

Characterisation of brainstem proopiomelanocortin neurones **Teodora Georgescu**

Co-supervisors: Prof. Lora Heisler Dr. David Lyons

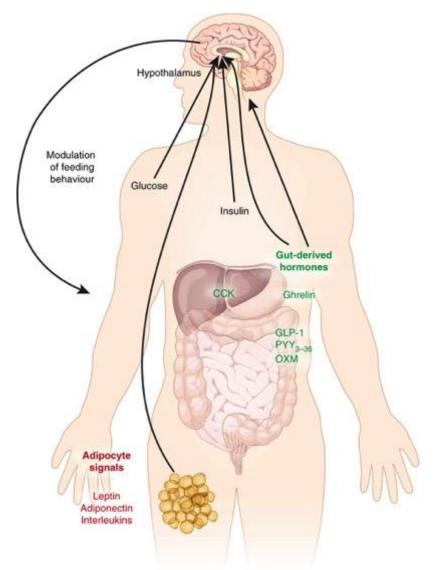
Rowett Institute of Nutrition and Health

Obesity Epidemic



- with >30 bmi in 2008 (compared with 147 million in 1980)
- Major risk factor for type 2 diabetes, cardiovascular disease and hypertension
- Enormous toll on human health and leading to large healthcare costs

+ Control of food intake and energy balance

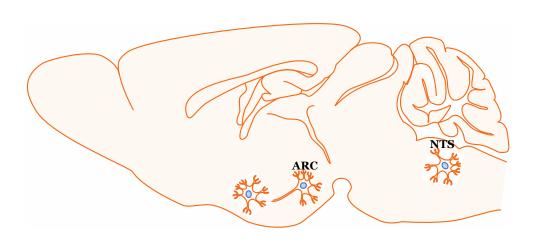


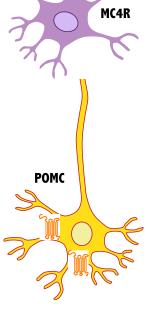
Melanocortin System

■ Pro-opiomelanocortin (POMC) neuropeptides are crucial regulators of appetite

The POMC neurons of the central nervous system are situated primarily in the Arcuate Nucleus of the hypothalamus (ARC) and a smaller group is localized in the Nucleus Treatus Solitorius (NTS) of the brainstern

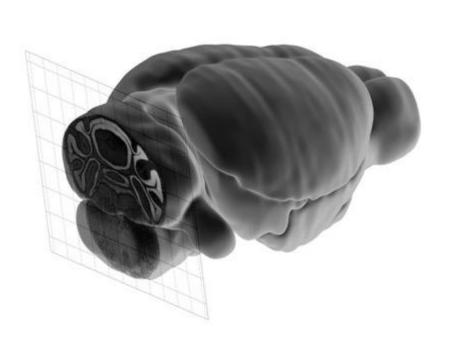
the Nucleus Tractus Solitarius (NTS) of the brainstem.

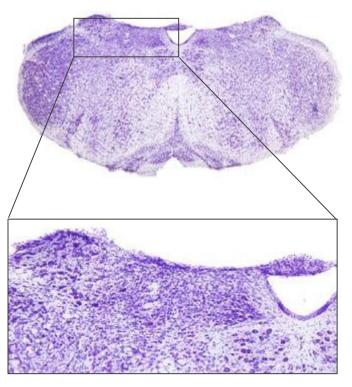




Nucleus of the solitary tract (NTS)

- The NTS plays an essential role in integration of gut derived factors and vagal afferents with central signals.
- The NTS is a crucial site for controlling short-term satiety



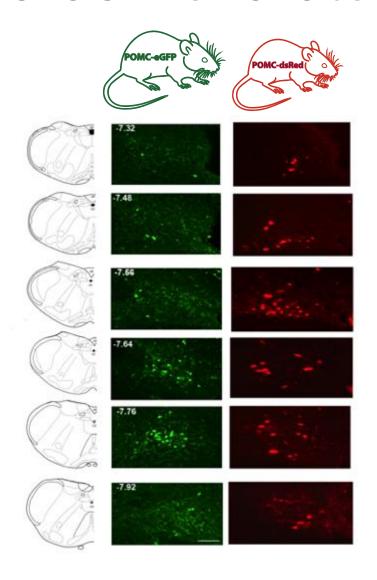


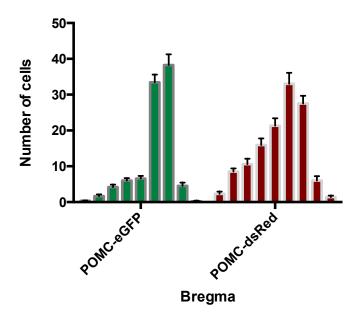
+ Aims

- Aim 1: Map the distribution of POMC cells in the NTS
- Aim 2: Characterise the endogenous regulators of POMC in the NTS
- Aim 3: Determine how these effects on cellular activity are achieved



