**Stress, eating and the reward system (Adam and Epel, 2007)**

**doi: 10.1016/j.physbeh.2007.04.011.**

**keywords: food**

-weight loss as a marker of stress in rats BUT when they have HPF stress increases intake of that HPF

-humans: bidirectional, 30% decrease intake during or after stress, the rest increase

-sympathetic adrenomedullary system (SAM) originates in the locus ceruleus and with the HPA build the effector limbs of the stress response

-CRH neurons of the PVN are the principle hypothalamic regulator of the HPA

-CRH stimulates secretion of ATCH from anterior pituitary

-ACTH on the adrenal glands where it stimulates the release of cortisol or corticosterone

-cortisol feedback back to shut off further secretion to protect the organism from prolonged secretion

-predictors of eating more during stress in humans: female, overweight, scoring high on dietary restraint

-human “threat stress” activates the HPA and cortisol which stimulates hunger and feeding

-human “challenge” activates the SAM and adrenaline which shuts down digestion

-excess glucocorticoids part of obesity via increase food intake and visceral fat deposition

-humans: greater basal cortisol or greater cortisol reactively in people with AN, BED, BN.

-naloxone suppressed intake of HPF.

-stress as a type of negative reinforcement for food intake

-rats: physical stress reduced sugar water intake (vs water) and emotional stress increased it

**Effect of restraint stress on feeding behaviours of rats (Ely et al., 1997)**

[**https://doi.org/10.1016/S0031-9384(96)00450-7**](https://doi.org/10.1016/S0031-9384(96)00450-7)

**keywords: food, stress**

-neural events guide and trigger behavior but there is peripheral physiological input

-products of digestion act on chemoreceptors

-adult male rats (60-90 days)

-1 hr/day

-“control animals were manipulated but not submitted to restraint”

-acute restraint stress did not increase the intake of fruit loops

-chronic model of moderate intensity increase food intake of fruit loops

**The hypothalamic-pituitary-adrenal axis in the regulation of energy balance (**Nieuwenhuizen and Rutters, 2008**)**

**DOI: 10.1016/j.physbeh.2007.12.011**

**keywords: HPA**

-cortisol binds to transporter in the blood

-binds to glucocorticoid and mineralocorticoid receptors

-GR: initiates or represses transcription, negative feedback of HPA axis

-MR: regulates basal HPA activity

-anorectic effects of adrenalectomy can be reversed by glucocortoid replacement

-CRH neurons in the PVN

-A diagram of a food chain

AI-generated content may be incorrect.

**Chronic stress, metabolism, and metabolic syndrome**

**(Tamashiro et al., 2011)**

**keywords: stress**

-stress has adverse effects including inferring with energy homeostasis and resulting in obesity

-responses to acute stress and protective and adaptive

-chronic stress impairs neuroplasticity

**Stress and obesity: the role of the hypothalamic–pituitary–adrenal axis in metabolic disease**

**(Bose et al., 2009)**

**keywords: HPA**

-stress is a challenge to the homeostasis of the animal

-respond by producing physiological stress response to regain equilibrium

-ANS and HPA

-acute short-term stress response is necessary for homeostatic recovery, chronic or prolonged stress can be harmful

-CRH from the PVN of the hypothalamus stimulates ACTH from pituitary

-physical stressors activate PVN neurons that express CRH

-ACTH cortisol from adrenal cortex

-adrenalectomy in Cushing’s syndrome (high cortisol) relives obesity

**Palatable foods, stress, and energy stores sculpt corticotropin-releasing factor, adrenocorticotropin, and corticosterone concentrations after restraint**

**keywords:HPA, food, stress**

**(Foster et al., 2009)**

-previous studies show reduced HPA response to acute and repeated stressors in rats

-adult male SD rats

-only rats with highly palatable sucrose ate more after 30 min restraint stress

**Glucocorticoids, chronic stress, and obesity**

**(Dallman et al, 2006)**

**keywords: stress, food**

-sustained stressors may leave prolonged traces of elevated glucocorticoids

-chronic elevations of glucocorticoids act differently depending on if they are presently elevated in the presence or absence of a chronic stressor

-stressor-glucocorticoid-induced plastic effects on the brain that result from persistent stressor may have “deleterious consequences for the chronically stressed organism”

-at high daily doses of glucocorticoids for 3 weeks, it takes days-weeks to return to basal HPA activity after the treatment is stopped

