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Hypothalamus Dysfunction & Metabolic Disorders

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FULL CIRCLE FAMILY HEALTH

Objectives

In this presentation you will learn:

- Signs and symptoms of hypothalamus dysfunction and its pathophysiology in relation to metabolic disorders.
- Appropriate diagnostic testing to evaluate hypothalamus function.
- How communication between the gastrointestinal tract, adipose tissue and the hypothalamus controls metabolism.
- Therapies which can help mitigate hypothalamus microinflammation.
- The most effective lifestyle changes your patients need to make to improve their hypothalamus function to help mitigate their metabolic disorders.
- Integrative therapies to reverse hypothalamus microinflammation and optimize hypothalamus function.

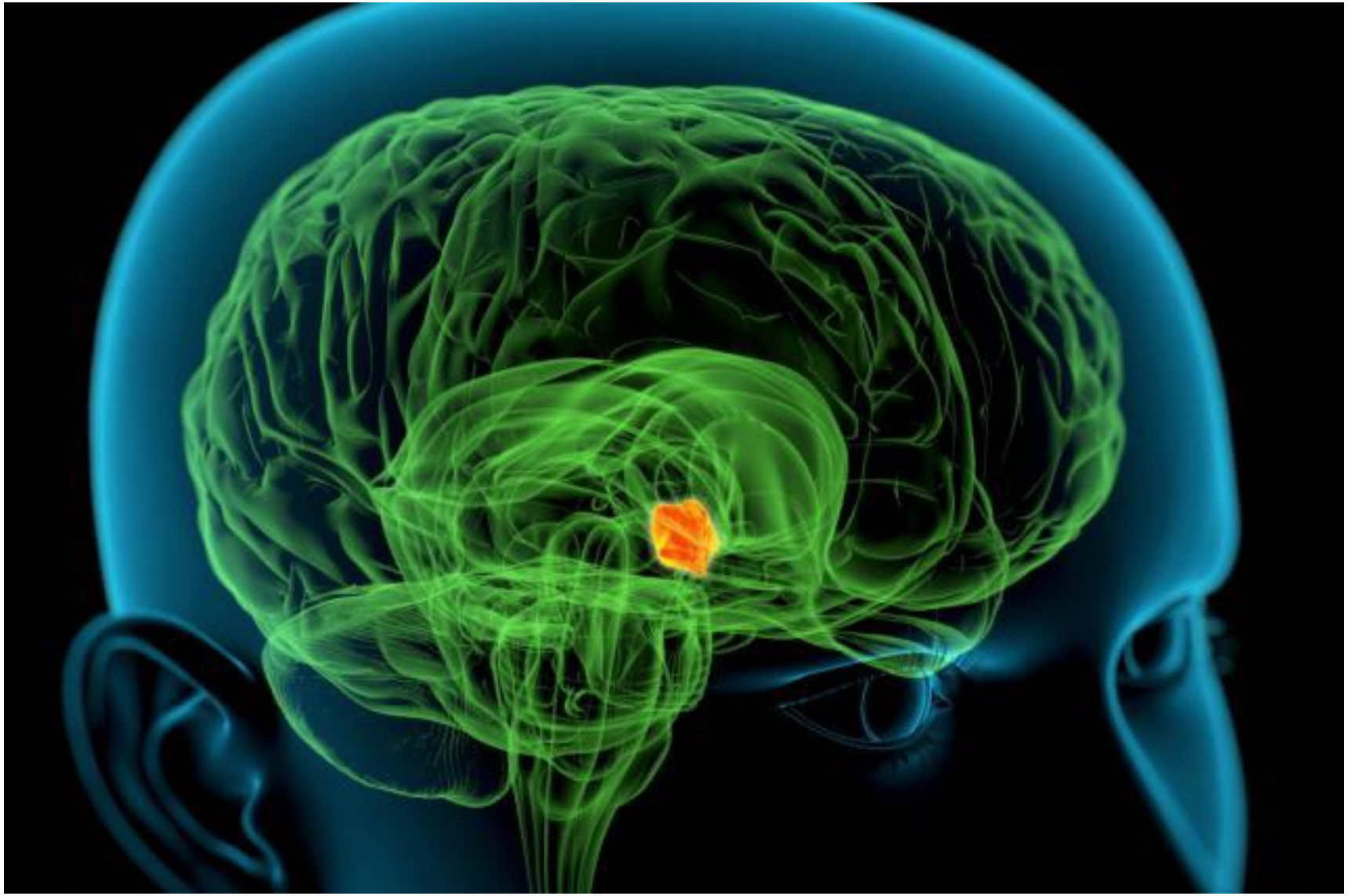
ForeFather of Neuroendocrinology

In 1969 discovered thyrotropin-releasing factor, a small peptide produced in the hypothalamus, which led to far-reaching effects on studies of metabolism, reproduction and growth.

Roger Guillemin (1924–2024)
Neuroscientist/Nobel prizewinner
Credit: Hulton Archive/Getty

“Recent research has demonstrated the mechanistic involvement of Hypothalamic Inflammation across multiple components of metabolic syndrome and diseases”

Focus on Root of Metabolic Disorders → **HYPOTHALAMUS**



What is Hypothalamus Dysfunction?

Hypothalamus no longer effectively controls and communicates with the endocrine system, neurological system, immune system, gastrointestinal tract and adipose tissue leading to wide spread metabolic dysfunction

- Obesity
- PCOS
- Cardiovascular disease
- Diabetes
- Neurological disorders
- Immune disorders
- Hormonal imbalance
- Circadian rhythm disorders
- Mood and cognitive disorders
- Aging

Hypothalamic Neuron Dysfunction

- **AgRP** - HI affects regulatory signaling of glucose and energy metabolism (agouti-related protein = orexigenic)
- **POMC** - HI impairs function leading to glucose, adrenal, thyroid and diurnal dysregulation
- **BDNF** - HI decreases expression (brain-derived neurotrophic factor)
- **GABAnergic** - HI alters feeding regulation
- **Glutamatergic** - HI enhances sympathetic excitation and raises BP
- **GnRH** - HI affects reproduction and neurogenesis
- **PVN** - HI dysregulates SNS
- **Astrocytes** - HI induces loss of immune cells and increase In pro-inflammatory cytokine production
- **Microglia** - HI increases fatty acid accumulation, impairs immune function and increases cytokine production
- **htNSCs** - HI impairs neurogenesis (hypothalamic neural stem cells)

