# Ghrelin Acts in the Supramammillary Nucleus to Regulate Food Intake in Rats

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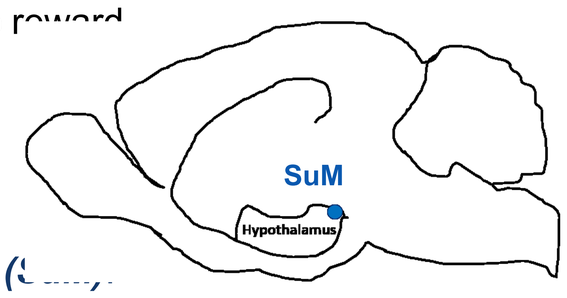
## Background

### *Ghrelin*

- An orexigenic hormone secreted by the empty stomach before a meal.
- Induces food intake and food-motivated behaviour when delivered centrally or peripherally to rats[1,2].
- Neural substrates for these effects include those where ghrelin receptors are located[3] and include hypothalamic, brainstem areas as well as midbrain areas linked to reward.

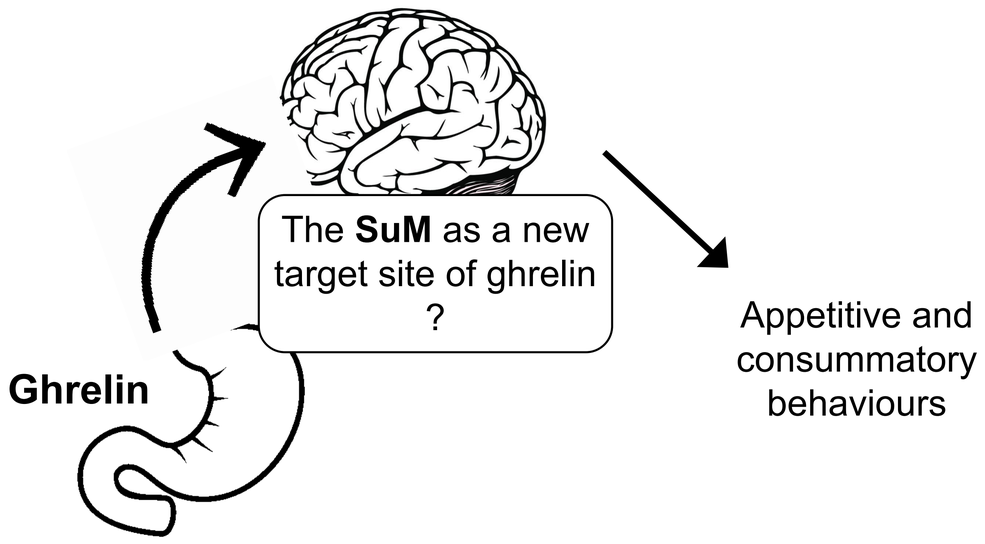



### *The supramammillary nucleus (SuM)*

- Located in the posterior hypothalamus
- Associated with food intake and food reward behaviours[4]
- Centrally delivered ghrelin binds to the SuM[5]

## Aim

To determine whether the SuM is a neural substrate for ghrelin and whether ghrelin action at this site contributes to it's orexigenic effects.




## Methods

### *In vivo electrophysiology:*

Rats were anaethetised, a jugular catheter implanted and the ventral surface of the brain exposed using a transpharyngeal approach. Extracellular recording electrodes were positioned in the SuM under visual control.
Single cell activity was recorded before and after an intravenous (i.v.) injection of 10 µg ghrelin. Significant changes in firing rate were detected at $p<0.01$ (t-test; threshold of 0.5 spikes/sec) comparing 20x30 seconds bins before and after injection.

### *Food intake measurement:*

Guide cannulae were implanted in the SuM under anaesthesia. Conscious rats were intra-SuM injected on different days with ghrelin (2 doses: 1µg and 0.5µg) and vehicle in a cross-over design so each animal was its own control (N=13). Chow intake was measured at 3, 6 and 24 hours after intra-SuM injection. Injections were performed early in the light phase.

## Results

We recorded 53 SuM cells that were spontaneously active. Of these, 17 cells (32%) were significantly activated by i.v. ghrelin (Fig. 1), 11 cells (21%) were significantly inhibited and 25 cells (47%) did not change their firing rate.

Ghrelin injected into the SuM increases intake of normal chow (Fig 2).

