The effect of GLP-1RA Therapy on CNS Hedonic Responses & Monoamine Signaling

NASEM

GLP-1 in CNS Disorders Workshop

Jon Davis

9-10-2024

Financial Disclosure

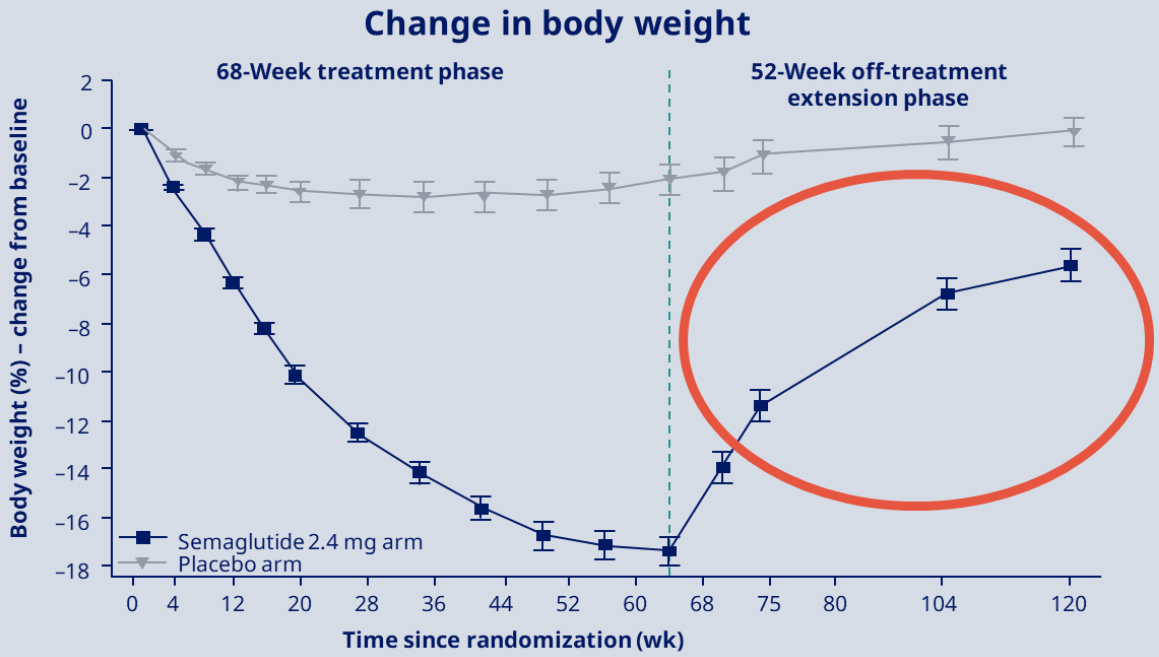
Jon Davis has a financial interest in novo nordisk

Agenda

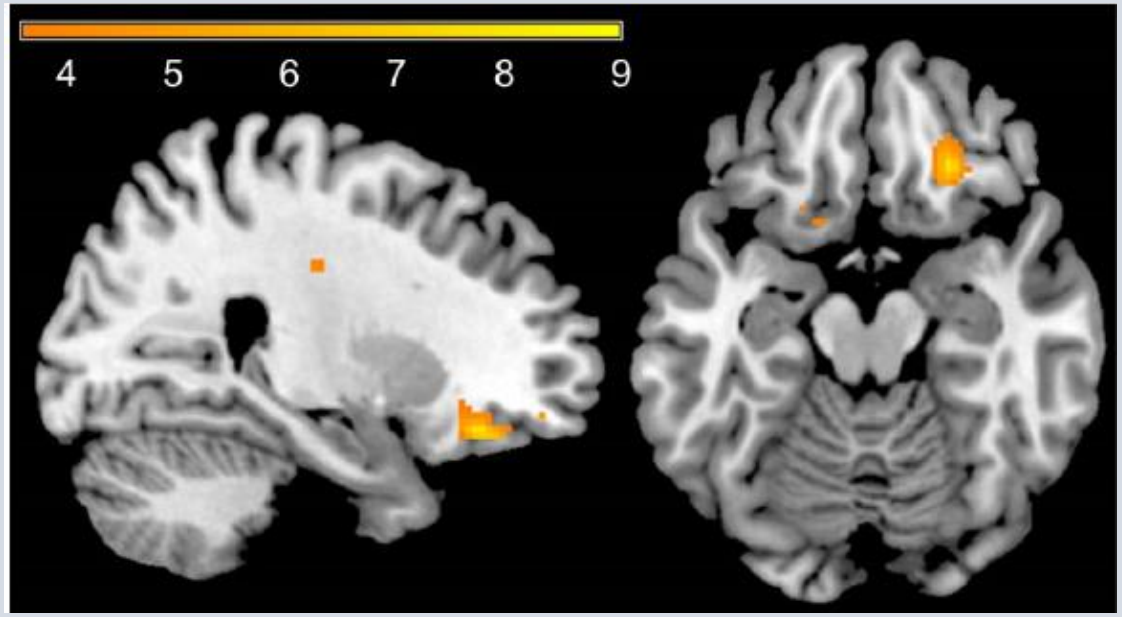
- Review Clinical Data
- Overview of CNS Dopamine System
- Preclinical impact of GLP-1RA on CNS Dopamine

