The Role of Leptin in Anorexia Nervosa: Clinical Implications

THE INSULINATORS
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Anorexia Nervosa (AN)

1. Summarize Leptin Related findings
2. Leptin Pathway Review
3. Intro to AN
4. How it relates to leptin
5. Clinical perception in AN
6. Effects of weight gain
7. Reproductive axis + how it relates to the real work
8. Bone mineral density + how it relates to the real world
9. Hyperactivity + how it relates to the real world
10. Overview
LEPTIN
RELATED
FINDINGS
+
PATHWAY
Introduction

What is leptin?
- Discovered in 1944
- Folds like cytokines (Cytokines + Hormones)
- A peptide hormone
- Tertiary structure resembling that of members of the long-chain helical cytokine family
- Produced by adipocyte in proportion to fat size stores \textit{Leptin=fat cells=body fat}
- Operates directly + indirectly on pathophysiological processes
- Most important: Insulin works with systems that deal with energy regulation, growth, immune response and cell function
- It is involved with general endocrinology, metabolism, reproduction, immunology, <3 pathophysiology, respiratory function and wound healing, growth and development
JAK-STAT Pathway

- **JAK**
  - Janus Kinase
  - 4 Members of the Janus Kinase family: JAK1, JAK2, JAK3, TYK2
  - Related to non-receptor tyrosine kinases
  - Leads to a phosphorylation cascade

- **STAT**
  - Signal Transducer and Activators of Transcription
  - 7 STAT-encoding Genes (1,2,3,4,5A,5B,6)
  - Involved in proliferation, apoptosis, and immune system
  - Dysregulation leads to angiogenesis= growth of a tumor
**Leptin Receptors**

- The receptors involved look extremely similar to class 1 cytokine receptors

<table>
<thead>
<tr>
<th>There are Amino Acids that make Leptin work</th>
<th>There are isoforms (different forms of Leptin)</th>
<th>The isoforms and their location</th>
</tr>
</thead>
<tbody>
<tr>
<td>o 4 cysteine residues</td>
<td>o OB-R: OB-Ra, OB-Rb, OB-Rc, OB-Rd, OB-Re</td>
<td>o <strong>OB-R = hypothalamus</strong> and other areas associated with food and energy regulation</td>
</tr>
<tr>
<td>o WSXWS</td>
<td>o They are short, long, secreted</td>
<td>o <strong>OB-Rb = hypothalamus</strong></td>
</tr>
<tr>
<td>o Extracellular domain contains 2 cytokine-like receptors</td>
<td>o Main difference between them is their <strong>intracellular</strong> part</td>
<td>o <strong>Ra and Rb =</strong> in extraneuronal tissue</td>
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<tr>
<td></td>
<td></td>
<td>o <strong>Ra and Rc =</strong> choroid plexus, seem to be involved with leptin transport</td>
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<td></td>
<td></td>
<td>o <strong>OB-Re =</strong> buffering for free leptin</td>
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THE JAK/STAT Cascade

Box1 and Box2 - the binding sites of JAK proteins on the receptor
The intra-cellular domain of all OB-R isoforms contains in the juxta-membrane region the box1 JAK-binding domain, whereas OB-Rb also includes the box2 motif and STAT-binding sites.
JAK2 associates with the receptor via the box1 motif.

The long isoform leptin (L) receptor (OB-Rb) contains four important tyrosine residues (*Tyr974, Tyr985, Tyr1077 and Tyr1138*).
These phosphorylated tyrosine residues provide docking sites for signaling proteins with SH2 domains.
Most importantly, Tyr1138 recruits the transcription factor STAT3

It is phosphorylated by JAK2, dimerizes and translocates to the nucleus

Here, it induces SOCS3 and POMC (pro-opiomelanocortin) expression, while repressing AgRP (agouti-related peptide).
SOCS proteins inhibit signalling by binding to phosphorylated JAK proteins or interacting directly with tyrosine-phosphorylated receptors.

The ability of SOCS3 to inhibit leptin-stimulated phosphorylation of JAK2 and ERK provides a negative-feedback mechanism on the leptin signalling system. Grb-2, growth factor receptor binding-2.
A. Upon leptin (L) binding, a conformational change takes place (A) that allows JAKs, to then become activated.