-normal response to acute stressor in a **stressor-naïve animal**: afferent activation of the hypothalamic CRF neuron, secretion to the median eminence to activate the pituitary corticotrope, then ACTH secretion into general circulation, then adrenal cortex where glucocorticoids increase within 2-5 minutes of the stimulus, and soon act to inhibit the CRF and ACTH “secretory responses”

-rapid action of glucocorticoids shorten the duration but not the peak magnitude of stimulus-induced ACTH secretion which is key to limiting the duration of action of the HPA to be able to respond to the threat but not so much that it could be harmful

-(**concurrent stress**) “sensitization of HPA activity in response to a novel stimulus in chronically stressed rats” only if the glucocorticoids levels are elevated above the normal daily mean

-“sustained treatment with glucocorticoids in the **absence of concurrent stress** inhibits both basal and acutely stimulated activity in the HPA axis… likely that the inhibition is at the pituitary with **less central inhibition**”

-“however, many low-intensity repeated stressors like restraint, cold, noise, and ethanol provoke habituation rather than sensitization in the HPA”

-highly likely that LC noradrenergic (NE) activate the HPA and that LC lesions decrease HPA response to acute stress

-glucocorticoids act catabolically in the periphery, and anabolically in the brain/centrally

-in the brain glucocorticoids promote caloric intake (opposite to in the periphery)

-“in the absence of stress, glucocorticoids strongly stimulate in a dose-related fashion, the ingestion of substances that are pleasurable to the animal”

-incidence of chronic social stress is increase, high calorie HPF are readily available and physical effort needed to acquire them is decreased

-the system of glucocorticoids needed to survive in chronic stress has not yet adapted to our modern climate with ease of access to these foods

**ENDOCRINEOLOGY OF THE STRESS RESPINSE**

**(Charmandari et al., 2005)**

**keywords: stress, hormones**

-when homeostasis is threatened (or perceived to be threatened)  
-central parts of the stress system are in the hypothalamus (HPA) and brainstem (SAM)

-CRH is an anorexigenic (loss of appetite) peptide

-glucocorticoids inhibit the PVN CRH and NE sympathetic systems

-diurnal variation in secretion of cortisol and ACTH (which is normal) can be disrupted by changed in lighting, feeding, activity, and following stress

-glucocorticoids are the final effectors of the HPA

-neg. feedback of glucocorticoid on CRH and ACTH

-stress influences appetite satiety centers in the hypothalamus

-acute elevation in CRH concentration causes anorexia

-stress response is supposed to be short/limited

-increased HPA axis activity: chronic stress, anorexia, DM, Cushing syndrome, hyperthyroidism

-prolonged activation of HPA suppresses growth hormone secretion

-glucocorticoids induce insulin resistance

**Understanding the relationships between physiological and psychosocial stress, cortisol and cognition (James et al., 2023)**

**keywords: stress**

- “In the event of experiencing acute stress, the initial response to this is facilitated via the SAM, which regulates the release of catecholamines (including noradrenaline, adrenaline, and small amounts of dopamine) and ultimately triggers the “fight or flight” response (70, 71). These processes lead to activation of the HPA axis.”

-“ The release of this hormone [glucocortocid] is the best characterised marker of the HPA axis response to psychosocial stress.”