Semaglutide STEP Trial Data

Weight loss is variable, plateaus at 68 weeks, strong regain of body weight

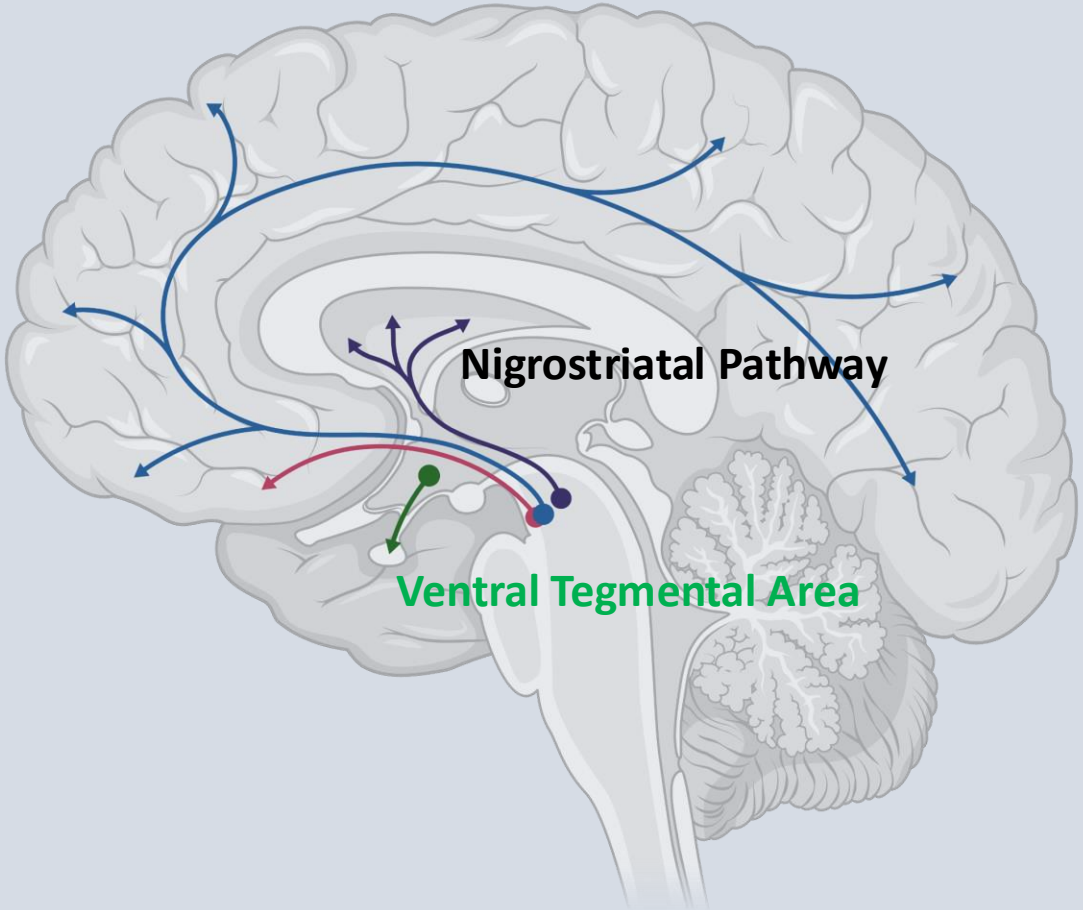


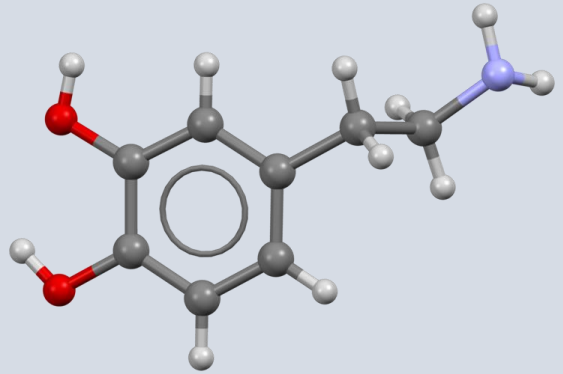
Chronic GLP-1 agonism leads to Augmentation of CNS Reward Regions in response to palatable food cues