SX Hypothalamus Dysfunction

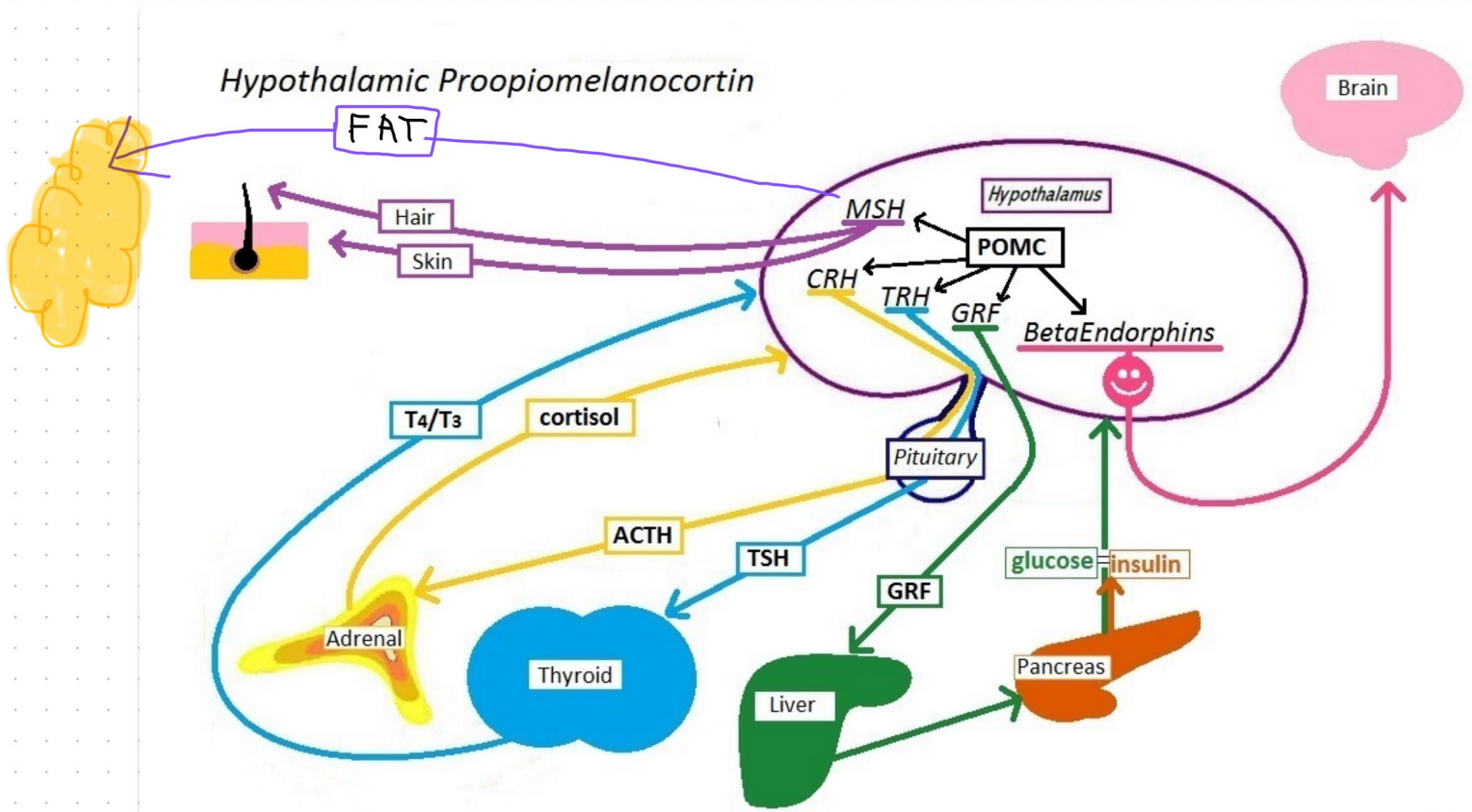
- Fatigue
- Temperature dysregulation
- Anorexia/ Hyperphagia
- Obesity/ Cachexia
- Insomnia
- Hypertension/Orthostatic Hypotension
- Sympathetic Sx - palpitations, sweating, insomnia
- Parasympathetic Sx - arrhythmias, somnolence
- Maladaptive Stress Response
- Mood disorders - anxiety, depression
- Insulin Resistance/Hypoglycemia/Hyperglycemia
- GI Sx - maldigestion, malabsorption, IBS, constipation, diarrhea
- Libido issues/Infertility
- Amenorrhea /Irregular periods
- Osteoporosis /Osteoarthritis
- Delayed puberty/Premature aging
- Lack of motivation/Inability to bond with others
- Edema/ Dehydration
- Polydipsia /Polyuria
- Skin rashes, acne, eczema
- Pain – neuropathy, trigger point tenderness

Hypothalamus regulates metabolism and appetite

- First-order neurons of arcuate nucleus (ARC) - antagonistic express insulin and leptin receptors
  - Orexigenic = Neuropeptide Y & agouti-related peptide
  - Anorexigenic = POMC
  - Paradoxical orexigenic effect of cannabis on POMC by inducing **β-Endorphins**
- ARC project to second-order neurons in paraventricular (PVH), ventromedial (VMH), dorsomedial (DMH), lateral (LH) Hypothalamus
- Second-order hypothalamic neurons project to brainstem and midbrain

- Bidirectional gut-brain axis & fat-brain axis
- Molecular messengers provide homeostatic feedback of energy availability to Hypothalamus via bloodstream and via brainstem through afferent vagal pathways to Hypothalamus
- Hypothalamus communicates with gut via PNS
- Hypothalamus communicates with fat via SNS