They are able to tyrosine-phosphorylate other JAKs and tyrosine residues on the receptor.
B. Activation of JAK2 occurs by transphosphorylation and subsequent phosphorylation of tyrosine residues in the cytoplasmic region of the receptor. Phosphorylation of Tyr1138 allows association of STATs, which then become substrates of receptor-associated JAKs. Phosphorylation of STATs leads to their dissociation from the receptor and the formation of active dimers (a molecule or molecular complex consisting of two identical molecules linked together).
C. This translocate to the nucleus to regulate gene expression, binding to the promoter regions of target genes (D).
THE JAK/STAT Cascade in BASIC terms
JAK-STAT Pathway, Step 1:

The plasma membrane has these JAK-STAT components in it, we see that some parts of it lie intracellularly and some extracellularly.
JAK-STAT Pathway, Step 2:

The extracellular region is compromised with a certain receptor type called: **CYTOKINE RECEPTORS**, these kinds of cytokines receptors are mostly in the direction of binding cytokinase on them.
JAK-STAT Pathway, Step 3:

In the intracellular part, the cytokine receptors are associated with **2 JAK** (Janus Kinase) proteins.
JAK-STAT Pathway, Step 4:

SO when you have a presence of any kind of **Cytokinase** such as the (red blob drawn here) it attaches to the cytokine receptors = LIGAND BINDING
After it binds to the receptor, it brings to 2 JAKs into a very close proximity, and the JAKs trans-phosphorylate each other, this increases the activity of the TYROSINE-KINASE-domains
In this next step we see these phosphorylated JAK kinases, then phosphorylated **tyrosine kinase** on the receptors, this creates phosphotyrosine-binding sites for STAT proteins.
Next, the STAT proteins dock the phospho-tyrosine cites as shown and its by the SH2 domain, of STAT protein, which mediates the docking of STAT2 toward phosphorylated tyrosine. Why? -> (Domains)
After STAT docks on phosphorylated tyrosines on the receptor, JAK comes in and phosphorilates them.
JAK-STAT Pathway, Step 9:

Then, phosphorylation of STAT proteins cause the STATS to dissociate from the receptor.

So the phosphorylation detaches the STAT protein from the phospho-TYROSINE.
Finally, the dimerization of the STAT translocates to the **NUCLEUS** with the help of **DNA** binding domain of the STAT protein. The STAT protein simply attaches itself to the DNA and initiates the transcription AND we get the **GENE EXPRESSION!**
Importance of Leptin Take Away Message

- Leptin is distributed everywhere in your body, and by doing research on it we can find effective ways on how to fight pathologies, different disorders and understand the regulation of human body homeostasis

- Energy regulation is important for your brain + cognitive function

- Leptin is involved in adaptive responses emotional stress and starvation, lets go ahead and explore what happens in starvation aka Anorexia Nervosa (AN)
What is Anorexia Nervosa?

(AN)

Box 1 | Description and diagnosis of anorexia nervosa

Core features
- Behavioural disturbance related to eating or weight control practices that leads to a significantly low body weight
- Disturbance in the experience of body shape and/or weight
- Disturbance results in substantial impairment in physical, social and/or mental functioning
- Disturbance is not secondary to any other medical or psychiatric disorder

Possible laboratory abnormalities
- Endocrine: low serum oestrogen (female) or testosterone (male) levels; and low-to-normal thyroid hormones levels (T3 and/or T4)
- Haematological: mild leukocytopenia with apparent lymphocytosis; anaemia; and thrombocytopenia
- Cardiovascular: abnormalities on echocardiogram; sinus bradycardia; and significant prolongation of the QTc interval
- Gastrointestinal: delayed gastric emptying; and decreased colonic motility (with laxative use)
- Other abnormalities: electrolyte disturbance; significantly increased osteopenia, osteoporosis and risk of fracture; pseudoatrophy (enlarged cerebral ventricles and external cerebrospinal fluid spaces); reduction in resting energy expenditure; dehydration; and hypercholesterolaemia
Behaviors & Possible Psychobiology

- Feeding problems
- Low BMI
- Social difficulties

- Coping by avoidance
- or perfectionism

- Over-control of eating
- Weight control behaviours

- Social isolation
- Impaired physical and mental quality of life

High risk
- Low reward and high
- threat sensitivity
- Social cognition problems
- Cognitive rigidity

Prodromal
- Compulsivity
- Anxiety

Full syndrome
- Cognitive control over drives
- Emotional avoidance
- High ability to delay reward
- Impulsivity and high reward sensitivity can lead to loss of control of eating (binge–purge subtype)

Severe enduring
- Habits, not goal-directed
- behaviours
- Increased threat sensitivity
- Decreased social cognition

Behavioural features          Psychobiological features
Somatic and Psychosocial Effects