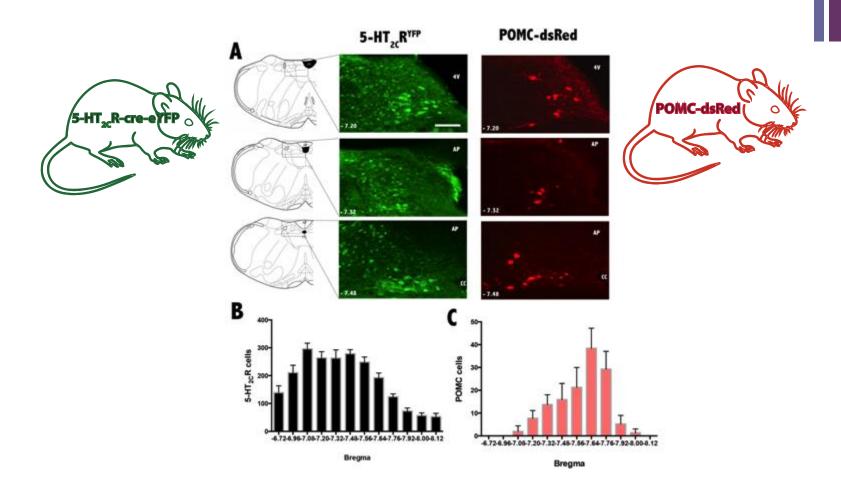
+ POMC-GFP vs. POMC-dsRed distribution NTS



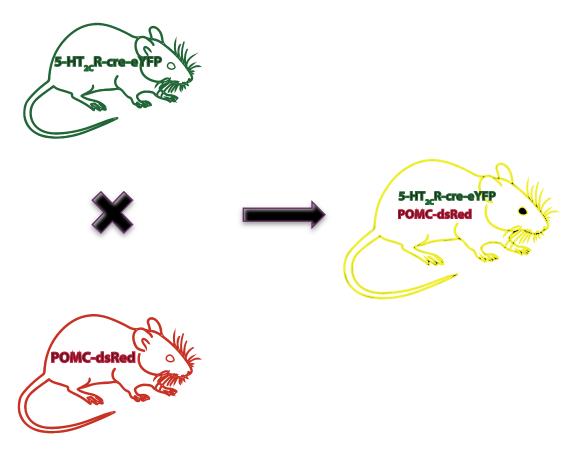


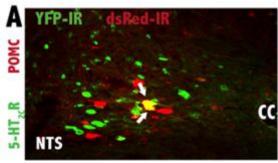


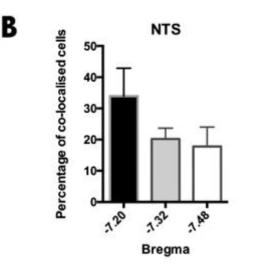
Distribution of 5-HT $_{2C}$ R and POMC cells in the NTS