POMC > Core Hypothalamic Hormone

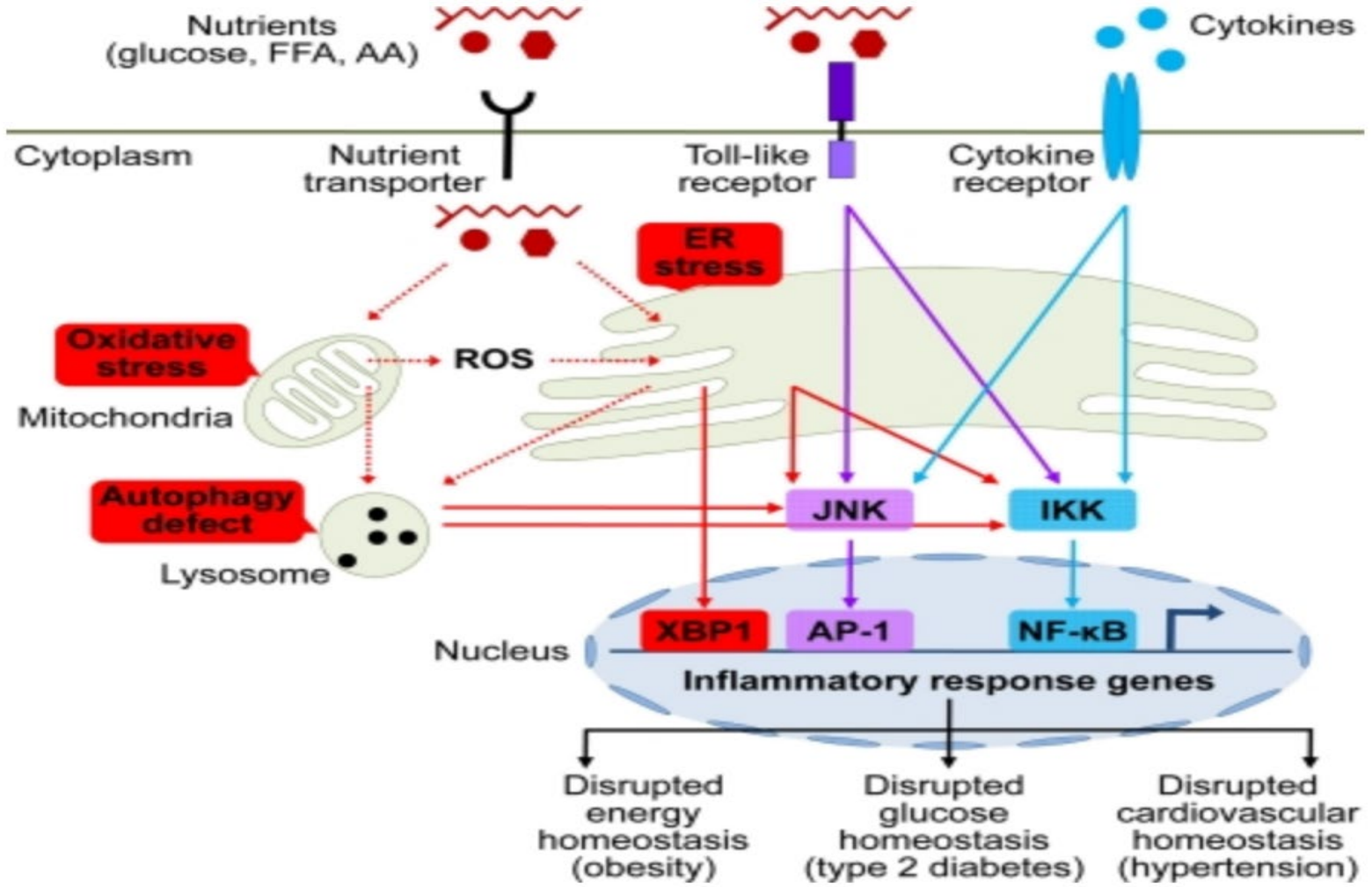


Causes of Hypothalamus Inflammation

- Dietary triggers
  - High fat
    - Impairs insulin signaling and expression of inflammatory cytokines in the hypothalamus
    - Saturated fatty acids increase the secretion of pro-inflammatory mediators.
  - High Carb
    - High carb diets activate microglia and hypothalamic inflammation
    - High monosaccharides increase astrogliosis and pro-inflammatory cytokines
- Imbalanced gut microbiome
- Age-related changes
- Neuronal overactivity (stress induced activation of HPA)

Pathophysiology of Hypothalamus Inflammation

- Acute central over-supply of glucose or lipids - induce hypothalamic inflammation within a few hours to three days.
- Hypothalamic inflammation affects hypothalamic hormonal signaling to cause central dysregulation of energy balance leading to obesity development.
- Hypothalamic inflammation disrupts peripheral insulin and glucose homeostasis in the development of systemic insulin resistance and T2D and cardiovascular dysfunction, such as hypertension.



Research Perspective Volume 4, Issue 2 pp 98—115

Characteristics of Metabolic Inflammation

- Chronic duration
- Low grade intensity
- Inflammatory stimuli
  - Primary: over nutrition
  - Secondary: low-grade cytokines in the circulation and CNS
- Source of inflammation
  - Primary: local subcellular changes in the Hypothalamus
  - Secondary: chronic but low-grade production of circulating cytokines associated with metabolic diseases
- Positive effect on energy balance
  - increased food intake
  - increased fat mass
- Effects on glucose homeostasis
  - Hyperglycemic from glucose intolerance and insulin resistance

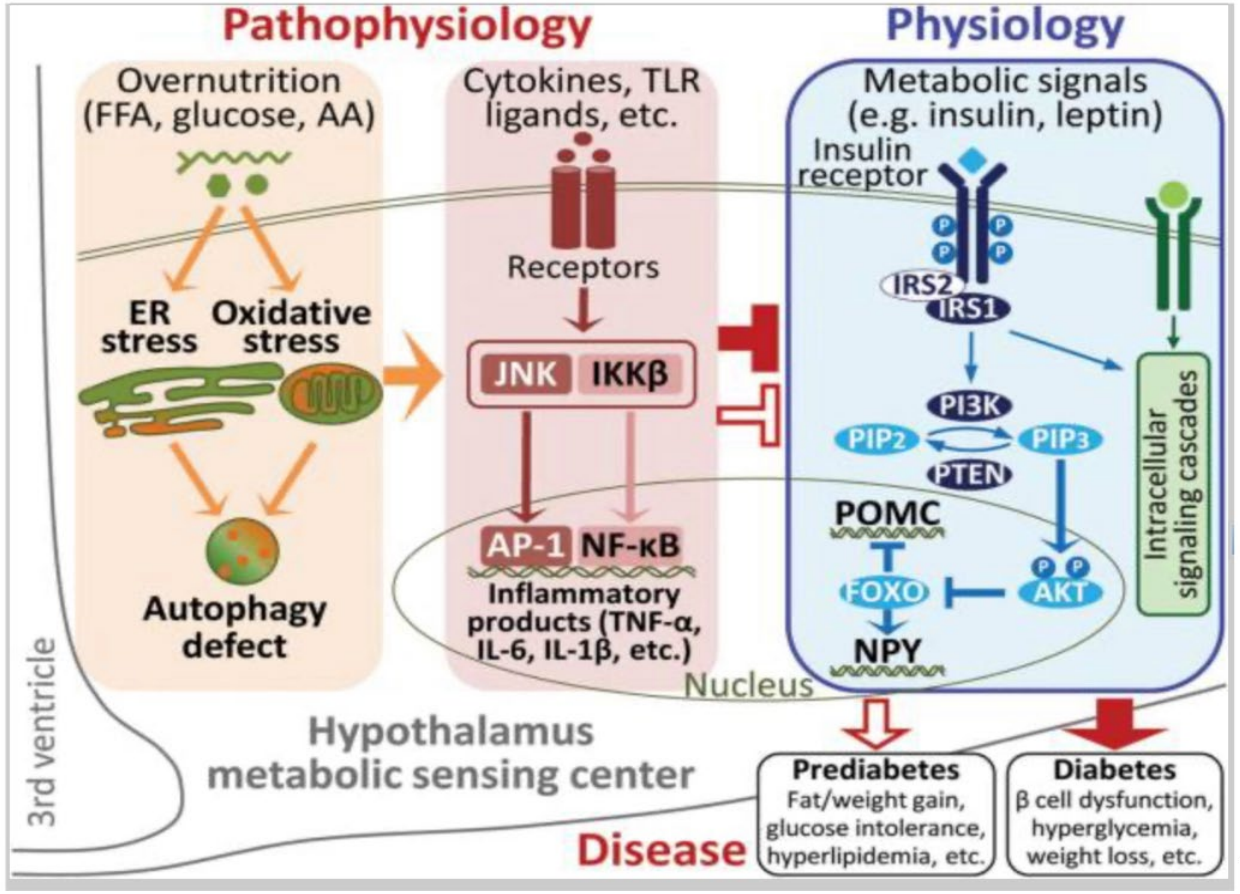
Metabolic Syndrome (MetS)