Psychosocial effects
- Sexual disinterest
- Poor social functioning
- Isolation
- Relationship dysfunction
- Carer "burn out"
- Psychosocial dysfunction
- Suicidal ideation
- Depression
- Financial dependency

Anorexia nervosa

Somatic effects
- Gastrointestinal
  - Abdominal bloating
  - Constipation
- Orthopaedic
  - Osteoporosis
  - Spinal compression
- Cognitive
  - Poor flexibility

Haematological
- Anaemia
- Leukocytopenia

Reproductive
- Amenorrhoea

Cardiovascular
- Hypotension
- Bradycardia

Dental
- Poor dental status
- Dental caries

Renal
- Hypokalaemia
- Hypophosphataemia
- Nephrolithiasis
- Hyponatraemia
- Oedema
Neurobiological Model
Possible pathway to AN development

Predisposing traits (biology)
- Anxiety and sensitivity to salient stimuli
- Unstable dopamine circuitry
- Larger orbitofrontal cortex

Precipitating cues
- Menarche stimulates dopamine receptors
- Exposure to food restriction sensitizes dopamine receptors

Precipitating factors
- Low self-esteem
- Social pressure
- Stress
- Food restriction

Perpetuating factors
- Eating over-stimulates dopamine receptors
- Food restriction tempers over-stimulation, leading to ‘improvements’ in mood
- Food restriction further sensitizes dopamine receptors
Reward Neural Circuits

Brain structures associated with reward pathway
Factors influencing circulating leptin levels in AN

1995: AN may react with upregulation of leptin production after adequate caloric intake; low body weight “psychological” only

Later using radioimmunoassays, hypoleptinaemia was discovered as a *cardinal* feature of acute AN

Based on patients in in-patient treatment, leptin levels are **below** the 5th percentile

Leptin concentrations are also subnormal in CSF of AN patients
Treatment for AN

Psychotherapy

- Family based treatment
- Focal psychodynamic psychotherapy
- Enhanced Cognitive behavioral therapy
- Specialist supportive clinical management
- Maudsly Model of Anorexia treatment of adults

Pharmacotherapy

Table 4 | Evidence base for pharmacological and nutritional treatments in anorexia nervosa

<table>
<thead>
<tr>
<th>Treatment*</th>
<th>Weight</th>
<th>Eating disorder psychopathology</th>
<th>Psychological co-morbidity$</th>
<th>Physical co-morbidity$</th>
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<td><strong>Antidepressants (acute phase)</strong></td>
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<tr>
<td>SSRIs: fluoxetine and citalopram</td>
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<td>Negative</td>
<td>Negative</td>
<td>Lack of evidence</td>
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<tr>
<td>TCAs: clomipramine and amitriptyline$</td>
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<td>Negative</td>
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<td>Lack of evidence</td>
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<tr>
<td><strong>Antidepressants (relapse prevention)</strong></td>
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<tr>
<td>SSRI: fluoxetine</td>
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<td>Negative</td>
<td>Weak</td>
<td>Lack of evidence</td>
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<tr>
<td><strong>Antipsychotics (acute phase)</strong></td>
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<td>Olanzapine$</td>
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<td>Lack of evidence</td>
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<td>Negative</td>
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<td><strong>Nutritional supplements</strong></td>
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<tr>
<td>Zinc$</td>
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<td>Lack of evidence</td>
<td>Weak</td>
<td>Lack of evidence</td>
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<td><strong>Hormones or drugs to treat osteoporosis$</strong></td>
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<td>Gonadal steroid replacement$</td>
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<tr>
<td>Recombinant human growth hormone$</td>
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<tr>
<td>Insulin-like growth factor 1$</td>
<td>Negative</td>
<td>Lack of evidence</td>
<td>Lack of evidence</td>
<td>Weak</td>
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<tr>
<td>Biphosphonates: alendronate$, risedronate and etidronate</td>
<td>Negative</td>
<td>Lack of evidence</td>
<td>Lack of evidence</td>
<td>Weak</td>
</tr>
</tbody>
</table>
How does anorexia and reproductive function relate to each other

- Primary amenorrhea (not menstruating) in young patients
- Secondary amenorrhea in postmenarcheal females (for at least 3 months)
- Typically sets in after weight loss
- Ovaries of severely emaciated patients are small
Important players of the female reproductive system

- Gonadotropin Releasing Hormone (GnRH)
- Luteinizing Hormone (LH)
- Follicle Stimulating Hormone (FSH)
- Estrogen
- Inhibin
Leptin’s role in reproduction

