ω-3)
Anti-inflammatory



How does the brain encode sufficiency vs. need states for ω-6 and ω-3 to sustain life?

Why this proposal?

- **No** FDA-approved pharmacological or interventional psychiatry **treatment** for anorexia → most severe and enduring patients are seeking physician-assisted suicide
- Published RCTs for anorexia shy away from using weight/BMI gain as a primary outcome
- Built-in **controlled parameters** and **follow-up mechanisms**
- A pioneer in trial design based on neural circuity control of innate behavioral drives

RCT proposal designed to take advantage of a typical treatment course for anorexia

Inpatient (IP) or residential → Partial hospitalization program (PHP) → Intensive outpatient program (IOP) → Outpatient (OP)

Hypothesis: compared with no nutraceutical intervention, increasing omega-6/omega-3 ratio via nutraceutical supplementation

- accelerates **weight restoration** during **IP/residential** treatment
- increases the likelihood of **long-term weight maintenance**

Method:

Consecutively admitted adolescent and adult anorexia patients, (parental) consented to

- participate **while IP/residential**
- AND to be **followed for at least 6 months** after discharge, at their PHP, IOP, and/or OP visits

Rolling randomized 1:1 to receive

- omega-6 (or omega-6/omega-3 combo formulation) that **targets published omega-6/omega-3 ratio in HC,** or placebo
- Aim for sample size = 60, 30 in each group.
- After discharge, patients will continue in **the same randomized group** for 6 months

ACUTE at Denver Health


Johns Hopkins

ω-6 or ω-6/ω-3 combo

placebo

Primary outcomes:

- **Rate of BMI increase** during IP/residential treatment: ΔBMI / days
- **% of patients** maintaining **BMI > 18.5** in supplemented vs. control groups 6 months after discharge

Secondary outcomes:

- **Rate of BMI change** (gain, maintenance, loss) **when "out and about"** (PHP, IOP, and OP)
- Safety and target engagement **Labs**
  - **Hemodynamic stability**: CBC, CMP, Ca, Mg, phosphorous
  - **Systemic and end-organ inflammation** markers: ESR, high-sensitivity CRP, AST, ALT
  - **Plasma levels of ω-6, ω-3** and their respective metabolites
- Severity of **eating disorder psychopathology** measured by validated clinical tool