Mu opioid receptos antagonism in the nucleus accumbens shell blocks consumption of a preferred sucrose solution in an anticipatory contrast paradigm

Binge eating

- Feature of multiple eating disorders
- Elevated food consumption over short periods of time
- Palatable food are preferred during this events

Binge eating –> palatable food intake

If binge eating is a behavior related to (hedonic) palatable food intake:

We know that

- Opioid signaling controls food-intake
- MOR (mu opioid receptor) signaling in Nacc promotes hedonically drive feeding
- MOR agonists –> increases palatability (++licking bout duration)
- MOR activation in NAcc –> increases consumption of preferred flavor (non-caloric)
- Orosensory cues are sufficient for DAMGO-induced hyperfagia

MOR signaling in NAcc could be related to binge eating

However, authors proposes a more specific binge-like behavior

- Increased intake of palatable food in short periods of time *AND*
- Selective binge-event (towards preferred food) *AND*
- Hypophagia for non-preferred if preferred food is anticipated

The specfic binge-like behavior

More accurately models real-life scenario where all kinds of food are available but binged episodes are directed toward palatable (often non-healthy) food options.

The behavioral model: anticipatory contrast paradigm

- A variable quality or quantity is changed from block to block
- A variable quality in any given block provides complete information of the variable quality in the next block
- Block A: high sucrosose -> BlockB: low sucrose
- Expects learning via temporal association

Experiment: determine if MOR signaling in NAcc controls this specific binge behavior

The specific method

- Male Long-Evans rats (300-400 g)
- Bilateral cannulae to NAcc core (n = 28); NAcc shell (n = 56)

Anticipatory contrast paradigm

- 1 h sessions
- Group A: first 30 min –> 4% sucrose free access water, last 30 min –> 0% sucrose free access water
- Group B: first 30 min –> 4% sucrose free access water, last 30 min –> 20% sucrose free access water

The specific method

Drug infusion protocol

- Naltrexone (nonspecific opioid antagonist): {0, 1, 10, 50 micrograms}
- Naltrindole (delta opioid receptor antagonist): {0, 0.5, 5, 10 micrograms}
- Beta-FNA (irreversible MOR antagonist): {0, 0.5, 5, 10 micrograms}
- Injected 10 mins prior to testing

Results

Contrast paradigm

- 4% sucrose 4-0 $>$ 4-20
- 4-0 first block $>$ second block
- 4-20 first block $<$ second block

