

# Regulation of food intake: a focus on central nervous system and stress influence

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## Introduction

- Obesity is one of the major health problems in developed world. Current weight loss therapies targeting the reduction of food intake have been proven to be relatively ineffective, because many central and peripheral factors are implicated in the regulation of energy homeostasis. In addition, a lot of studies have defined a strong relationship between the regulation of food intake and stress.
- The aim of this review is to discuss the regulation of food intake by the central nervous system and the interconnection of different pathways in our brain and peripheral. Also, this review will discuss the action of hypothalamic-pituitary-adrenal axis (HPA) in the regulation of food intake.

## Material and methods

- **Scientific literature search on PubMed database:** recent papers and reviews of central nervous system and regulation of food intake research were selected according to their quality and date of publication (2006-2015).
- **Key words:** NPY, AgRP, POMC, CART, hypothalamus-pituitary-adrenal axis, melanocortin, leptin, insulin, ghrelin, obesity, stress.

## Results

### Central nervous system

Several brain regions are involved in the regulation of food intake:

- Hypothalamus, amygdala and nucleus accumbens (NAc) of the cortico-limbic systems.
- Key hypothalamic sites (Figure 1) include:
  - arcuate nucleus (ARC),
  - paraventricular nucleus (PVN),
  - dorsomedial hypothalamic nucleus (DMH)
  - lateral hypothalamic area (LHA)
  - ventromedial hypothalamic nucleus (VMH).