- Prevalence - 42% of adults in US, 30% worldwide
- Metabolic syndrome related diseases:
  - Obesity
  - PCOS
  - Type 2 diabetes
  - Obesity-related hypertension
  - Coronary artery disease
  - Atherosclerosis
  - Hepatic steatosis
  - Aging-related neurodegenerative disease

- **Diagnostic characteristics** =
  - high blood pressure ≥130/85 mmHg
  - high fasting blood-glucose level, ≥100 mg/dL
  - high serum triglycerides ≥150 mg/dL
  - low HDL-C level
    - <40 mg/dL in men
    - <50 mg/dL in women

Hypothalamus Inflammation, IR & T2D

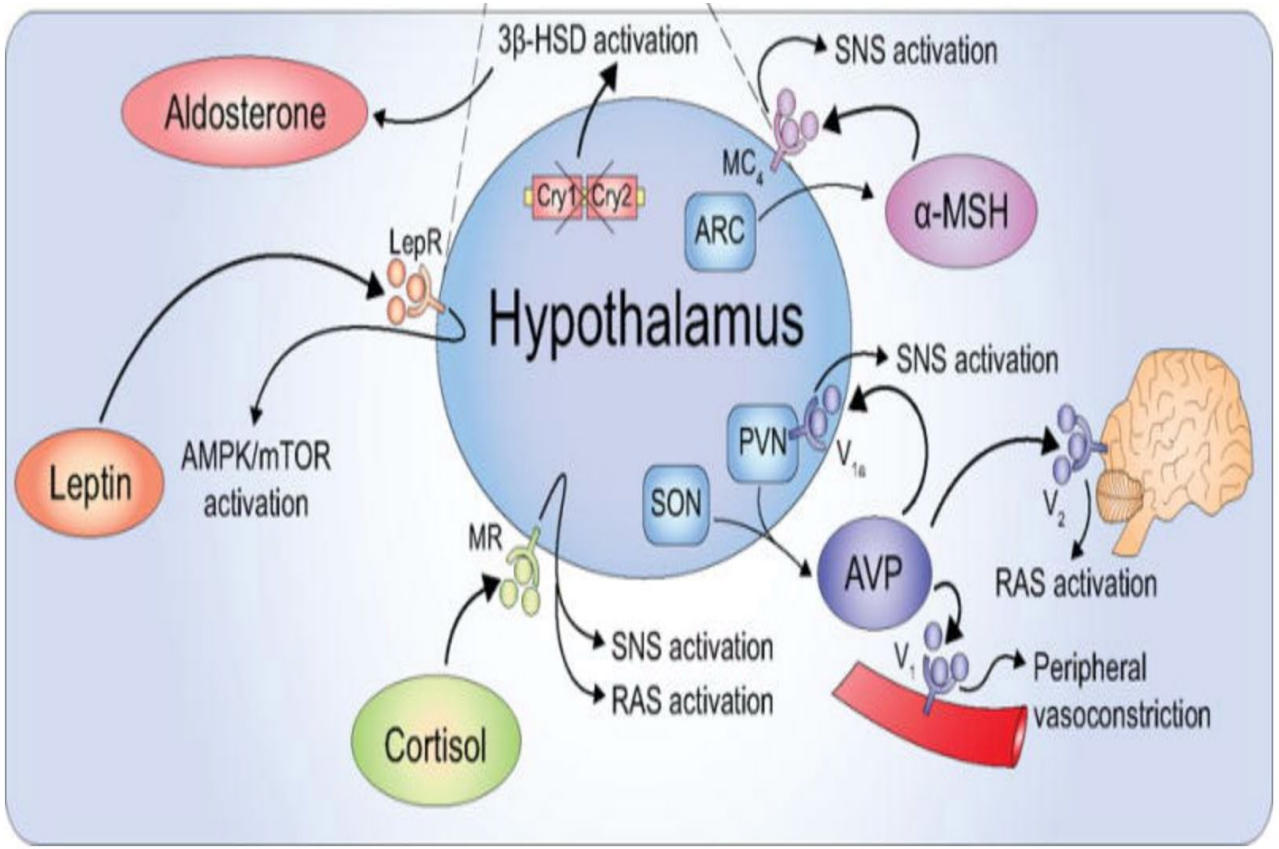
- Studies show HI has direct influence on peripheral insulin sensitivity and glucose tolerance.
- HI direct effect on central glucose regulation in an obesity independent manner and may be pathogenic factor of pre diabetes and overt diabetes



Endocrinology. 2012 Mar; 153(3): 1010–1013.

Hypothalamus & Blood Pressure

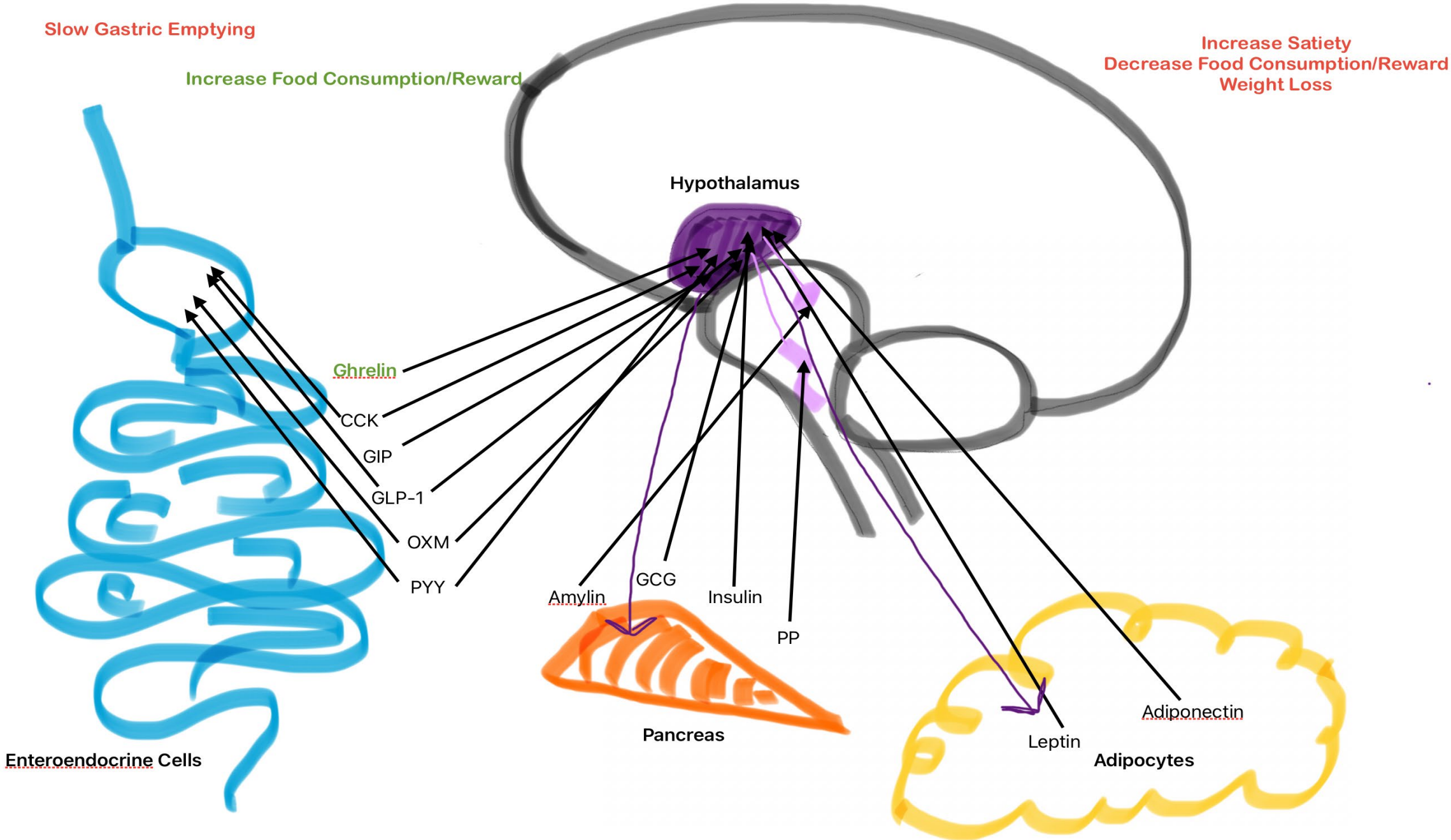
- Hypothalamus controls BP through ANS regulated by vasopressin, cortisol and leptin
- HI can dysregulate BP through increased renin-angiotensin system activity



