**Obesity or EDs (Disordered Eating) (1.1) ~half a page**

The brain’s relationship with food is changing. As the global food system becomes increasingly saturated with processed and ultra-processed foods, the obesity epidemic grows in parallel (Moubarac et al., 2014). More than half of adult Canadians are overweight or obese and more than 54% of Canadians eat out at least once a week (Moghimi and Wiktorowicz, 2019). Access to these processed foods is easier than ever, and it takes very little energy to get them (Dallman et al., 2006). Ultra-processed foods are more energy dense, with more sugar, sodium, and saturated fats. They are also highly palatable. The typical Canadian’s grocery list becomes increasingly dominated by ultra-processed foods, while unprocessed foods (ingredients) disappear (Moubarac et al., 2014).

Stress, the perceived threat to homeostasis, is an adaptive mechanism that has become a challenge in modern life (Smith and Azevedo, 2025). The body has many mechanisms to return to that homeostasis, vital to resistance and adaption (Smith and Azevedo, 2025). Transition sentence. Glucocorticoids are hormones, part of the stress response system, a system that has not adapted to our world of high chronic social stress and landscape of easily accessible high calorie, highly palatable foods (Dallman et al., 2006).

High calorie, highly palatable foods are easily accessible, and it takes very low physical effort/energy expenditure to get them (Dallman et al., 2006).

-glucocorticoids induce insulin resistance (Charmandari et al., 2005)… obesity

**Stress (1.2) ~one page**

Physiologically, stress is a challenge to the homeostasis of an organism (Bose et al., 2009), or the perceived threat to homeostasis (Charmandari et al., 2005). The organism then responds to regain equilibrium (Bose et al., 2009). In humans, stress activates the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic adrenomedullary system (SAM) which originates in the locus ceruleus (LC), to different degrees (Adam and Epel, 2007; Charmandari et al., 2005). Activation of the SAM activates epinephrine which suppresses appetite and stops digestion (Adam and Epel, 2007). The HPA includes corticotrophin releasing hormone (CRH) release from the paraventricular nucleus (PVN) of the hypothalamus which stimulates adrenocorticotrophin hormone (ACTH) release from the pituitary gland which stimulates cortisol release from the adrenal cortex (Bose et al., 2009; Adam and Epel, 2007). In an acute, short-term stressor, cortisol should negatively feedback on CRH and ACTH to prevent prolonged secretion of cortisol (Adam and Epel, 2007; Charmandari et al., 2005) since the acute stress response is necessary for homeostatic recovery, but chronic or prolonged stress can be harmful (Bose et al., 2009).

Cortisol binds to glucocorticoid and mineralocorticoid receptors and when initiates or represses transcription of x to negatively feedback on the HPA axis, or regulate basal HPA activity, respectively (Nieuwenhuizen and Rutters, 2008).

**Stress and appetite (1.2.1) ~two pages (**sex difference can be here: pandemic example**)**

As part of the normal response to an acute stressor in a stressor-naïve animal, there is afferent activation of the HPA, with glucocorticoid levels increasing within 2-5 minutes of the stimulus (Dallman et al., 2006). This rapid action is critical to shorten the duration of ACTH secretion and the HPA so that the threat can be responded too, but not so much that there could be negative consequences (Dallman et al., 2006). Cortisol, a glucocorticoid, stimulates hunger and feeding (Adam and Epel, 2007). Chronic stress and excess glucocorticoids play a role in obesity by interfering with energy homeostasis (Tamashiro et al., 2011) and increasing food intake and visceral fat deposition (Adam and Epel, 2007).

In the periphery, glucocorticoids act catabolically to mobilize energy stores, ensuring enough fuel for tissues such as the heart and muscles, allowing for the energy to escape stressors (Dallman et al., 2006). In contrast, glucocorticoids act anabolically in the brain, driving caloric intake (Dallman et al., 2006). Meaning of that. Chronic elevation of glucocorticoids in the absence of chronic stress inhibits basal HPA activity and HPA activity stimulated by an acute stressor, but this is likely due to inhibition at the pituitary, not central inhibition (Dallman et al., 2006). Norepinephrine neurons in the LC likely activate the HPA, evident by lesioning studies that find a decreases HPA response to acute stress (Dallman et al., 2006). This balance and crosstalk between the HPA and SAM are critical in the stress response.

Under prolonged stress, the ability of glucocorticoids to negatively feedback stimulated ACTH secretion is decreased (Dallman et al., 2003). Chronic stress increases consumption of highly palatable “comfort foods”, reinforcing neural pathways leading to consumption of these foods (Tryon et al., 2013). Factors that predict eating more under stress in humans include being female, overweight, or having a history of food restriction (Adam and Epel, 2007) and women who report more chronic stress also report being emotional eaters (Tryon et al., 2013).

Davies et al. (2023) found females were at higher risk for pandemic stress-induced binge eating, and females ages 10 to 19 showed the greatest increase in eating disorder released hospitalizations during this time (Auger et al., 2023). Hunger and satiety signals are driven by the hypothalamus (Tryon et al., 2013; Smith and Azevedo, 2025). When under stress, this communication is dysregulated, causing alterations in hypothalamic neurons that lead to altered feeding behaviour (Smith and Azevedo, 2025).