**The Neuroendocrine Impact of Acute Stress on Synaptic Plasticity**

**(**dos-Santos et al., 2023**)**

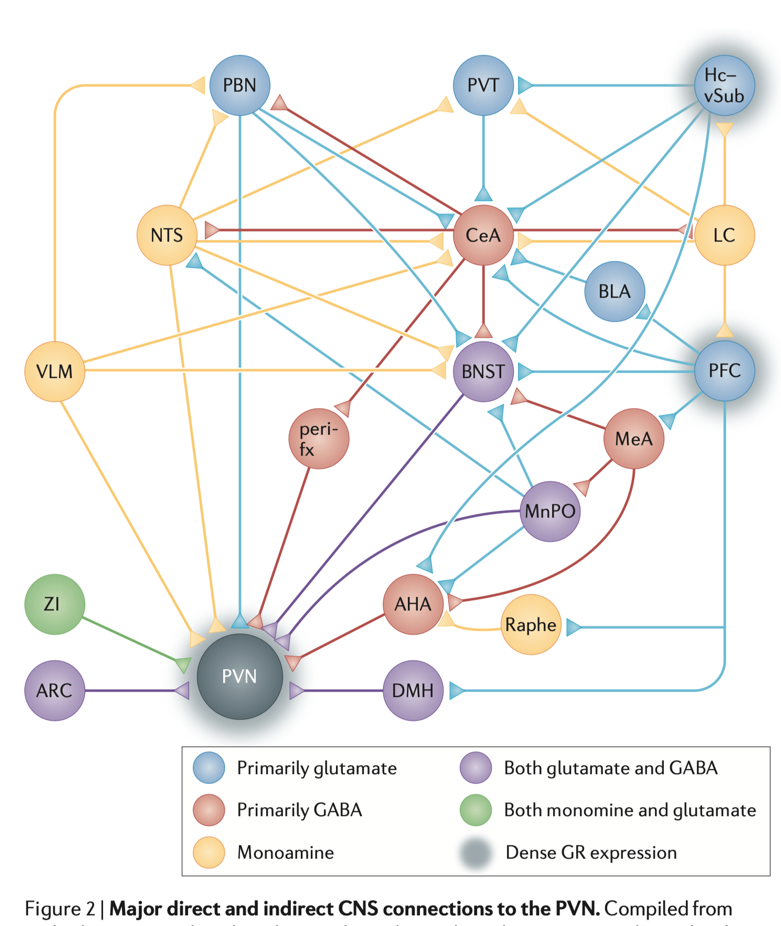
**keywords: stress, neurons**

-“Glucocorticoids act on CRH neurons to inhibit excitatory synaptic transmission via the retrograde release of the endocannabinoid 2-arachidonoylglycerol (2-AG), which suppresses presynaptic glutamate release (36) and inhibits HPA activation”

-“Glucocorticoids also rapidly alter the postsynaptic intrinsic excitability of PVN neurons via modulation of membrane potassium channels. ”

**Stress-related synaptic plasticity in the hypothalamus**

**(Bains et al., 2015)**

-

-Moreover, microinjection of glutamate into the PVN stimulates HPA-axis output, whereas administration of an ionotropic glutamate receptor antagonist before exposure to stress blunts the neuroendocrine stress response

-Endocannabinoids (eCBs) have been implicated repeatedly in the negative regulation of HPA-axis responses

-A single acute stress alters signalling at glutamatergic synapses on PNCs. This manifests as an increase in the ratio of AMPAR- to NMDAR-mediated transmission35

-Surprisingly, this is not due to an increase in signalling via AMPARs, but rather to a long-lasting decrease in NMDAR signalling35 that results from the downregulation of postsynaptic NMDARs by local release of CRH during stress.

-STP is not due to an increase in postsynaptic glutamate signalling or an increase in release probability; instead, it is due to a switch in the mode of release at glutamatergic synapses from univesicular (that is, a presynaptic action potential releases, at most, a single vesicle of glutamate) to multivesicular (that is, a presynaptic action potential can release more than one vesicle).

-These observations suggest that CRH-mediated decreases in NMDAR-dependent Ca2+ entry during stress prevent the release of a retrograde messenger that normally blocks the multivesicular release of glutamate following high levels of presynaptic activity

-There are various dendritically released factors that could be responsible for suppressing glutamate release84, but experiments have ruled out eCBs acting at CB1, opioids or adenosine35

**Synaptic regulation of the hypothalamic–pituitary–adrenal axis and its modulation by glucocorticoids and stress**

**(Levy and Tasker, 2012)**

**keywords: stress, HPA**

-Glutamatergic synaptic inputs to CRH cells are suppressed by rapid glucocorticoid actions that appear to be involved in the glucocorticoid-mediated fast negative feedback of the HPA axis

-Importantly, this glucocorticoid effect was blocked by antagonists and mimicked and occluded by agonists of the cannabinoid type 1 receptor (CB1R), suggesting the involvement of the endocannabinoid system.

-We recently corroborated this with the finding that the rapid glucocorticoid effect is absent in CB1R knockout mice

-Consistent with the endocannabinoid acting as a retrograde messenger to inhibit glutamate release at glutamate synapses, the glucocorticoid effect was prevented by blockade of G protein and protein kinase activity and Ca2+ signaling specifically in the postsynaptic cell

-glucocorticoids trigger a form of endocannabinoid-mediated long-term depression of synaptic excitation

-preliminary evidence for the desensitization to the rapid glucocorticoid-induced suppression of glutamate release in brain slices from animals that had been subjected to an acute 30-min restraint stress prior to sacrifice

-This effect is likely due to the long-term depression of glutamatergic synaptic inputs by a tonic activation of presynaptic CB1 receptors via glucocorticoid-induced retrograde endocannabinoid release, since a CB1 receptor-mediated inhibitory tone was observed in glutamate inputs to parvocellular neurons from acutely stressed rats, but not from unstressed rats.