+ POMC cells co-localise with 5-HT_{2C}R cells in the NTS

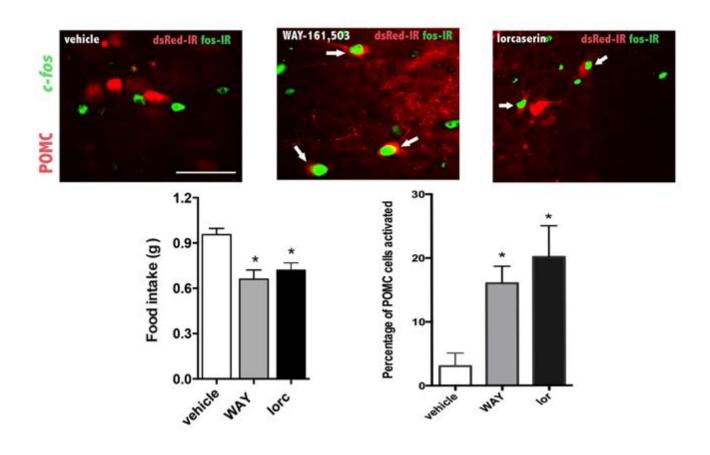






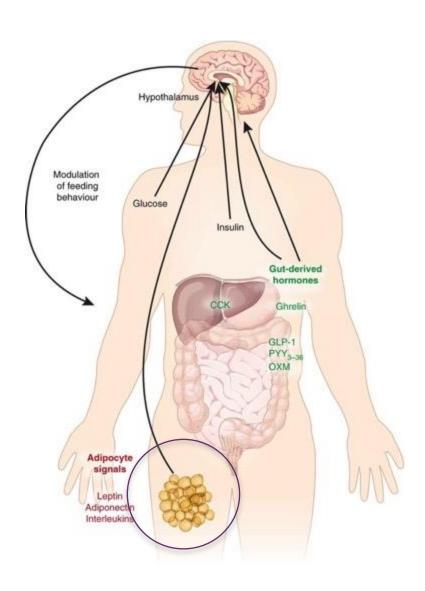


+ 5-HT_{2C}R agonists increase the activity of POMC neurons in the NTS

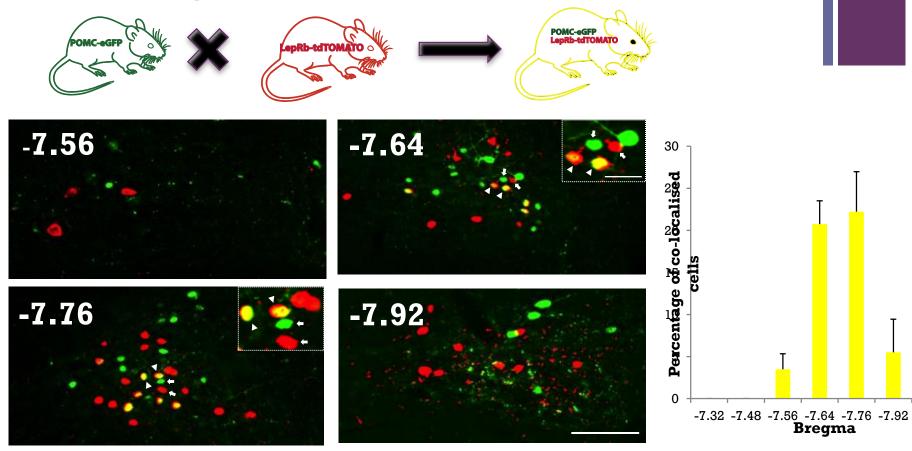




+ Leptin regulates energy balance

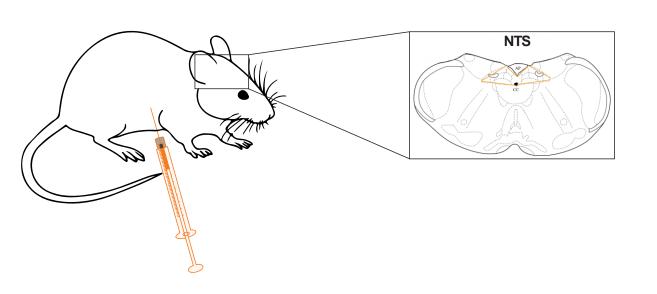


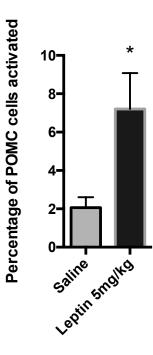
NTS POMC-GFP cells co-localise with LepRb-TOM expressing cells





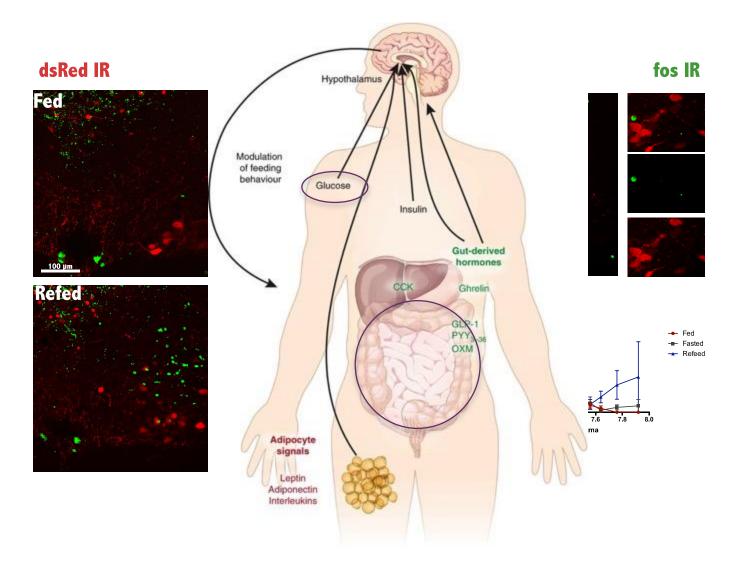
Leptin activates POMC-GFP neurones in vivo