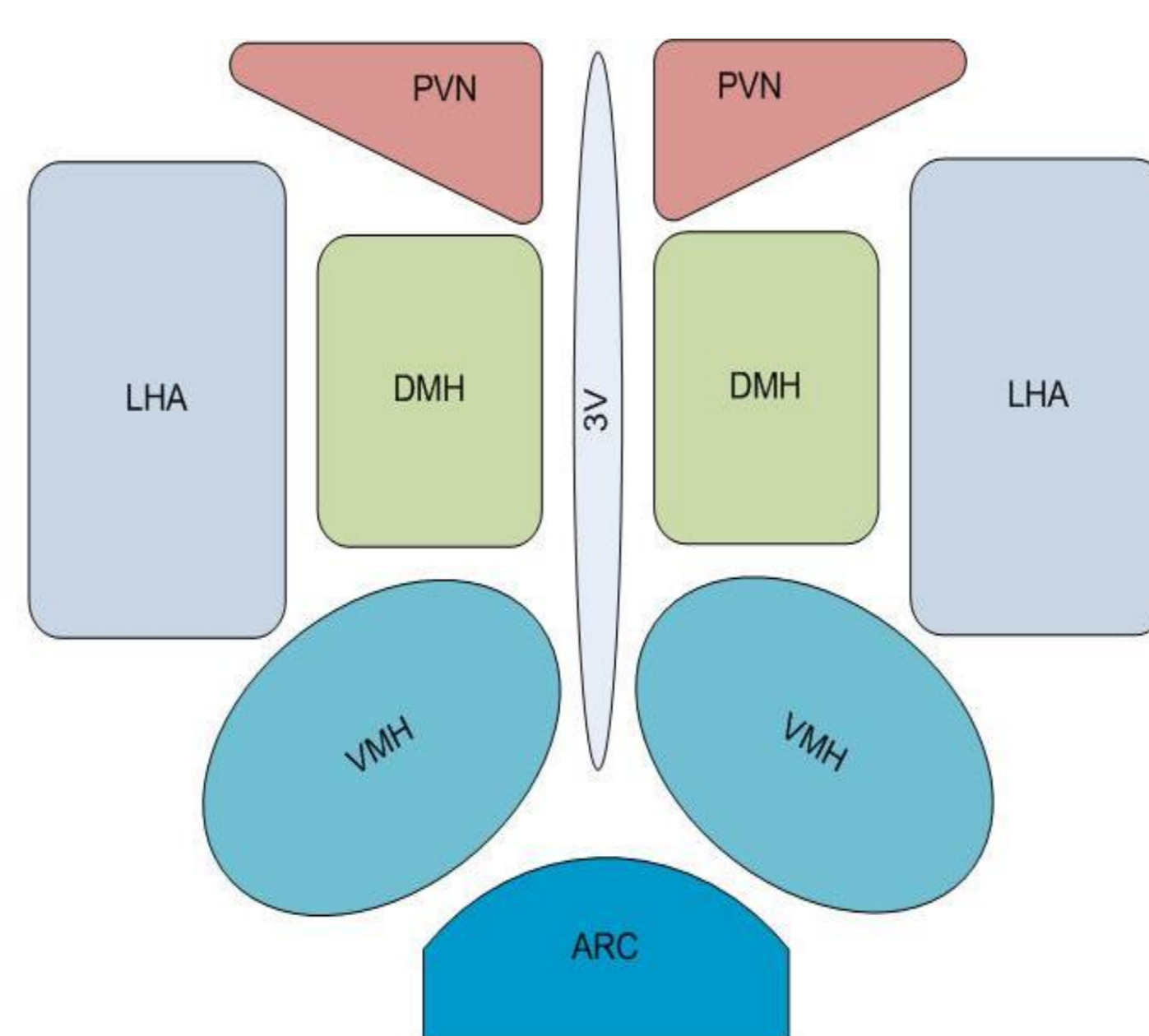


Fig.1. Nucleus of hypothalamus. (Adapted from Parker, J.A. et al, 2012)

**ARC** contains two populations of neurons with opposite effects on food intake which are named after the neuropeptides they contain:

- Neuropeptide Y (NPY) and agouti-related protein (AgRP) have orexigenic effects, which means they increase food intake.
- Pro-opiomelanocortin (POMC) and cocaine and amphetamine-regulated transcript (CART) have anorexigenic effects, which means they decrease food intake.

### Peripheral signals

The main peripheral signals are:

- Leptin and insulin: secreted mainly from adipocytes and  $\beta$ -cells of the pancreatic islets of Langerhans respectively, both have anorexigenic effect in ARC.
- Ghrelin: secreted mainly from stomach in response to hunger, stimulate food intake.