CNS Mesolimbic Dopamine System

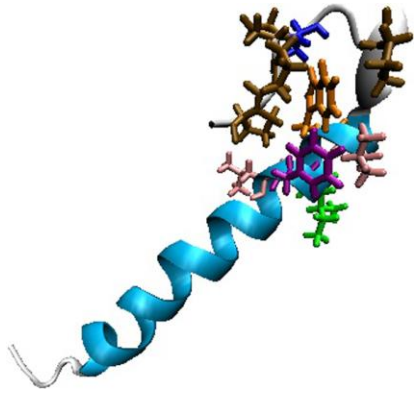
Mesolimbic System:
Reinforced Behavior



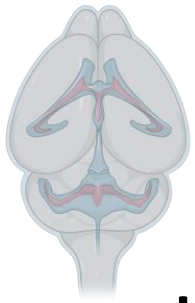


Dopamine

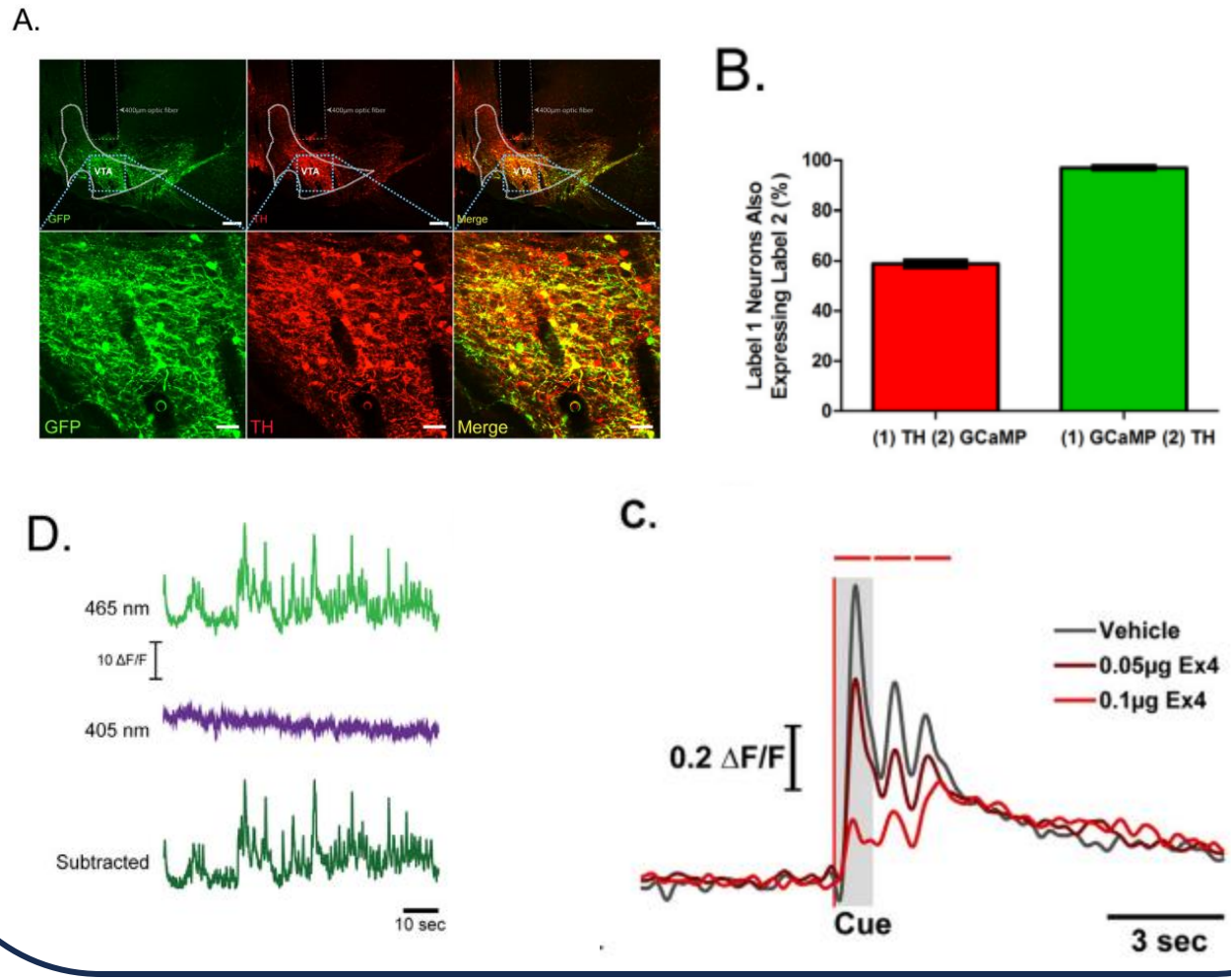
GLP-1RA Modulation of CNS Dopamine Neurons