- Regulates oscillations in levels of LH and oestradiol
  - Regulates nocturnal LH profile in mid-to-late follicular phase that comes before ovulation
- Has direct relationship in secretions of the hypothalamic GnRH
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  - Regulates nocturnal LH profile in mid-to-late follicular phase that comes before ovulation
- Has direct relationship in secretions of the hypothalamic GnRH
Cascade into amenorrhoea

1. Loss in fat mass & low calorie intake (AN)
2. Drop in leptin
3. Shuts down hypothalamic-pituitary-gonadal axis
4. Drop in FSH and LH
5. Curtailment in ovarian oestrogen production
6. Amenorrhoea
Magic leptin level number?

- Critical threshold value for amenorrhea
- HOWEVER, there are normally menstruating females who are below this level.
  - Note: most *have been* amenorrhoeic before
  - Leads to question: Perhaps the body can adjust itself?
What happens when leptin is injected?

- **Experiment 1:** Realimentation induced increments in leptin levels and then followed by FSH and LH
  - AN patients with low leptin levels and undetectable FSH
  - Result: FSH detectable upon admission
  - Threshold leptin level for normalization was 1.85 µg/l

- **Experiment 2:** in a further study...
  - Threshold leptin level for normalization was 1.2 µg/l

- This discrepancy suggests that threshold ranges may differ with amount of energy depletion
Inhibin B

- Hormone that is an early marker for gonadal activity
- Not detectable in severely underweight AN patients
- Inhibin B increases during weight gain > “awakening” of reproductive system
- Correlated with leptin (leptin receptors in ovary) and BMI
Female Reproductive Recovery

- May take many months before ovarian function normalizes
- Emergence of follicle occurs when there is normal weight, increase in uterine area, and increased levels of LH, oestradiol, and high LH:FSH ratio (>2)
- Achievement of body weight (90% of body weight)
  - Resumption in menses (85% of patients within 6 months)
Alternative treatment for women who did not menstruate following treatment

- 17 adults who did not menstruate after 6-12 months of treatment were given clomiphene treatment (medication that stimulates ovulation)
- Result: this led to on average five and 50 fold increase in LH and oestradiol levels
- Serum leptin levels remained the same regardless of whether people menstruated or not
- Proves that the hypothalamic pituitary axis was intact
Males?

- Only records of 3 male AN patients were investigated
- Leptin levels were low; 0.25 ug/l
- Testosterone levels were initially low and increased *simultaneously* during leptin realimentation
Proof of Principle study: Conclusion for leptin and reproduction

● Study
  ○ 8 females with amenorrhea due to excessive exercise or low weight (cases)
  ○ 6 females with amenorrhea (control)
  ○ Cases given recombinant leptin for 3 months

● Results
  ○ 3 cases menstruated & 2 had preovulatory follicle, while no controls menstruated
  ○ Increased follicular diameter, number of dominant follicles, endometrial thickness, ovarian volume
  ○ LH patterns improved and oestriadiol hormones increased

● Critical role of leptin in regulating hypothalamic-pituitary-gonadal axis

● Directly proven that leptin treatment improves reproductive function
  ○ Typically triggering hormonal changes that led to ovulation
  ○ Most cases had leptin levels over 2 ug/L
Bone mineral density

- Complication of AN: **Decrease** in bone density
- Higher risk for bone fractures, osteopenia, and osteoporosis
- Bone mass deficiency persists for a long time
What happens to your bones during starvation?

- High serum cortisol
  ○ Enhances bone resorption
- Low serum oestradiol
  ○ Important for bone mineralization
- Bone density in recovered AN patients
  ○ Inversely related to duration of amenorrhea
  ○ Directly related to duration of postmenarcheal menses before onset of AN-induced amenorrhea
How can you increase bone mass?

Oestrogen (in postmenopausal women)

Weight gain (stronger predictor)
Oestrogen + Leptin

- Oestrogens increase in bone mass in healthy postmenopausal females but not in adolescents with AN. Why?
- Leptin! Which is a regulator in bone mass
  - Inverse relationship between bone resorption marker (CTX) and leptin concentrations
  - Positive correlation between bone mass and serum leptin levels suggest something. Was observed in non-obese women after adjustment for body weight and fat mass
  - Not fully understood
- Recent findings indicate leptin induces bone loss via CNS and by regulating input from SNS
Neuropeptide CART neurons

● Suggests that CART seems to inhibit bone loss
● CART neurons found in regions rich with high concentrations of sex steroid receptors
● Leptin and sex steroids possibly coordinate the CNS regulation of bone mass (in the hypothalamus)

On another note...