**Figure 1:** Mean change in firing rate of all SuM cells that were significantly activated by i.v. ghrelin injection in anaesthetised rats. Data were normalised to the control period and expressed as mean+SEM for each 30 seconds bin.

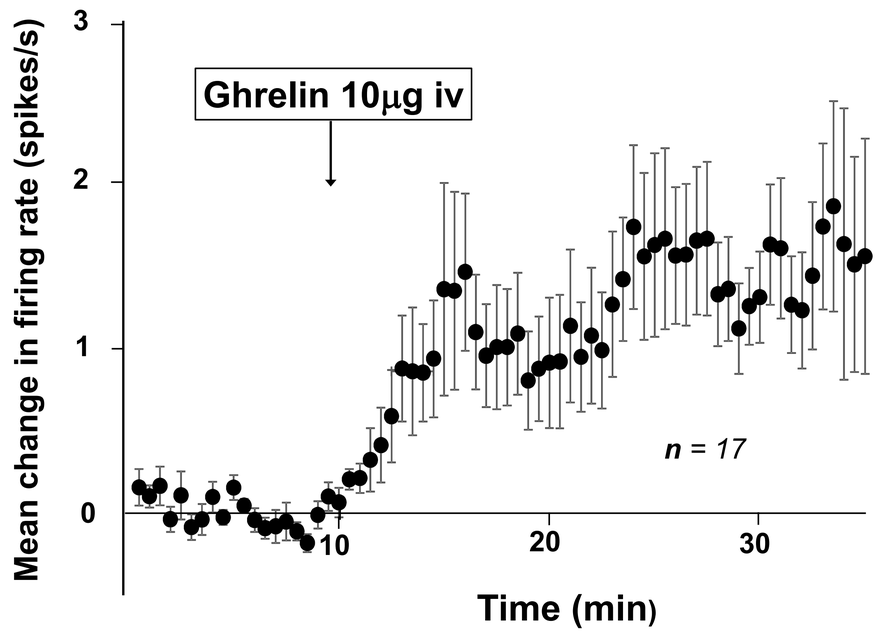
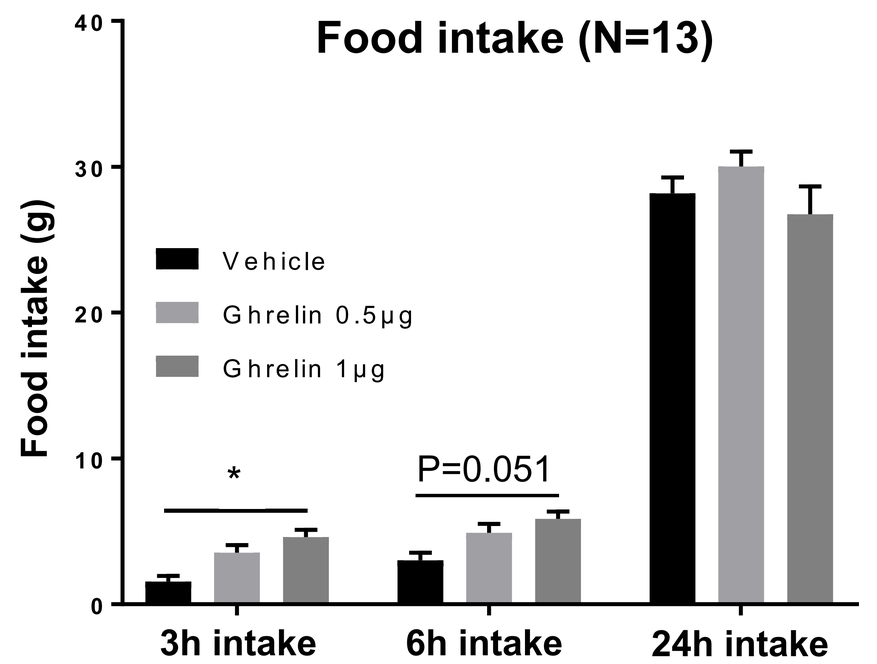



**Figure 2:** Effect of intra-SuM ghrelin injection on food intake (3, 6 and 24 hours after injection) in conscious rats. Treatments were administered in a cross-over design so each animal is its own control. *$p<0.05$ as determined by two-way ANOVA corrected by Dunnett's post hoc test.




## Conclusions

**Peripheral ghrelin alters the activity of SuM cells, eliciting predominantly excitatory but also inhibitory responses.**
**The SuM is a neural substrate from which ghrelin can drive feeding behaviour.**

References:
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