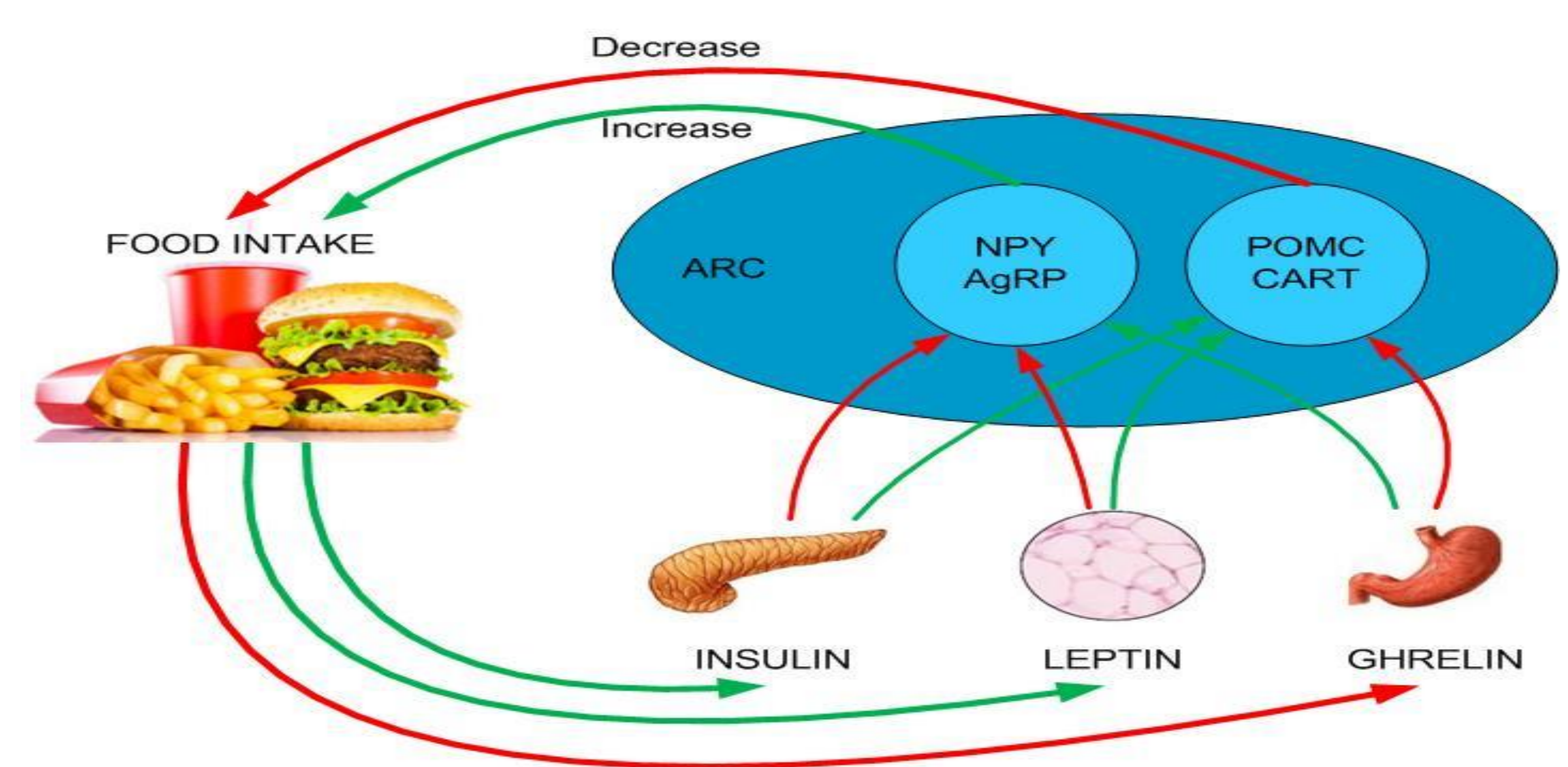


Fig.2. Peripheral signals in ARC increasing/decreasing food intake

### Anorexigenic neurons

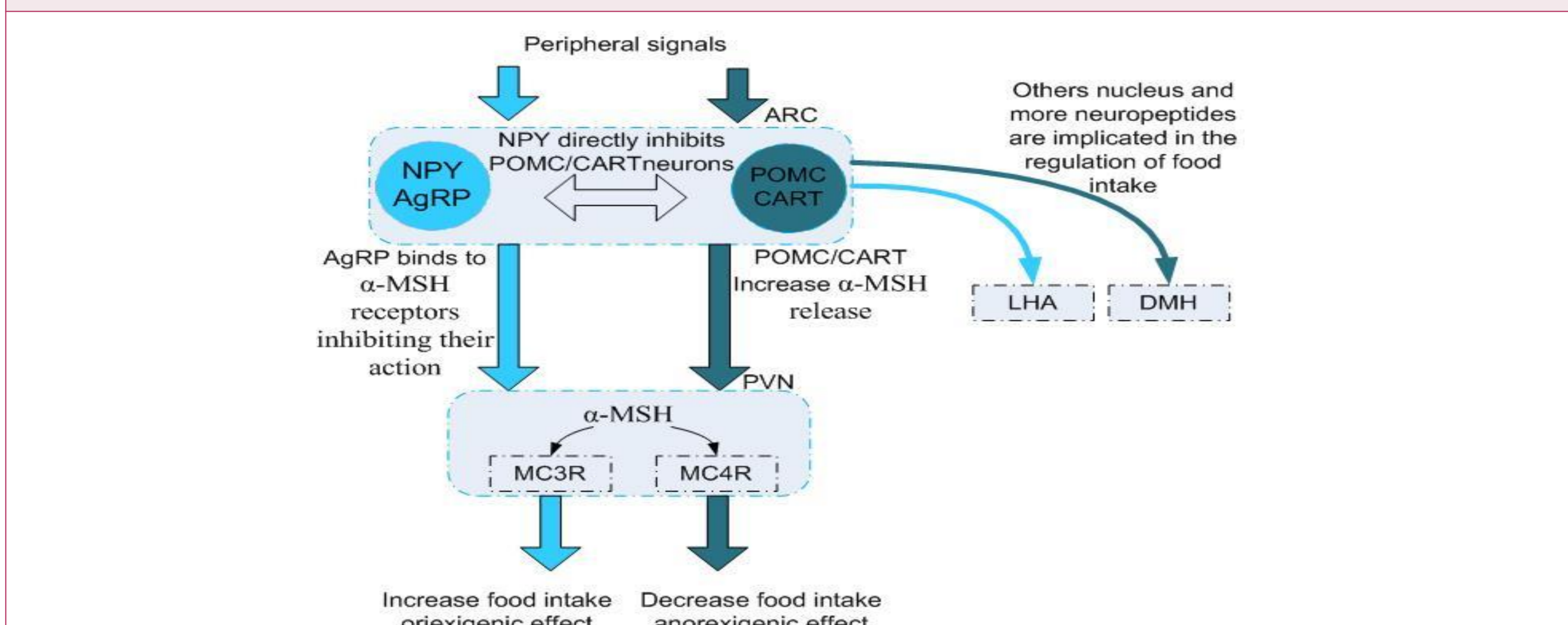
POMC & CART are distributed through hypothalamus (ARC, PVN, DMH) and other regions of SNC.