● Starvation reduces norepinephrine turnover in hypothalamus
● This, with hypoletenaemia, could be a possible explanation for impairment of bone metabolism in AN
Exogenous application of leptin to leptin-deficient human adults was shown to have **sustained effects on tissue composition in the human brain**.
DLPFC: Self control center!

Dorsolateral prefrontal cortex
A self-control center of the brain. The DLPFC acts like a brake system to curb impulsive behaviors. In anorexics, the DLPFC may work overtime to keep people from giving in to the temptation to eat.
**PSYCHOLOGICAL: Brain Regions**

Ventral striatum
Part of the brain’s reward circuitry. The ventral striata of anorexics may be hypersensitive to flavors healthy people find pleasurable, such as sugar. This oversensitivity could affect patients' enjoyment of food.
PSYCHOLOGICAL: Brain Regions

The way you see food, and a person with anorexia sees food differ a lot.
Insula is basically, your self awareness; do you realize you're hungry? Are you listening to ghrelin?

PSYCHOLOGICAL: Brain Regions

*Insula*

Involved in self-awareness of body states, such as pain and hunger. The insula is the first brain region to register the taste of sweets. In anorexics, the insula may not correctly detect sweets and other signals.
A: “The striatum contains both dopamine and opioid receptors and is involved in reward approach and motivation (wanting), as well as hedonic experience (liking).”

BIOLOGICAL: Brain Regions

B: AMYGDALA-FEAR AND ANXIETY
C: INSULA-PRIMARY TASTE CORTEX
D: ORBITOFRONTAL CORTEX- REWARD
How does the biological tie in with the psychological together?

Anorexia:
- Underweight

Bulimia:
- Either be normal or overweight

Restricting
- Type: reduce food intake --> loose weight

Binge Eating/
- Purging:
  - by vomiting or taking laxatives

Binge eating/purging can be a factor of Bulimia, as well.
Hyperactivity

Defined to be the condition of being abnormally or extremely active.

'Semi-starvation-induced hyperactivity (SIH)'

SIH is suppressed by Leptin, it results in the rats to reduce their intake of ad libitum food intake for 1 week (n = 7 in each treatment group)
RESULTS:

In essence, rats with access to a running wheel develop hyperactivity upon food restriction.

SIH: ‘Anorexia-based activity’ or ‘semi-starvation-induced hyperactivity (SIH)’
ad libitum: as much or as often as necessary or desired.

Rats were restricted from their ad libitum amount of food

Due to this restriction the rats resulted in hyperactivity

WHY?
GLUCOSE: Starvation stimulates a decrease in the production of the hormone leptin.

Leptin determines the energy expenditures.

Purging or self-induced vomiting affects resting glucose levels and leptin levels.

LEPTIN: In which starvation results in a decrease production of Leptin.

Metabolic rate increases exponentially during weight restoration in anorexia.
LEPTIN: in which starvation results in a decrease production of Leptin

Metabolic rate increases exponentially during weight restoration in anorexia.

Metabolism: Decreased lean body mass results in reduced metabolism.

Binge-eating and purging decreases metabolic rate for months or even years.

Restoration of normal metabolism is contingent upon normalized eating patterns.
Motor Restlessness

- **MOTOR RESTLESSNESS**: characterised by an irresistible urge to move about, can be a manifestation of many underlying disorders
So why would this result in HYPERACTIVITY?

Hyperactivity can be a variant of anorexia nervosa, which has the same effects, as weight loss. Hyperactivity can also be considered as a kind of obsessive compulsive disorder.

The SIH triggered by hypoleptinaemia suggests that the same mechanism might underlie the hyperactivity in patients with acute AN.

As leptin levels increased, motor restlessness decreased

As leptin levels decreased, motor restlessness, increased

Meaning that:
Nevertheless, increased nervousness, anxiety and motor activity have anecdotally been reported in starved humans.

ANXIOUS

ANOREXIA NERVOSA:

- As leptin levels increased, motor restlessness decreased
- As leptin levels decreased, motor restlessness increased

MEANING THAT:

Hyperleptinemia could affect activity levels directly and/or indirectly via specific psychopathological features. For example, independent effects of anxiety on activity levels need to be considered.

HUMANS:
ENERGY CONSERVATION MODE?
WHERE’D I HERE THAT BEFORE?