Repeated restraint stress enhances glutamatergic transmission in the paraventricular nucleus of the rat hypothalamus (<https://www.researchgate.net/publication/259200098_Repeated_restraint_stress_enhances_glutamatergic_transmission_in_the_paraventricular_nucleus_of_the_rat_hypothalamus>)

**Acute stress facilitates glutamatergic long-term potentiation in PVN magnocellular neurons through beta-adrenergic receptor/PKA cascade in vitro in rats**

**(Jin et al., 2024)**

**keywords: stress, neurons**

-age and sex of wistar rats not specific

-HFS-induced NMDAR-independent LTP of PVN MNCs in acute stress rats was mediated by β-AR

-HFS-induced NMDAR-independent LTP of PVN MNCs in acute stress rats through postsynaptic PKA signaling pathway

**Sex differences in the murine HPA axis after acute and repeated restraint stress**

**(Nalepa et al., 2025)**

**keywords: stress, HPA**

-Plasma CORT was increased after ARS in both males and females (p < 0.0001) compared to NS mice. Additionally, CORT levels were higher in female mice after ARS compared to male mice (p = 0.0004), while no sex differences were found in the NS condition (p = 0.9856)

-After acute stress, female mice consistently produced a larger peak CORT response compared to male mice. An enhanced acute CORT response in female rodents is in accordance with previous reports (Aoki et al., Citation2010; Iwasaki-Sekino et al., Citation2009; Weinstock et al., Citation1998) and the general perception that females are more stress-reactive than males

-no significant sex differences in plasma ACTH levels were observed, which could point to increased adrenal ACTH sensitivity in female compared to male mice.

-Despite the enhanced peak CORT response in female mice after ARS, we found no sex difference in the stress recovery period up to 1.5h post-stress, where female mice returned to baseline CORT levels similarly to male mice. This suggested a steeper increase in CORT after acute stress and a steeper decrease in CORT levels after stress.

**The intricate link between glucocorticoids and endocannabinoids at stress-relevant synapses in the hypothalamus**

(Crosby and Bains, 2012)

**keywords: stress, endocannabinoids, hypothalamus**

-DMH activation needed for autonomic response to stress (increases in HR, BP, RR when stimulated)

-eCBs bind to CB1Rs in the brain

-eCBs are not stored in vesicles like classical NTs, synthesized as needed in response to a rise in postsynaptic Ca2+ or activation of mGluRs and other GPCRs.

-released from post synaptic cell and travel across the synaptic cleft and activate CB1Rs on the presynaptic cell which supresses adenylate cyclase activity, voltage sensitive ca2+ channels, and some k+ channels which supress neurotransmitter release

-blocking CB1Rs results in activation of the HPA seen as an increase in plasma cort.

-CORT increases eCB levels and depresses glutamate synapses in PVN slices

-“ CORT, through activation of a putative membrane-bound glucocorticoid receptor, triggers the local synthesis of eCBs in PVN neurons (Di et al., 2003). This process is dependent on the Gαs G protein subunit and the cAMP-PKA signaling pathway (Malcher-Lopes et al., 2006). Following synthesis, eCBs then act in a retrograde fashion to curtail glutamate release onto CRH neurons through activation of presynaptic CB1Rs (Di et al., 2003).”

Chronic:

-chronic stress or prolonged treatment with CORT reduces CB1R expression in hippocampus

-A screenshot of a computer

AI-generated content may be incorrect.

**Regulating the Fast-Food Landscape: Canadian News Media Representation of the Healthy Menu Choices Act**

(Moghimi and Wiktorowicz, 2019)

**keywords: food**

-Availability of fast food is high, with more that 54% of Canadians eating out at least once a week

-more than half of adult Canadians overweight or obsese

**Processed and Ultra-processed Food Products: Consumption Trends in Canada from 1938 to 2011**

(Moubarac et al., 2014)

**keywords: food**

-obesity epidemic paralleled by global food system dominated by an increasing amount of processed and ultra-processed food

- ultra-processed food are more energy dense with more free sugars, sodium, saturated fats with less fibre

-typically, in large portion sizes

-rising in how much of grocery budget they take up, of how much of the energy in a diet they provide

-“ In the late 1930s, Canadian diets mostly consisted of unprocessed and minimally processed foods made into freshly pre- pared and cooked meals and dishes. This dietary pattern was not ideal. Canadian nutrition policies at that time addressed deficiencies in minerals and vitamins (such as vitamins C and D)”