Clin Sci (Lond). 2017 Feb 1; 131(3): 211

Disruption of hypothalamic control > metabolic dysregulation

- POMC & Agouti Related Protein neurons detect and respond to metabolic and hormone signals of short and long term deficit or surplus.
- Hormones bind to their receptors (LepT, InsR,GHSR, GLP-1R)
- Energy surplus, elevated leptin & insulin stimulates POMC neurons
- Energy demand and ghrelin stimulates AgRP neurons which release NPY. Leptin and insulin inhibit AgRP.
- PVH receives stimulus from POMC and AgRP - highest number of melanocortin expressing neurons in CNS
- Anorexigenic melanocortin suppress food intake and enhance energy expenditure
- Orexigenic AgRP peptides inhibit melanocortin to increase food intake


Slow Gastric Emptying
Increase Food Consumption/Reward
Increase Satiety
Decrease Food Consumption/Reward
Weight Loss
Hypothalamus
Ghrelin
CCK
GIP
GLP-1
OXM
PYY
Amylin
GCG
Insulin
PP
Pancreas
Enteroendocrine Cells
Leptin
Adiponectin
Adipocytes

Peripheral Hormonal Signals to Hypothalamus

Adipose

- **Adiponectin** <wt, lipids
- **Leptin** <food intake, wt

Enteroendocrine

- **Ghrelin** >food consumption & reward
- Cholecystokinin (**CCK**) >satiety <gastric emptying
- Glucose-dependent insulinotropic polypeptide (**GIP**) <food intake, >LPL (lipoprotein lipase), postprandial insulin
- Glucagon-like peptide-1 (**GLP-1**) >satiety, postprandial insulin, <gastric emptying, food reward
- Oxyntomodulin (**OXM**) >satiety <gastric emptying, food intake
- Peptide tyrosine tyrosine (**PYY**) >satiety <gastric emptying, motility

Pancreas

- **Amylin** >satiety <gastric emptying, food intake
- Glucagon **(GCG)** >satiety, glucogenolysis, gluconeogenesis
- **Insulin** <food intake, weight
- Pancreatic polypeptide (**PP**) >satiety <gastric emptying

Adipose Hormones

- **Leptin**
  - crosses the blood-brain barrier, binds to ARC down-regulating appetite stimulators and up-regulating anorexigenic **α-MSH**
  - Normal body-weight maintenance requires intact leptin-hypothalamic circuit
  - Obesity is hyperleptinemic state. due to leptin resistance
  - Elevated leptin affects the vascular structure, leading to hypertension, angiogenesis, and atherosclerosis
- **Adiponectin**
  - secreted mostly by visceral than subcutaneous adipose, crosses BB barrier to hypothalamus - decreases body weight and plasma lipids, enhances insulin suppression of hepatic glucose production
  - Obesity leads to decreased production of adiponectin, increases gluconeogenesis, reduces glucose uptake, generating hyperglycemia and contributing to IR
  - Low levels of adiponectin can also cause hyperlipidemia, correlates with CVD
  - Adiponectin levels are inversely proportional to abdominal fat mass and IR,

Pancreatic Hormones

- **Insulin**
  - T2DM development - increased workload of the endocrine pancreas > β-cell decompensation
  - obesity-associated insulin resistance - decreased surface INSR content and impaired insulin signal transduction > generating a hyperglycemia state and causing micro and macrovascular damage
- **Glucagon**
  - metabolic adaptation to starvation. Plasma glucagon level increases after 24–48 h of fasting, inducing hepatic insulin resistance that prevents glucose from being stored.
  - Glucagon promotes gluconeogenesis and ketogenesis

Gut Hormones

- **Ghrelin**
  - Gastric peptide hormone produced by stomach cells, hypothalamus, hypophysis and other tissues.
  - Promotes GH secretion, stimulates appetite, modulates pancreatic secretions, gastric motility and acid secretion.
  - Reduced in obesity, generating GH hyposecretion
  - Lower level of ghrelin in MHO & MUO
- **PYY (peptide YY)**
  - Synthesized and released from L-cells in distal gastrointestinal tract cells in response to food intake.
  - Acts on the hypothalamus to reduce intestinal motility, gastric emptying and gallbladder secretion, decreasing the appetite and increasing satiety
  - Negative association between circulating PYY and markers of adiposity.
- **GLP-1 (glucagon like protein-1)**
  - Released by the gut in response to food intake
  - Stimulates insulin secretion, β-cell growth and survival, preventing glucagon release and reducing appetite
  - Functional deficits in GLP-1 signaling caused by weight gain may maintain the obesity phenotype
  - Cardiovascular protector - inhibits thrombosis, prevents atherogenesis, protects against oxidative stress and vascular damage
- **CCK (cholecystokinin)**
  - Gut peptide hormone produced by small intestinal endocrine I-cells and cerebral neurons
  - Promotes satiety - affects exocrine pancreatic enzyme secretion, gastrointestinal motility, and gallbladder function
  - CCK interaction with leptin to promote more inhibition of food intake is disrupted in obesity