- Glucose is a critical part of digestion, it’s an essential energy source for cellular metabolism.
- Glucose is used as a substrate for glycolysis:
  - In muscle cells glucose is used to produce energy and stored as glycogen; also known as a secondary SHORT TERM energy source.
  - In fat cells, it is used as triglyceride production or ENERGY STORAGE MOLECULE.
Hyperactivity: STUDY

● “The fact that hyperleptinemia can induce hyperactivity in a rat model for AN has led to a series of studies in AN patients, which support the notion that application of leptin to severely hyperactive patients might prove beneficial.”

● Elevated levels of physical activity have consistently been reported in patients with AN
SIH could potentially only arise if leptin levels fall below a specific concentration, the degree of hyperleptinemia then influencing the severity of the hyperactivity. Studies of short term fasted females revealed that changes of leptin levels within the physiologic range have no major physiologic effects in leptin-replete humans, substantiating the critical role of sub-threshold leptin concentrations for the initiation of the physiologic adaptation to a semi-starvation.
Conclusion: Leptin secretion is profoundly perturbed in this eating disorder. Normalization of secretion after weight recovery requires time, the recovery of leptin-dependent somatic and behavioral symptoms may take even longer.
TREATMENTS?

TALK THERAPY: WHICH CAN RESTORE SELF ESTEEM

FUTURE? - Leptin injections in small doses, and Psychobehavioral Therapy → to normal production of Leptin and increase the metabolic rate to normal.

AMANDA’S SLIDE:
Leptin is a versatile 16 kDa peptide hormone, with a tertiary structure resembling that of members of the long-chain helical cytokine family. It is mainly produced by adipocytes in proportion to fat size stores, and was originally thought to act only as a satiety factor. However, the ubiquitous distribution of OB-R leptin receptors in almost all tissues underlies the pleiotropism of leptin. OB-Rs belong to the class I cytokine receptor family, which is known to act through JAKs (Janus kinases) and STATs (signal transducers and activators of transcription). The OB-R gene is alternatively spliced to produce at least five isoforms. The full-length isoform, OB-Rb, contains intracellular motifs required for activation of the JAK/STAT signal transduction pathway, and is considered to be the functional receptor. Considerable evidence for systemic effects of leptin on body mass control, reproduction, angiogenesis, immunity, wound healing, bone remodelling and cardiovascular function, as well as on specific metabolic pathways, indicates that leptin operates both directly and indirectly to orchestrate complex pathophysiological processes. Consistent with leptin’s pleiotropic role, its participation in and cross-talk with some of the main signalling pathways, including those involving insulin receptor substrates, phosphoinositide 3-kinase, protein kinase B, protein kinase C, extracellular-signal-regulated kinase, mitogen-activated protein kinases, phosphodiesterase, phospholipase C and nitric oxide, has been observed. The impact of leptin on several equally relevant signalling pathways extends also to Rho family GTPases in relation to the actin cytoskeleton, production of reactive oxygen species, stimulation of prosta glandins, binding to diacylglycerol kinase and catecholamine secretion, among others.

Key words: adipocyte, cytokine, Janus kinase/signal transducer and activator of transcription pathway (JAK/STAT pathway), leptin receptor, obesity, signalling cascade.
Anorexia nervosa

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Abstract | Anorexia nervosa (AN) is a psychiatric condition characterized by severe weight loss and secondary problems associated with malnutrition. AN predominantly develops in adolescence in the peripubertal period. Without early effective treatment, the course is protracted with physical, psychological and social morbidity and high mortality. Despite these effects, patients are noted to value the beliefs and behaviours that contribute to their illness rather than regarding them as problematic, which interferes with screening, prevention and early intervention. Involving the family to support interventions early in the course of the illness can produce sustained changes; however, those with a severe and/or protracted illness might require inpatient nursing support and/or outpatient psychotherapy. Prevention programmes aim to moderate the overvaluation of ‘thinness’ and body dissatisfaction as one of the proximal risk factors. The low prevalence of AN limits the ability to identify risk factors and to study the timing and sex distribution of the condition. However, genetic profiles, premorbid features, and brain structures and functions of patients with AN show similarities with other psychiatric disorders and contrast with obesity and metabolic disorders. Such studies are informing approaches to address the neuroadaptation to starvation and the other various physical and psychosocial deficits associated with AN. This Primer describes the epidemiology, diagnosis, screening and prevention, aetiology, treatment and quality of life of patients with AN.
1. Pull out your phone
2. Search Kahoot.it
3. Input the code on the screen
4. Choose your username
5. Let’s play!