-“ After 1938/1939, household food avail- ability in Canada changed significantly. The percentage of the total food expenditure for unprocessed or minimally pro- cessed foods fell rapidly and then levelled out in the 21st century. Fresh potatoes almost disappeared. In the United States, and probably in Canada, this decline has been offset by a clear and steady growth in consumption of ultra-processed products, such as frozen French fries, chips, and other packaged snacks”

-“ On the other hand, increased consumption of ultra-processed food products is the most striking change, along with the near disappearance of culinary ingredients from Canadians' grocery shopping lists.” (not the processed foods, but the ultra-processed)

-each generation spends less time in the kitchen

**Hunger Games: A Modern Battle Between Stress and Appetite**

(Smith and Azevedo, 2025)

**keywords: food, stress**

-“ Stress, an evolutionarily adaptive mechanism, has become a pervasive challenge in modern life, significantly impacting feeding-relevant circuits that play a role in the development and pathogenesis of eating disorders (EDs).”

-“ Stress activates the hypothalamic–pituitary–adrenal (HPA) axis, disrupts specific neural circuits, and dysregulates key brain regions, including the hypothalamus, hippocampus, and lateral septum.”

-“ Although chronic stress can have negative health impacts today, its evolutionary roots highlight its importance in animal resilience and adaptation.”

-“ From occasional stress-eating to more severe eating disorders (EDs), the relationship between stress and food is complex and multifaceted.”

-“ Allostasis refers to the body's ability to achieve stability through change in response to stressors (Goldstein and McEwen 2002; McEwen 2017b). Unlike homeostasis, which maintains fixed internal conditions, allostasis involves adaptive shifts in physiological and psychological states to cope with new demands.”

-allosteric load: “Over time, this stress-induced eating behavior places a constant demand on the body's regulatory systems, contributing to metabolic dysregulation, obesity, and health issues like insulin resistance and cardiovascular disease”

-“ In response to ongoing stress, the brain can strengthen synapses, form new pathways, and enhance neural networks that help the body cope with future stressors (McEwen 2019). Whether these changes are beneficial or harmful depends on the nature, intensity, duration of the stress experienced, and the system's resilience to “wear-and-tear” highlighting the brain's capacity to both adapt and, in some cases, deteriorate in response to environmental demands”

-hypothalamus: “s the body's primary control center for hunger, satiety, and energy expenditure, the hypothalamus integrates multiple signals, including hormonal, metabolic, and neural inputs, to maintain homeostasis (Tran et al. 2022). However, when an individual experiences stress, these processes can be dysregulated, leading to alterations in the way that hypothalamic neurons respond to interoceptive signals, thus altering feeding behavior.”

-“the hypothalamus is sexually dimorphic, meaning it exhibits structural and functional differences between males and females (Heck and Handa, 2019). These differences are crucial for regulating sex-specific behaviors and physiological processes, as well as for contributing differentially to stress responses. For instance, in female mice, acute HPA function following a stressor is markedly greater than it is in males, and this difference has largely been attributed to modulation by the gonadal hormones testosterone and estradiol (Heck and Handa, 2019).”

-“ This stress response is adaptive in the short term, mobilizing energy stores and preparing the body for “fight or flight.” However, chronic stress can disrupt this system, leading to abnormal feeding behavior.”

**Chronic stress exposure may affect the brain's response to high calorie food cues and predispose to obesogenic eating habits**

**(Tryon et al., 2013)**

**keywords: stress, food**

- “Chronic stress, which can induce palatable “comfort” food consumption, may trigger or reinforce neural pathways leading to stronger reactions to highly rewarding foods.”

- “These results suggest that persistent stress exposure may alter the brain's response to food in ways that predispose individuals to poor eating habits which, if sustained, may increase risk for obesity.”

- “Women who had reported more chronic stress also reported being emotional eaters”

-higher chronic stress increase palatable snack food consumption

- hypothalamic-driven hunger and satiety

- “it was suggested that repeated stress-associated indulgence of comfort food, over the course of time, leads to adaptations in the brain that promote palatable food intake and hypocortisolemia”

- “Chronic stress has been linked to palatable food consumption and unhealthy eating habits. The neurophysiological basis for stress-eating is less clear.”

**Chronic stress and obesity: A new view of “comfort food”**

**(Dallman et al., 2003)**

**keywords: stress, food**

- “Acutely (within hours), glucocorticoids (GCs) directly inhibit further activity in the hypothalamo–pituitary–adrenal axis, but the chronic actions (across days) of these steroids on brain are directly excitatory.”

- “GCs increase the salience of pleasurable or compulsive activities (ingesting sucrose, fat, and drugs, or wheel-running). This motivates ingestion of “comfort food.” (iii) GCs act systemically to increase abdominal fat depots.”