White Adipose Tissue (WAT)

- Dominant body fat, adipocytes store energy as triglycerides, increase fat reserve (lipogenesis) or utilize fat as energy (lipolysis)
- Hypothalamic melanocortin signaling regulates lipid metabolism and adiposity via SNS
- SNS releases norepinephrine > initiates lipolysis
- Disruption of hypothalamic melanocortin promotes lipid uptake, triglyceride synthesis, fat accumulation in WAT
- Major source of inflammation associated with obesity
- Active endocrine organ producing and secreting a plethora of cytokines, hormones and other factors collectively called adipokines

HD and gut microbiome

- Sensitivity of gut microbiota to host genetic and dietary influences contribute to risk of development of obesity and related metabolic disorders
- Depletion of the gut microbiota attenuates diet-induced hypothalamic inflammation and enhances leptin sensitivity via GLP-1R-dependent mechanisms.
- SAD quickly leads to pro-inflammatory gut microbiota and early hypothalamic oxidative stress
- High-fat diet increases secretion of bile acids followed by alterations in microbial compositions.
- SIBO associated with non-alcoholic fatty liver disease, hypertension, and metabolic syndrome
- Fasting-induced adipose factor (Fiaf) - a key protein negatively regulated by intestinal microbes

Case Study

- 48y/o cisgender female c/o can't lose weight
- G3P2SAB1 Hx PCOS, preeclampsia, GDM, vasectomy
- Past 2 years - more irregular menses, increased PMS, 20# wt gain
- Diet - weight watchers, emotional eater,
- Exercise - Pilates 2x/wk, walks 2mi/day
- Sleep - interrupted by hot flashes
- GI: constipation
- FH: Mother overweight at menopause > DM, HTN
- No meds, no, supps, no ETOH, mod caffeine, excess diet drinks

Is Weight the issue?

- 17% of overweight and obese participants found to be insulin sensitive
- approximately 20% of the general population can be categorized as obese but metabolically healthy.
- 18% of the population were found to have a normal body weight but suffered from severe metabolic abnormalities.

Obesity research suggests that hypothalamic inflammation could be a cause and not merely a consequence of obesity.

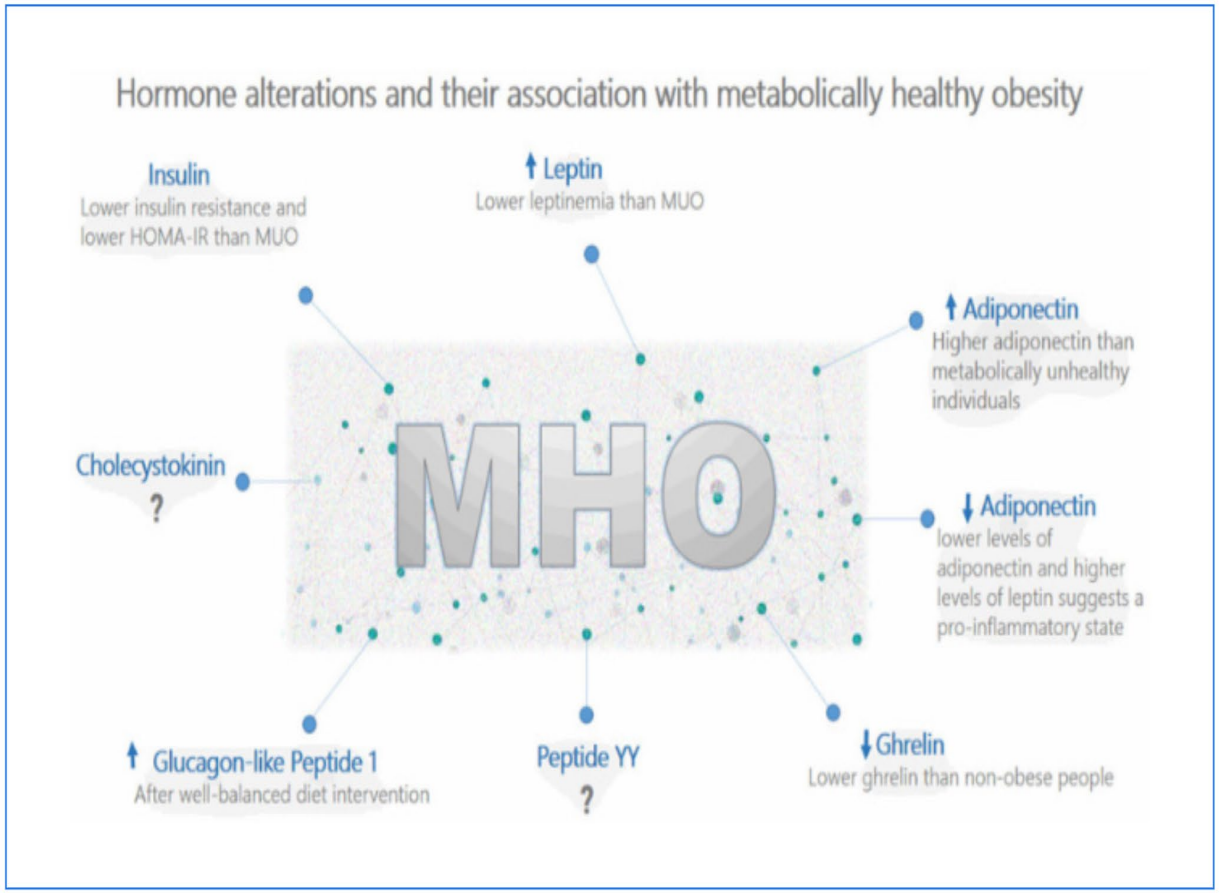
Obesity > Metabolic Syndrome

- Obesity > major risk factor for CVD, CA, DM > over 70% of early deaths worldwide
- Obesity = excess energy intake + poor physical activity + dysregulation of hormonal production, inflammatory cytokines and microcirculatory function
- Macrophages in adipose tissue produce proinflammatory cytokines - contribute to subclinical inflammation and promote IR, T2DM and MetS

- **Where fat is matters**
- Subcutaneous adipose tissue - lower infiltration of macrophages, lower production of proinflammatory cytokines compared to visceral adipose tissue
- Visceral fat is key to Metabolic Unhealthy Obesity
- MUO = BMI $\geq$30 Kg/m^2 + MetS criteria

Metabolic Unhealthy Obesity vs Metabolically Healthy Obesity

- MHO = BMI ≥30 Kg/m^2 without any MetS criteria
- MHO individuals are at increased risk for death and CVD events over the long-term compared with MHNW.
- Insulin resistance index and insulin values lower in MHO compared to MUO
- MHO and MHNW have lower concentrations of TNF-a and IL-6 compared to MUO