Exendin-4: GLP-1 Agonist

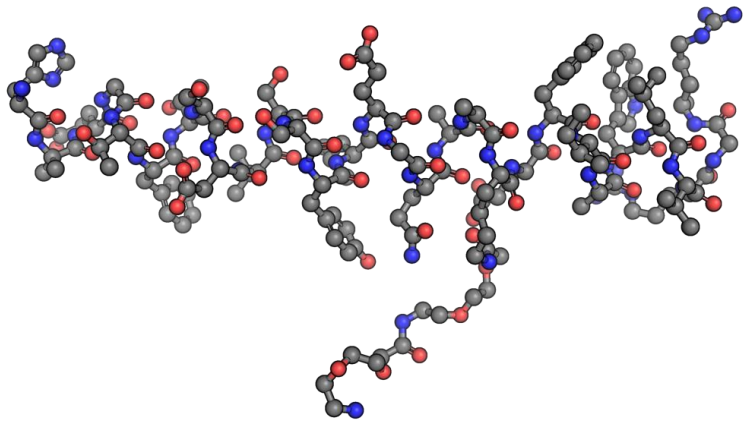


Lateral Ventricle

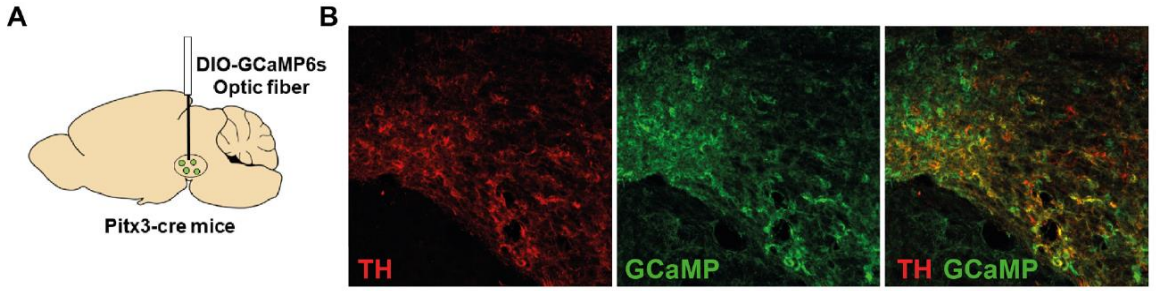


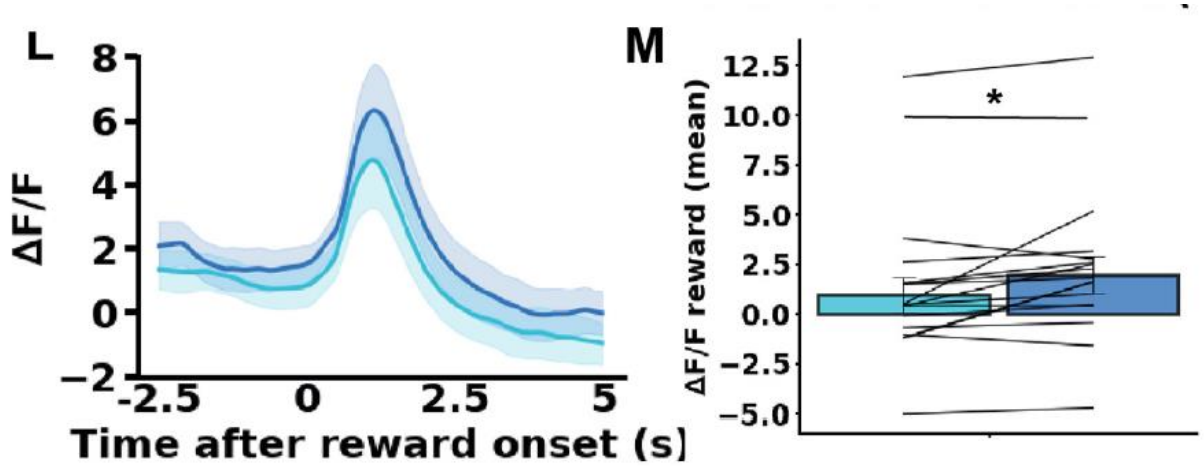
Phasic dopamine responses to a food-predictive cue are suppressed by the glucagon-like peptide-1 receptor agonist Exendin-4 (sciencedirectassets.com)

GLP-1RA Modulation of CNS Dopamine Neurons



Semaglutide: GLP-1 Agonist





GLP-1 receptor agonist semaglutide reduces appetite while increasing dopamine reward signaling - ScienceDirect

Summary

ICV GLP-1RA reduces phasic dopamine activity

Systemic semaglutide augments activity of dopamine neurons

More studies are needed to clarify the role of GLP-1RAs on CNS dopamine responses


novo nordisk®