- “The long-term consequences of such output modification in chronically stressed individuals may include deleterious weight gain, abdominal obesity, type II diabetes, increased cardiovascular morbidity, and mortality… also stroke [later on]”

- “Canonical GC-feedback inhibition of subsequent adrenocorticotropin (ACTH) secretion is easily demonstrated acutely, within the first 18 h after stress. Acute feedback inhibition occurs in brain and pituitary (Fig. 1 Left), probably through nongenomic mechanisms”

- “However, under a persistent stressor, or long after administration of a single stressor of high intensity (2), there is marked diminution of the efficacy of glucocorticoid feedback inhibition of stimulated, but not basal, ACTH secretion”

- “Another key effect of GCs on the central nervous system appears to be to increase the compulsive nature of some activities.”

- “Those with disordered eating, whether it be bingeing or ingesting most of the daily calories during the night, generally characterize themselves as chronically stressed (52, 53) and are obese. The foods that are overindulged-in typically have high fat and carbohydrate caloric content and may be characterized as comfort food. GC concentrations in these patients are slightly but not markedly elevated”

- “In contrast, patients with anorexia nervosa have very high cortisol concentrations and very low insulin concentrations”

**Learning-related synaptic plasticity: LTP and LTD**

(Siegelbaum and Kandel, 1991)

**keywords: plasticity**

-in hippocampus in 1973 after a brief high frequency train of Aps, there was an increase in excitatory synaptic potentials which could last for hours or even weeks (facilitation LTP)

-LTP only occurs if postsynaptic cell is depolarized

-glutamate exerts action in 3 ways: ligand-gated NMDA receptor channels, AMPA ligand gated channels, ACPD (mGluRs) receptors.

-ion channels with NMDA receptors allow Ca2+ influx (and prob. Protein phosphorylation)

-NMDA-receptor channel is blocked at restring membrane potential by extracellular Mg2+ ions (voltage dependent) when membrane is depolarized Mg2+ is expelled and Ca2+ influx happens

-LTD involves prolonged inhibition of synaptic transmission

-LTD is enhanced by picrotoxin, so it doesn’t require GABA-mediated inhibitory inputs

-like LTP, LTD is thought to be initiated by a rise in internal Ca2+, but not through NMDA type channels

**Glutamate as a Neurotransmitter in the Brain: Review of Physiology and Pathology**

(Meldrum, 2000)

**keywords: glutamate**

-principle excitatory neurotransmitter in brain

-3 families of ionotropic receptors (permeable to cations): NMDA, AMPA, kainite

-3 groups of metabotropic (mGluR) that use g-proteins and second messengers like diacylglycerol and cAMP

-most abundant AA in diet

-glutamate release produces EPSP primarily related to AMPA receptor activation

-AMPA receptors have lower glutamate affinity than NMDA receptors but have faster kinetics

-“ A distinctive feature of the NMDA receptor is its voltage-sensitive block by Mg++. This is operative under normal circumstances but is overcome by partial depolarization of the resting membrane potential.”

-“ The synaptic release of glutamate is controlled by a wide range of presynaptic receptors. These include not only the Group II and Group III glutamate metabotropic receptors (see Fig. 1 and below) but also cholinergic (nicotinic and muscarinic) receptors, adenosine (A1), kappa opioid, γ-aminobutyric acid (GABA)B, cholecystokinin and neuropeptide Y (Y2) receptors (see Meldrum 1998).”

-changing the receptors subunits can alter their properties

**Molecular mechanisms of neurotransmitter release**

(Fon and Edwards, 2001)

**keywords: neurotransmitter**

-NT released from presynaptic neuron diffuses across cleft and transudes signal by binding to receptors on the post synaptic neuron, so the receptors determine the nature of the signal

-chemical neurotransmission allows for high flexible and regulation (in comparison to electrical transmission) and can vary in intensity, speed.

-release occurs in quanta

-classical NT (ACh, GABA, glutamate) made in cytoplasm so need to be packaged into synaptic vesicles using an ATPase that pumps H+ into vesicles

- classical NT (ACh, GABA, glutamate) recycle locally in the nerve terminal where they accumulate in SV

-glutamate degraded by glutamine synthetase

- plasma membrane transport proteins mediate reuptake of classical neurotransmitters

-phosphorylation of glutaminase (enzyme) converts glutamine to glutamate

-synaptically released glutamate is taken up by glia, converted to glutamine, and then delivered back to the neuron for conversion to glutamate

**Glutamate, a neurotransmitter—And so much more**

(Hertz, 2006)