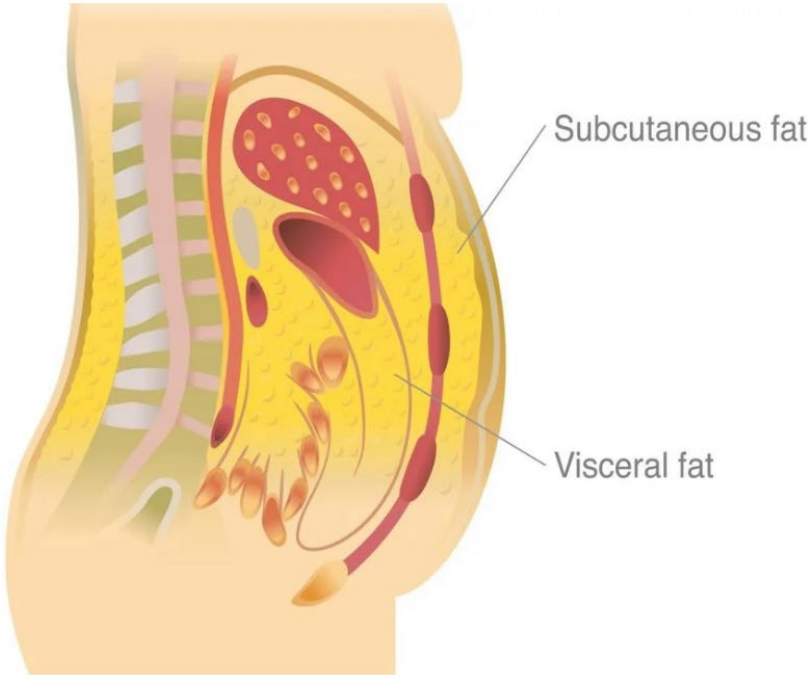
Am J Cardiovasc Dis. 2020; 10(2): 48–61.

Physical Examination

- 160# 62" BMI: 29.3
- Waist 38 Hips 44 ratio 0.86
- BF% 47% LBM 85#
- BP
  - Siting 148/92
  - Lying 134/88
  - Standing 142/92
- Apple weight distribution
- Stool noted in LLQ
- Acanthosis nigricans
- Androgenic body hair pattern

WAT – measure your patient

- Visceral obesity (abdominal, central, or ectopic obesity) increases risk
- **High risk waist circumference**
  - ≥102 cm (40”) in men
  - ≥88 cm (34”) in women
- **High risk waist-to-hip ratio**
  - >0.9 for men
  - >0.85 for women



Diagnostic Tests

- **Blood Analysis**
  - Hypothalamus function - TSH/fT4,fT3, DHEA-S, Prolactin, IGF-1, FSH if indicated
  - Lipid profile with subparticle sizes, LPa
  - Glucose metabolism - HGB A1C, insulin:glucose, c-peptide
  - Inflammation - CRP-HS
  - Vitamin D OH25
- **Stool Analysis**
  - microbiome diversity
  - function (butyrate production)
- **Abdominal Ultrasound**
  - Check visceral vs SQ abd fat
  - Check hepatic steatosis

Lab findings

- HGBA1C: 5.9% (IR)
- Chol 190 mg/dl, LDL 130 mg/dl, HDL 38 mg/dl, TGL 180 mg/dl , LP(a) 75 mg/dl, predominantly small particles (MetS pattern)
- CRP hs: 4.5 mg/L (inflammation)
- FSH day 5: 24 mIU/mL (perimenopausal)
- TSH 1.2 mU/L, fT4 0.8 mU/L, fT3 2.4 mU/L (HPT axis dysfunction)
- DHEA-S: 212 µg/dL (PCOS)
- PLC 8am:17 ng/ml (dyscircadian)
- Igf-1: 50 ng/ml (increased ghrelin)
- Vitamin D: 32 ng/dl (mild deficiency)
- Abdominal US: mild visceral fat and mild hepatic steatosis (MetS)
- Stool: low diversity, low levels lactobacillus/bifidus species, no pathogens, high butyrate levels

Assessment

Hypothalamus Dysfunction E23.3

- perimenopause N95.9
- dyscircadian prolactinemia E22.1
- central hypothyroidism E03.8

Metabolic Syndrome E88.81

- insulin resistance E88.81
- hypertension I10
- elevated CRP R79.8

Therapies to mitigate HD and MetS

- Diet
- Exercise
- Sleep
- Stress reduction
- Medications
- Supplements

Hypothalamus Diet

- A diet rich in unsaturated fatty acids (UFAs), such as omega −3 and −9, instead of SFAs can reverse inflammation in the hypothalamus. UFA diet increases anti-inflammatory proteins, improves leptin and insulin signaling, decreases gut inflammation
- Diets rich in polyphenols to modulate the inflammatory response and oxidative stress in the hypothalamus
- (n-3) Fatty Acids alleviate adipose tissue Inflammation and insulin resistance
- Fiber rich increases protective butyrate
- Fermented foods fortify gut microbiome (treat SIBO first)

Exercise

- Exercise tempers hypothalamic inflammation by decreasing microglia activation and by improving glucose intolerance
- Exercise mediates anti-inflammatory cytokine secretion & improves adipocyte oxidative capacity.
- Diet + exercise reduce low-grade inflammation and macrophage infiltration in adipose tissue but not in skeletal muscle in severely obese subjects

Exercise makes Fat Fit

- Adipocyte lipolysis is stimulated strongly by catecholamines released during exercise
- Exercise-related improvements in WAT mitochondrial function reduces visceral adiposity through greater lipolysis and reduces inflammation
- Adiponectin levels significantly increase with both acute and short-term aerobic exercise training.
- Study investigated the effects of a 15-week exercise intervention in severely obese subjects.
  - Subjects experienced improvements in insulin sensitivity and reduced systemic inflammation

Medication options to treat MetS:

CVD

Antihypertensives for METs

1. angiotensin receptor blockers (ARBs) and angiotensin converting enzyme (ACE) inhibitors
2. Add - calcium channel blockers or low dose thiazide diuretic recommended

Lipid lowering agents

statins

Insulin Resistance

Metformin - inhibits hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

Benefits - weight reduction, lowers plasma lipid levels, prevention of some vascular complications.