Results

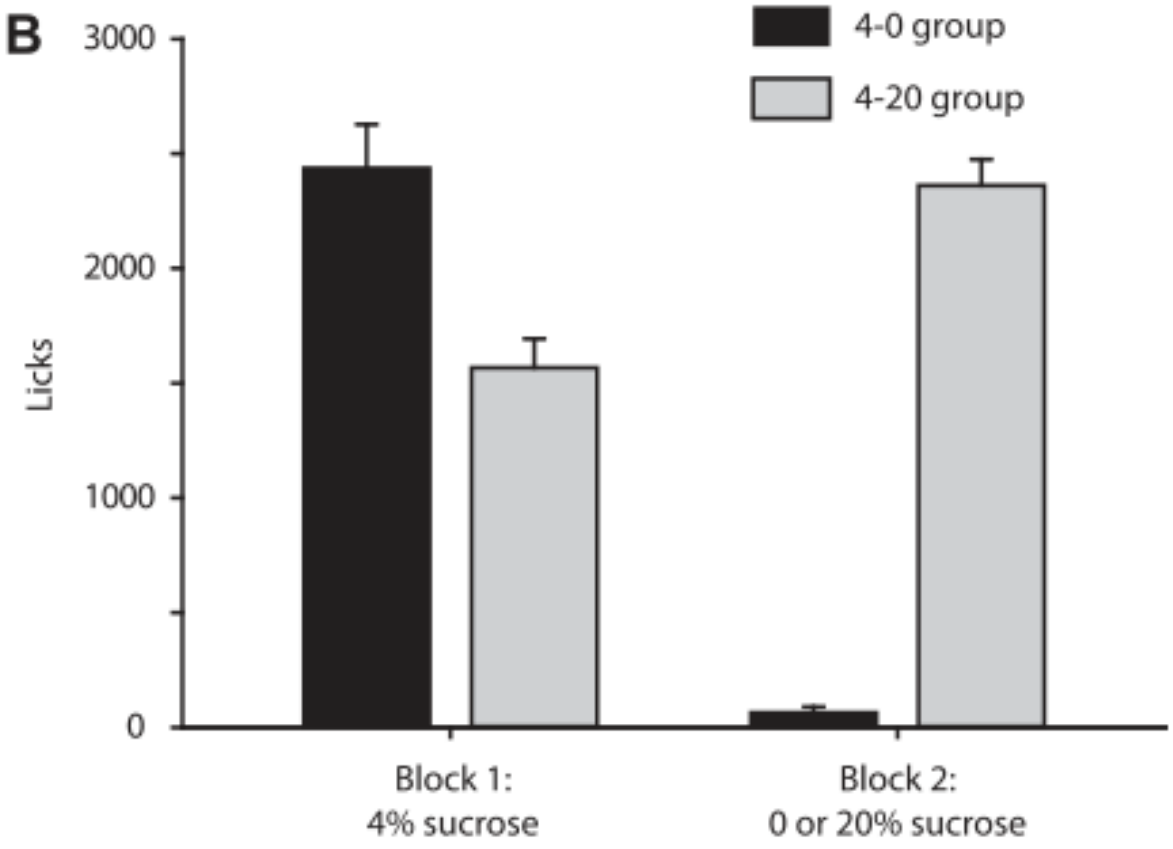

Fig. 1. (A) Anticipatory contrast paradigm. (B) After training in the anticipatory contrast paradigm, rats in the 4-0 group (black bars) consumed significantly more 4% sucrose in block 1 than rats in the 4-20 group (gray bars). Data shown include all rats in the 4-0 group ($n = 42$) and the 4-20 group ($n = 41$) and reflects performance in the final training session prior to drug infusion.

Results

Effects of naltrexone: NAcc shell

- Reduced licking in both groups
- Groups x Drug interaction: $p < 0.01$
  - 4-0 group reduced licking for 4% sucrose
  - 4-20 group did not reduce 4% sucrose consumption; reduced 20% sucrose consumption

Results

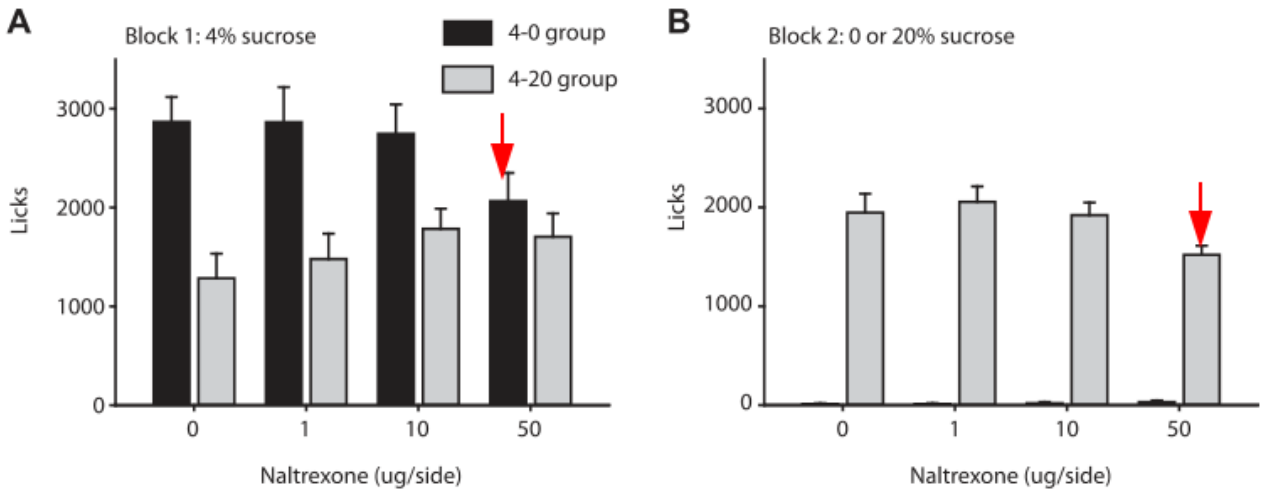

Fig. 2. Infusion of the nonspecific opioid antagonist naltrexone into the NAcc shell selectively decreased intake of the preferred sucrose solution in 4-0 and 4-20 groups. (A) Naltrexone infusion in the NAcc shell decreased licks devoted to 4% sucrose by rats in the 4-0 (black bars) group during block 1, but did not significantly change 4% sucrose consumption by rats in the 4-20 groups (gray bars). (B) Naltrexone infusion decreased 20% sucrose consumption in the 4-20 group during block 2.