**keywords: glutamate**

-Uptake of glutamate into astrocytes by GLAST and GLT1 and into neurons by EAAC1

- VGLUT1 and VGLUT2 are for glutamate uptake into vesicles for release, expressed in glutamatergic neurons

- VGLUT3 is expressed in many neurons that are not primarily glutamatergic

-glutamate is either converted to glutamine by the astrocyte-specific glutamine synthetase or oxidatively degraded after conversion to α-ketoglutarate by oxidative deamination or transamination

**The dorsomedial hypothalamic nucleus and its role in ingestive behavior and body weight regulation**

(Bellinger and Bernardis, 2002)

**keywords: DMH**

-stimulation in sheep produced hyperphagia

-DMH lesions (rats) = hypophagia, hypdispia, but normal % fat and lean body mass

-DMHL rats have normal plasma GH

- “The ad libitum-fed DMNL rats showed the typical lesion-induced hypophagia and lost BW compared to the ad libitum-fed sham-operated group.”

-“After about 20 days, the BWs of the ad libitum-fed lesioned rats stabilized on a lower growth curve.”

-“In sharp contrast to this, the restricted rats after DMNL lesioning showed an immediate hyperphagia and their food intake remained higher than that of the ad libitum-fed group for 10 days.”

-“ After DMNL, the restricted group immediately began to gain BW and approached the attenuated BW of the ad libitum-fed DMNL rats and began to parallel their weight gain.”

-“At the end of the 28-day study, body composition of the DMNL groups was comparable to the control animals. These data demonstrated that the DMNL rats not only actively regulated their BW, but also did so with normal body composition.”

- “DMNL rats given **high fat** or ‘junk food’ diets **did become obese** compared to chow fed DMNL rats”

- “However, DMNL rats given a **high-fat diet** do not become **as obese as control animals**, when fed **other palatable diets**, they can become **as obese or even more obese** than similarly fed sham-operated rats”

-”The data taken as a whole suggest that DMNL may attenuate high-fat induced obesity but do not completely eliminate it”

- “The DMNL groups showed their typical hypophagia, reduced BW gain, reduced linear growth, but normal body composition.”

-OVX does not change growth in DMHL rats vs sham (sex difference not caused by ovary homrones)

-“ These data [45] suggested that even though the DMNL lowered the rat's ‘BW settling point’, they appeared to be fully capable of responding to other regulatory challenges, i.e., the loss of estrogens that increased BW (fat and lean body mass) and linear growth”

**Central stress-integrative circuits: forebrain glutamatergic and GABAergic projections to the dorsomedial hypothalamus, medial preoptic area, and bed nucleus of the stria terminalis**

(Myers at al., 2014)

**keywords: DMH**

-“Glutamatergic and GABAergic neurons play important roles in stress regulation, directly exciting and inhibiting, respectively, paraventricular hypothalamic (PVN) corticotropin releasing hormone (CRH) neurons”

-DMH projects GABAergically to the PVN

-DMH projects glutamatergically to the PVN

-^ show pronounced activation by stress

-“Descending input from the limbic forebrain is thought to influence the role of the DMH, POA, and BST in stress integration”

-ventrolateral region of DMH sends stress-activated projections to the parvocellular PVN

-DMH got lots of vGluT2-psoitive input from extreme dorsal region of the PVT (paraventricular thalamus)

-input from periaqueductal gray involved dorsolateral DMH

-GABA neurons scattered

-“innervation of the predominantly GABAergic DMH, mPOA, and BST by GABAergic neurons of the MeA and CeA supports the hypothesis that these amygdalar regions promote HPA axis activation by disinhibition, using sequential GABAergic synapses.”

-“In contrast, there is evidence for excitatory innervation of the DMH, mPOA, and BST by hippocampal and prefrontal cortical neurons, consistent with the glutamatergic signature of outputs from these stress-inhibitory sites.”

-“all three PVN-projecting regions receive mixed GABA and glutamate input from hypothalamic nuclei which may be relevant to intra-hypothalamic mechanisms governing the integration of stress responses.”

-“As an upstream regulator of the PVN, the DMH is highly sensitive to psychogenic stressors”

-“With regard to HPA axis integration, the ventrolateral subdivision of the DMH sends stress-activated GABAergic projections to the PVN”

-“The vast majority of these PVN-projecting neurons contain GAD65, indicating that this is likely a stress-inhibitory region of the DMH. In contrast, the dorsomedial portion of the DMH predominantly expresses vGluT2 and provides glutamatergic innervation of the PVN”

-“Our group has demonstrated that local injection of a panionotropic glutamate receptor antagonist into the DMH enhances corticosteroid responses to restraint stress”

-“Microstimulation of the dorsal component of the DMH results in an increase in ACTH release while inhibition has the opposite effect”

-ventrolateral DMH = GABA projections to PVN

-dorsomedial DMH = glutamatergic projections to the PVN

-A diagram of a diagram

AI-generated content may be incorrect.