Behaviour is complex due to the balance between SAM (epinephrine -> decrease hunger) and HPA (cortisol -> increase hunger)

**The hypothalamus (1.3) ~paragraph**

The hypothalamus is a tiny, yet powerful brain region that exerts immense control over basic life functions and homeostasis such as energy metabolism and expenditure, autonomic activity, and hormone secretion (Saper and Lowell, 2014; Benedini, 2009). It is the regulator of the master, pituitary gland and the autonomic nervous system (Benedini, 2009). The hypothalamus integrates multiple signals such as hormonal, metabolic, and neural input both from within the hypothalamus and from other brain regions (Goel et al., 2025; Smith and Azevedo, 2025).

Transition sentence… contains nuclei… distinct nuceli

**The DMH (1.4) ~half page**

The DMH, located XYZ, is involved in energy expenditure, cardiovascular changes in response to stress, thermoregulation, food intake, and body weight regulation (Goel et al., 2025; DiMicco et al., 2002). Located here is a heterogenous population of cells. The DMH communicates with various brain regions through both glutamate, the major excitatory neurotransmitter, and GABA (*gamma*-aminobutyric acid), the major inhibitory neurotransmitter (Myers et al., 2014). The DMH receives input from many brain regions including the prefrontal cortex, amygdala, lateral septum, and pre-optic area and projects to the PVN, rostral raphe pallidus of the medulla oblongata, and the LC (Myers et al., 2014; Tran et al., 2022). and plays roles in sympathetic activation of heart rate (DiMicco et al., 2002), brown adipose tissue (Tran et al., 2022).

The DMH is a region of interest due to its integration of satiety and stress signals (Crosby et al., 2011).

**The DMH and Food Intake (1.4.1) ~one page**

Early DMH studies in sheep showed that stimulation resulted in hyperphagia, indicating the role of the DMH in appetite (Bellinger and Bernardis, 2002). Lesioning studies in rats later revealed destruction of the DMH resulted in hypophagia and hypodipsia while maintaining normal body fat percentage and lean body mass (Bellinger and Bernardis, 2002). On a normal diet, DMH lesion (DMHL) rats display hypophagia and loose body weight, in contrast, DMHL rats with restricted diet show immediate hyperphagia. When given high fat diets, DMHL rats become obese compared to regular diet DMHL rats, but not as obese as control animals (Bellinger and Bernardis, 2002). However, on other highly palatable diets, DMHL rats show that can become as obese or even more obese than control animals.

\*Where to put\* Weight loss is a marker of stress in rodents but when they have highly palatable food, stress increases the intake of that highly palatable food (Adam and Epel, 2007).

**The DMH and Stress (1.4.2) ~paragraph**

Something to transition from eating to stress…

Glutamatertgic neurons, located primarily in the dorsomedial region of the DMH, and GABAergic neurons, located primarily in the ventrolateral region of the DMH, to the paraventricular nucleus of the hypothalamus (PVN), respectively activating or inhibiting corticotrophin releasing hormone (CRH) neurons (Myers et al., 2014). As the DMH is an upstream regulator of the PVN, these projections are modulated by stress. This is evident in stimulation of the dorsal region of the DMH, which results in increased ACTH secretion, while inhibition of this region decreases secretion (Myers et al., 2014).

Many neurons in the DMH expresses glucocorticoid receptors (Cintra et al., 1990), so the glucocorticoids produced by the HPA may in turn modulate the activity of the DMH, a modulator of the HPA axis. Conclusion sentence.

**Synapses (1.5) ~one page**

Neurons communicate using electrical and chemical (neurotransmitter) signals. Classical …

-metabolotipic and ionotropic

**-Glutamate (1.5.1) ~one page**

-NMDA and AMPA receptors

**-Stress on synaptic transmission (1.5.2) ~half page**

-endocannabinoid retrograde signalling?

-glucocorticoids acting on CRH neurons inhibit presynaptic glutamate release via 2-AG (dos-Santos et al., 2023)

-glucocorticoid mediated negative feedback of the HPA is blocked by agonists of CB1Rs (Levy and Tasker, 2012).

-^ CB1R knock out mice don’t have that response either

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**Neuronal Excitability (1.6)**

-action potentials

**-Stress and Neuronal Excitability (1.6.1)**

**Current Study (1.7) ~one page**

-what is known about the relationship between food and stress

-DMH role in appetite and stress (projections to the PVN which modulate the HPA)

-ideal brain region to study

-impact on xyz is unknown but could allow greater insight into xyz.

-females under researched

We hypothesized that stress would alter neuronal excitability and communication in the DMH. We predicted that acute stress would decrease activity of DMH neurons (lesion = less hungry (normal diet) so less activity = less hungry) and that chronic stress will increase activity (resistance to GC = hungrier, so we would see more activity) of DMH neurons compared to naïve animals. This hypothesis was tested by performing acute and repeated stressors and assessing the neuronal activity and communication of the DMH using patch clamp electrophysiology.

WHERE TO PUT INFO ABOUT AM251?