These neuropeptides release  $\alpha$ -melanocyte-stimulating hormone ( $\alpha$ -MSH) from PVN that binds to melanocortin receptor (MC3R, MC4R) which inhibits food intake.

### Orexigenic neurons

NPY is distributed along SNV whilst AgRP is only in ARC. Both increase food intake inhibiting POMC & CART pathway:

- NPY directly inhibits POMC neurons. (Regulation of acute feeding behavior)
- AgRP is the antagonist of  $\alpha$ -MSH, so it blocks binding of  $\alpha$ -MSH receptors. (Regulation of long term feeding behavior)



### Stress- modulated obesity

- Corticotropin-releasing hormone (CRH) regulates secretion of adrenocorticotrophic hormone (ACTH) which controls secretion of adrenal steroids, glucocorticoids (GC).
- The regulation of food intake and stress axis shares the majority of nucleus in CNS and their neuropeptides modify each other.

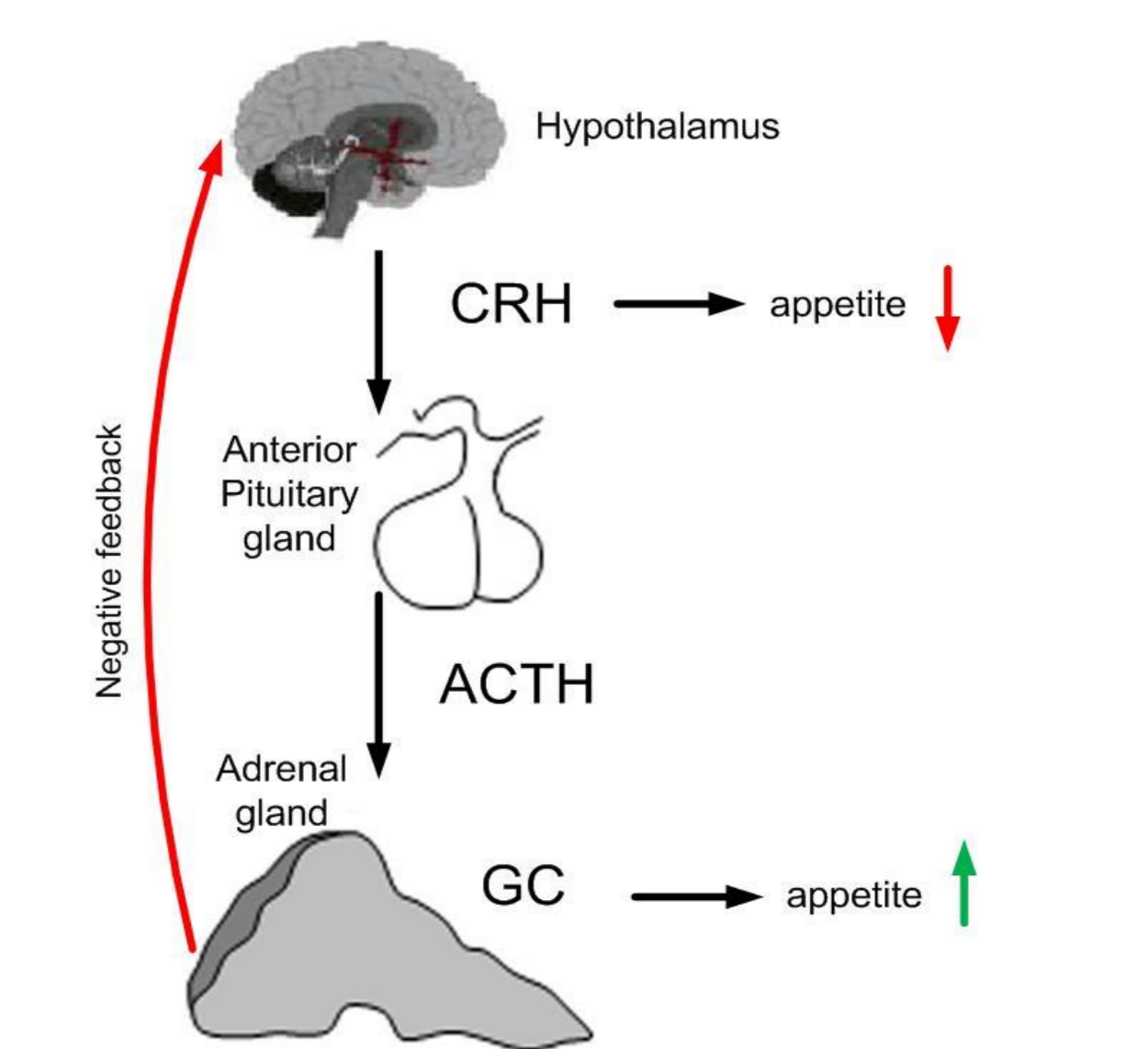


Fig.3. Hypothalamus-pituitary-adrenal (HPA) axis and its relation with the regulation of food intake. Adapted from Spencer, S.J. 2013).