**The dorsomedial hypothalamus and the response to stress: Part renaissance, part revolution**

(DiMicco et al., 2002)

**keywords: DMH, stress**

-“ The physiological response to emotional stress consists of an integrated pattern of endocrine and autonomic changes that is highly conserved across mammalian species.”

-picrotoxin (block GABAa) increases HR, sympathetic activity, and plasma catecholamines

-same thing^ if you add microinjections of excitatory amino acids

-disinhibition of DMH neurons = classic defence reaction (sympathetic)

**Ingestive behavior in adult rats with dorsomedial hypothalamic lesions**

(Dalton et al., 1981)

**keywords: DMH, food**

-adult male rats

-bilateral electrolytic lesions

- hypophagia, hypodipsia, loss of body weight immediately all during the first week

-food intake recovered within 2 weeks but was 10-12% lower than the control animals for the next 3 months

-body weight increased at same rate as the controls but never overcame the initial drop after surgery

-no difference in food intake per 100g of body weight in the first 2 weeks

-DMH lesions transiently disturbed food intake regulation but can permanently lower the animals body weight

-lesions are more severe and lasting when made to young weaning rats

**The Action Potential (saved as PDF, no DOI)**

(Barnett and Larkman, 2007)

**keywords: neurons**

-resting membrane potential is maintained by an electrochemical gradient, ion concentrations are maintained by ATP-dependent pumps , specifically the Na+-K+-ATP pump

A stimulus or neurotransmitters causes a local depolarization

-AP is a transient reversal in the polarity of the transmembrane potential which moves from point of initiation down the axons to the terminals

-Na+ and K+ cross the membrane though channels that open in response to a change in membrane potential

-three main phases: rapid depolarization (mediated by permeability to Na+), repolarization, hyperpolarization

-membrane potential reaches “threshold” depolarization rapid recruitment of all the voltage-sensitive Na+ channels causing that rapid depolarization

**Neurobiological and Systemic Effects of Chronic Stress**

(McEwen, 2017)

**keywords: stress**

<https://pmc.ncbi.nlm.nih.gov/articles/PMC5573220/>

-acute restraint stress elevates extracellular glutamate (dependent on adrenal glands)

-corticosterone acts directly via MR and GR to cause glutamate release

-blocking NMDA receptors interferes with ^

**Increased intrinsic and synaptic excitability of hypothalamic POMC neurons underlies chronic stress-induced behavioral deficits**

(Fang et al., 2023)

**keywords: neurons**

-chronic unpredictable stress increased intrinsic excitability of neurons in the hypothalamus\

**Hypothalamic control of food intake in rats and cats**

(Anand and Brobeck, 1951)

**keywords: DMH, food**

-variation in food intake due to injury in parts of the hypothalamus

-hyperphagia due to lesions in the medial hypothalamus leading to obesity

-FEMALE SD rats: electrolytic lesions

-bilateral disruption of the ventromedial nucleus stops eating

-overall: lesioning studies showed that damage to specific regions of the hypothalamus could produce a wide range of eating behaviours, leading to distinction and study of the hypothalamus’s distinct nuclei instead of as a whole.

Evidence for thyrotropin-releasing hormone and glucocorticoid receptor-immunoreactive neurons in various preoptic and hypothalamic nuclei of the male rat

(Cintra et al., 1990)

**keywords: neurons, stress, DMH**

-dorsomedial hypothalamus has lots of TRH-IR neurons, all of them show strong GR-IR (glucocorticoid receptor-IR (fluoresce)).

**Two Families of Postsynaptic Receptors (BOOK)**

(Purves et al., 2001)

**keywords: neurons**

-ionotropic: ligand-gated ion channel

-metabotropic: activation of G-proteins -> signal transduction

-ionotropic are faster: EPP at neuromuscular synapses by Ach, EPSP at some glutamatergic synapse, and IPSPs at some GABAergic synapses (occur a millisecond or 2 after an AP reaches the presynaptic terminal and last only tens of milliseconds)

-given neurotransmitter may activate both to produce both fast and slow post synaptic potentials at the same synapse

-response elicited by a NT is dependent on the postsynaptic receptors and their channels and the complement with the NT