Effects of naltrexone: NAcc core

Note non-preferrence specific effects

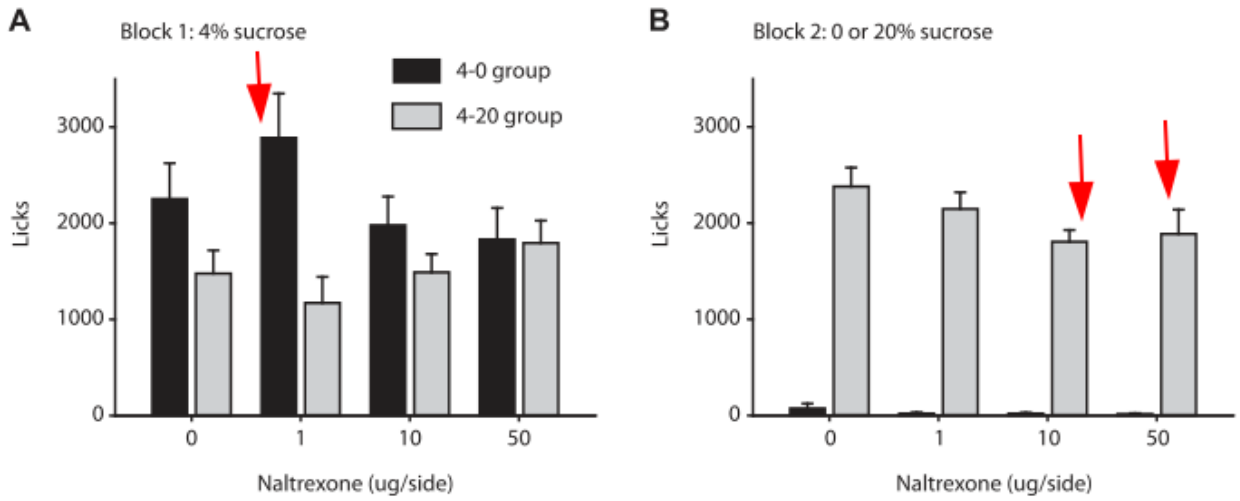

Fig. 3. Naltrexone infusion into the NAcc core. (A) Naltrexone infusion increased 4% sucrose intake in 4-0 group after the 1-µg dose only. In the 4-20 group, 4% sucrose was decreased after the 1-µg dose. (B) 20% sucrose consumption was significantly decreased by NAcc core naltrexone. Conventions in Figs. 3–5 are identical to those in Fig. 2.

Effects of naltridone

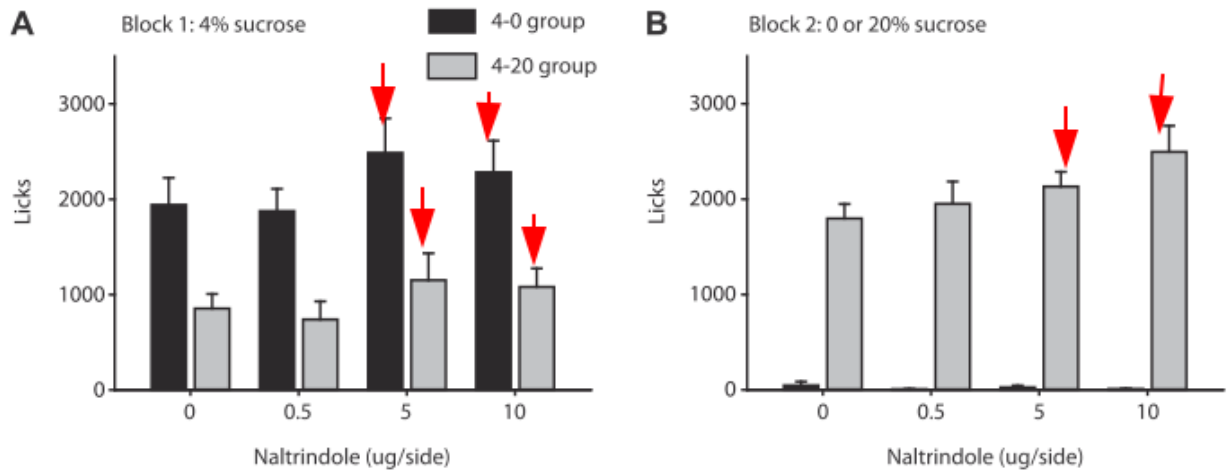

Fig. 4. Naltrindole infusion into the NAcc shell. (A) Naltrindole infusion increased 4% sucrose consumption for both 4-0 and 4-20 groups. (B) 20% sucrose consumption in block 2 was significantly increased by naltrindole infusion.