### Opposite effects:

- GC have orexigenic effects, increasing NPY and AgRP secretion, whilst CRH secreted in the PVN has anorexigenic effects.

### Stress and reward pathway:

- Chronic stress can decrease appetitive behavior, unless people have access to palatable food. Eating fatty food activates the brain reward system and decreases stress.

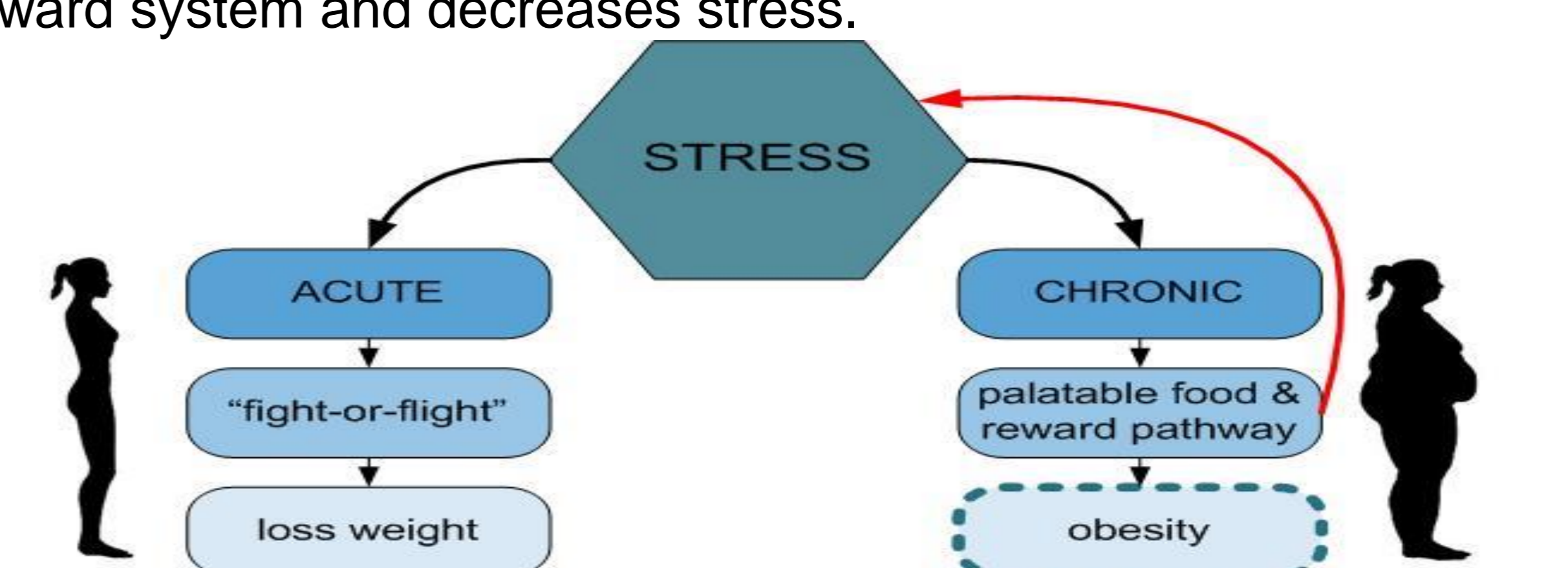


Fig.4. Acute and chronic stress pathways in the regulation of food intake

## Conclusions

- There is a strongly relationship between peripheral and central signals in the regulation of food intake.
- Although neuropeptides implicated in food intake are well-known, further research is necessary to completely understand other roles of these neuropeptides and their receptors, as well as their distribution in SNC.
- Feeding behavior after chronic stress is difficult to define because more pathways such as reward system are involved.

## References

- Parker, J. A. & Bloom, S. R. Hypothalamic neuropeptides and the regulation of appetite. *Neuropharmacology* 63, 18–30 (2012).
- Spencer, S. J. Perinatal programming of neuroendocrine mechanisms connecting feeding behavior and stress. *Front. Neurosci.* 7, 109-22 (2013).