Side effects - 30-40% of patients experience diarrhea, vomiting, or general gastrointestinal discomfort

Obesity

Glucagon-like peptide-1 receptor agonists – works centrally on ARC to suppress appetite and potential satiety, improve glycemic control and insulin resistance resulting in 15% wt loss. SE = thyroid C-cancer, pancreatitis, cholecystitis

Naltrexone/buproprion ER – buproprion stimulates POMC release of a-MSH decreasing food intake and increasing energy expenditure, naltrexone blocks b-endorphin mediated negative feedback , 5-6% wt loss. Contraindications = HTN, seizures, eating disorders, MAO inhibitors

Phentermine/topiramate ER – phentermine centrally acting sympathomimetic increases hypothalamic norepinephrine, topiramate suppresses appetite by increasing hypothalamic dopamine, inhibiting glutamate receptors, modulating NPY. >10% wt loss. Contraindications = CVD, glaucoma, hyperthyroidism, on MAO inhibitors

Hormones role in MetS & HD

Sex steroids

Progesterone – anti-inflammatory

Estradiol – promotes collagen and bone and joint repair

Testosterone – improves LBM

Adrenal/Thyroid

Cortisol – anti-inflammatory

DHEA – anabolic tissue repair

Pregnenelone - anti-inflammatory

Thyroxine/ Leiothyronine– promotes metabolism

Pituitary

Prolactin – modulates immune system

Growth Hormone – repairs and builds tissues, improves LBM

Dietary supplements

- Berberine
- Curcumin
- Omega-3 Fish Oils
- Vitamin D, Niacin
- Magnesium, phosphorus
- Polyphenols
- Ginseng
- White mulberry
- Bergamot
- Quercetin
- Black Rice

Berberine

- Modulation of gut microbiota to reduce wt, inflammation and IR
- Regulates mitochondrial energy metabolism
- Significantly increases fasting-induced adipose factor expression in intestinal and visceral adipose tissues.
- Regulates central obesity-related pathway
- Reduces IR > insulin sensitivity and insulin receptor (InsR) are increased
- Inhibits lipid synthesis in hepatocytes > reduces steatosis
- Lipid-lowering effects by upregulating LDL receptor
- Dose = 500mg with meals

Curcumin

- Alters Gut Microbiota - modulates intestinal permeability, reduces inflammation and oxidative stress in the gastrointestinal tract, and has an anti-microbial effect on bacterial, parasitic, and fungal infections.
- Significantly reduces adiposity and total macrophage infiltration in WAT
- Reduces expression of other key pro-inflammatory genes
- Dose: 1000-2000mg/d taken with fat for enhanced absorption

Omega-3 Fish Oils

- Modulates lipid metabolism
- Regulates adiponectin and leptin
- Alleviates adipose tissue inflammation; promotes adipogenesis,
- Alters epigenetic mechanisms
- Ongoing studies (REDUCE-IT and STRENGTH) will help to more firmly establish the role of omega-3 fish oils for cardiovascular protection
- Dose: 3 g of fish oil per day (360 mg DHA/ 540 mg EPA)

Dietary Supplements

Vitamins

- Vitamin D - correlates with significant improvements in plasma concentrations of adiponectin and leptin.
- Niacin - high dose, nonflush increases HDL and lowers triglycerides

Minerals

- Phosphorus - effects on blood pressure regulation through its role in plasma membrane structure.
- Magnesium – regulates vascular tone and endothelial function.

Dietary Supplements

Botanicals

- Ginseng supplementation lowers cholesterol and LDL-C by suppression of β-hydroxy-β-methylglutaryl-CoA reductase.
- White mulberry extract has a significant impact on the changes in the LDL-C subfractions
- Quercetin has antioxidant effects since it protects against H_2O_2-induced lipid peroxidation and reduces the cytokine-induced cell-surface expression of vascular cell adhesion molecule-1.

Food based

- Inulin, β-glucan, blueberry anthocyanins, and blueberry polyphenols reduce plasma ghrelin concentrations and improve blood glucose tolerance.
- Bergamot juice (neoeriocitrin, neohesperidin, naringin) has an effect on metabolic parameters, including plasma lipids, atherogenic lipoproteins and subclinical atherosclerosis.
- Black rice and its pigment fraction have shown anti-atherogenic activities.

Hypothalamus nutraceutical

Amino acids

Modulate hypothalamus function

Essential: phenylalanine, valine, tryptophan, threonine, isoleucine, methionine, histidine, leucine, and lysine

Conditionally essential: arginine, cysteine, glutamine, tyrosine, glycine, proline, and serine.

cannot be synthesized in sufficient quantities during certain physiological periods of growth, including pregnancy, adolescent growth, recovery from trauma and hypothalamic inflammation

PUFAs

Studies show omega-3 Fatty Acids induce neurogenesis of POMC expressing cells in the Hypothalamus

Phytonutrients

Whole plant food derived rich in antioxidants, vitamin and mineral cofactors

Sea vegetation

Sprouted grains and seeds

Herbs and botanicals

Sleep

- Causal association between short sleep duration and MetS
- Key role of the hypothalamus in sleep-wake regulation become increasingly recognized
- Relationship between abnormal sleep symptomatology and hypothalamic pathology is now widely accepted for a variety of medical disorders
- Growing evidence supports a hypothesis that a decline in the hypothalamic neurogenic process, caused by chronic neuroinflammatory signaling is a contributor to sleep–wake and other hypothalamic dysfunctions in aging.

Case study therapeutic plan

- To reduce visceral fat and inflammation
  - IRD phase shift q6weeks
    - 80gm protein/day 40gm fat/day
    - No artificial sweeteners
    - Increase water consumption 80 oz/day
  - HIT 3x/wk, wt resistance 2x/wk
- To improve perimenopause symptoms and reduce inflammation
  - Progesterone TD 100mg bid day 12-26
- To improve gut microbiome
  - Fiber 25gm/day (increase protective butyrate)
  - Colonize w 40 billion lactobacillus/bifidus species daily X 60
- To optimize Hypothalamus function
  - Full spectrum nutraceutical support 12gm daily
- To improve MetS symptoms
  - Berberine 500mg ac
  - Curcumin 500mg qd
  - Omega 3 2000mg qd
- Monitor BP at rest and 30 mins after exercise
- Sleep hygiene modification
- Stress reduction
- Support group for accountability

Three month followup

Assessment

- Menses regulated with progesterone
- Luteal sleep improved
- On phase 2 IRD
- Consistent HIT and wts
- BP lower after exercise
- Wt 150 BMI 27.4
- Waist 35, Hips 42 ratio 0.83
- BF 41% LBM 88#
- BP: 124/80

Labs

- HGBA1C 5.7
- Chol 180, LDL 110, HDL 48, triglycerides 110, LPA 50, shift to large particles
- CRP hs 2.2
- TSH 2.4, fT4 1.2, fT3 2.8
- DHEA-S 155
- PLC 8am - 9

Plan

- Add 25mg progesterone QHS in follicular phase
- IRD 5D/wk
- Add 1 LSD/wk change type of HIT
- Break from berberine x one month
- Continue rest supps

Six month followup

Vitals

Sleeping well

phase 3 IRD cycling

consistent HIT and wts

Wt 142 BMI 26

Waist 32, Hips 40 ratio 0.8

BF 35% LBM92#

BP: 122/78

Labs

HGBA1C 5.5

Chol 178, LDL 98, HDL 56, triglycerides 95, LPA 38, large particles

CRP hs 1.3

Plan

D/C berberine

Continue progesterone, hypothalamus nutraceutical

Continue new lifestyle habits

Cycle IRD, adding more high fiber carbs


Nutraceutical Support
Healthy Diet
Adequate Activity
Restorative Sleep
Healing Mindset
5 Pillars of Hypothalamus Healing

Thank you

Deborah Maragopoulos MN FNP

Intuitive Integrative Health

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