Effects of beta-FNA

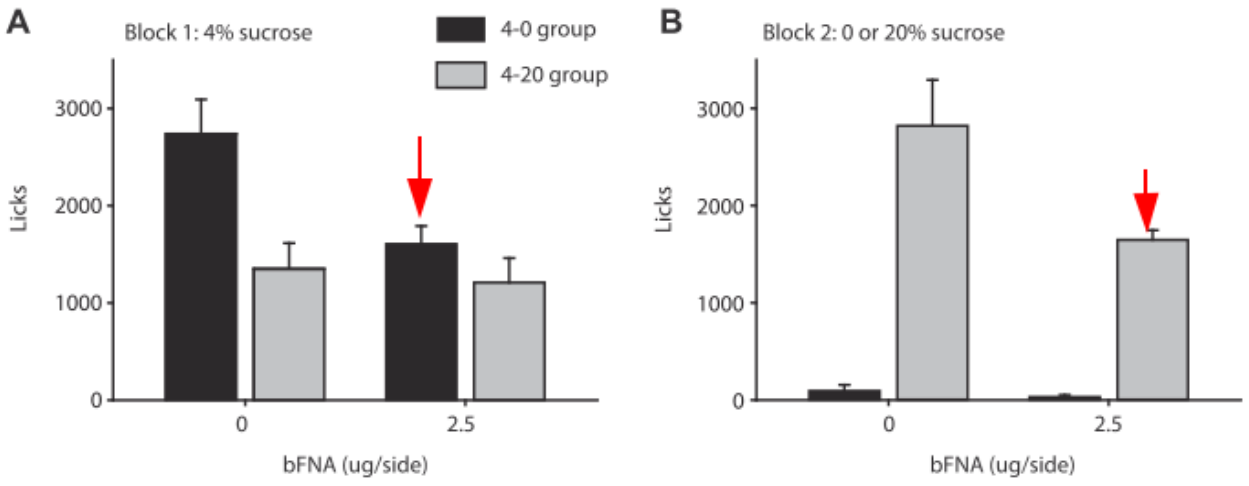

Fig. 5. Beta-FNA infusion into the NAcc shell. (A) Beta-FNA significantly decreased 4% sucrose consumption in the 4-0 but not the 4-20 group. (B) Beta-FNA significantly decreased 20% consumption in the 4-20 group.

Effects of beta-FNA

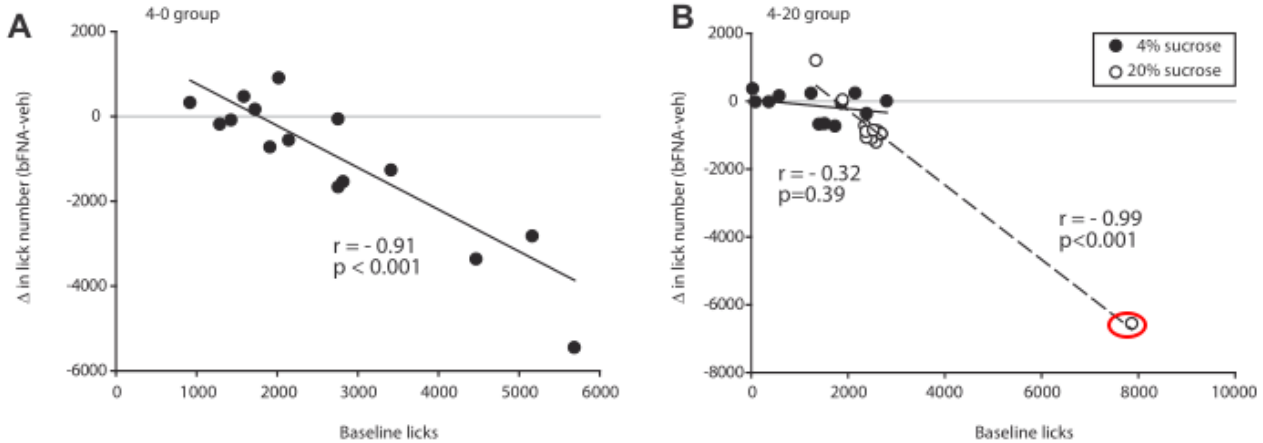

Fig. 6. Beta-FNA suppression of sucrose intake was correlated with baseline intake. (A) In the 4-0 group, the effects of beta-FNA were inversely correlated with baseline 4% sucrose intake (licks after control vehicle infusion). *y*-Axis shows the change in consumption after beta-FNA relative to baseline intake; the *x*-axis shows baseline intake (B) beta-FNA effects in the 4-20 group were negatively correlated with baseline intake of 20% but not 4% sucrose.

Discussion

- MOR signaling promoted intake of learned preferrences
- Adaptive role to consume the most paltable option
- Nacc shell mediated reinforcing properties of reward
- Signalining: NAcc core != NAcc shell
  - NAcc shell –> direct projection to lateral hypothalamus
- Signalining can be macronutrient specific: NAcc core signaling interruption decreases high-fat intake, while in NAcc core decreases sweet solution intake

My take

- NAcc MOR signaling controls learned preferrence intake
- Binge eating in the real world equates to a learned preferrence of paltable food over healthy foods
- However, I see no evidence of NAcc MOR signalining controlling learned hypophagia of non-preferred option
- Good model for controlling food properties (and isolating preferrence), but not precisely typical binge model