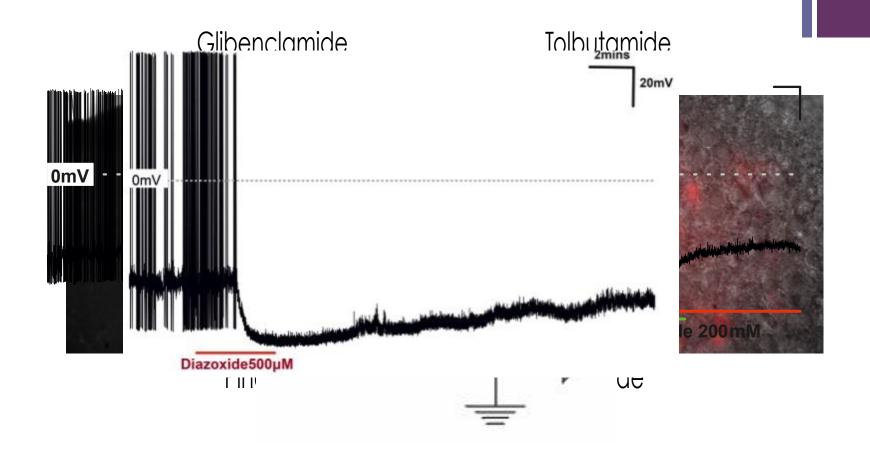


+ NTS POMC neurones increase their activity in response to food intake



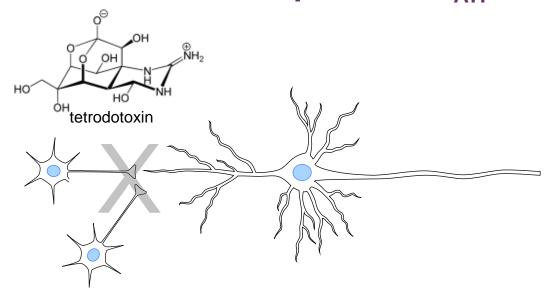


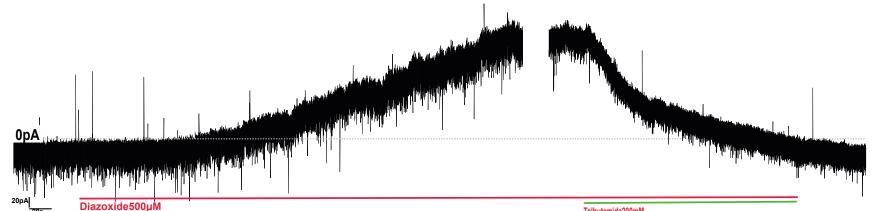
POMC cells in the NTS are metabolically sensitive





NTS POMC neurones possess K_{ATP} channels





Tolbutamide200mM

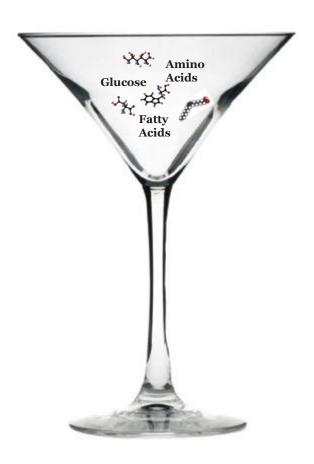


Conclusions

- Established the anatomical distribution of NTS POMC neurones
- Brainstem POMC cells co-express 5-HT2CR and LepRb and respond to their cognitive ligands
- NTS POMC neurones respond to energy state

Future work

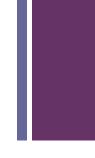
- Systematically characterise their response to nutrient availability e.g.: glucose, amino acids, lipids
- Characterise their cellular response to other functionally relevant neurotransmitters
- Employ mouse transgenics and optogenetics to map the functional connectivity of these neurones to other brain regions
- Use these technologies to investigate their behavioural output



Many thanks!

Rowett Institute of Nutrition and Health





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- Prof. Lora Heisler
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