Review

Is obesity a brain disease?☆

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IS OBESITY A BRAIN DISEASE?

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WHICH CAME FIRST
"CHICKEN & EGG"

OBESITY?
BRAIN CHANGES?
does it matter?
Is obesity a brain disorder?

- What is the evidence to support obesity is a brain disorder?
- Environmental, biological, and behavioral issues
- Over-nutrition: a biological trap?
- Old school: animals select food only for growth and survival
- Obesity stigma – lack of understanding the biology
- Body not keeping up with changes in nutrient availability
Recall:

- Leptin resistance
- Hyperphagia
- High Blood Pressure
- Hyperinsulinia (excess insulin in plasma)
Over-nutrition: A trap?

Obesity Trap

How is obesity perpetuated?

How did this happen? Pathogenesis
Does obesity depend on energy control circuitry?

Is it a function of critical periods?

Early development

Adolescence

How is obesity perpetuated?

How did this happen? Pathogenesis

Obesity trap
Does obesity Δ energy control circuitry?

Are the changes reversible?

Structural & functional changes

Regional blood flow

Reduction in brain volume

Hippocampal size

Inflammation hypothalamus

Gliosis
Tozuka et al., 2009 - high fat diet from pre-mating to lactation led to offspring with increased hippocampal lipid peroxidation and decreased neurogenesis.
Naim et al., 1985 - Set multiple choice cafeteria diet in rats → it resulted in increase in hyperphagia and obesity.

Srinivasan et al., 2008 - Exposed rat pups to high-carbohydrate (HC) milk formula → develop chronic peripheral hyperinsulinemia and adult onset obesity despite replacement to regular rat chow.

Miesel et al., 2010 offered hypertensive rats a choice between cafeteria diet and regular chow → the rats experienced increase body weight but also featured leptin and insulin resistance and higher blood pressure than control rats fed with regular chow.
EAT DURING THE DAY

CIRCadian RHYTHM MATTERS

WHEN YOU EAT ALSO MATTERS

SLEEP

NO NIGHT TIME EATING
Boitard et al., 2012 - exposure to high fat diet in adults and juvenile mice; but only juvenile - resulted in reduced hippocampal neurogenesis and reduction in rational memory flexibility.
Lipid peroxidation

Lipid peroxidation refers to the oxidative degradation of lipids. It is the process in which free radicals “steal” electrons from the lipids in cell membranes, resulting in cell damage. This process proceeds by a free radical chain reaction mechanism. It most often affects polyunsaturated fatty acids, because they contain multiple double bonds in between which lie methylene bridges (–CH2–) that possess especially reactive hydrogens. As with any.

Initiation [edit]

Initiation is the step in which a fatty acid radical is produced. The most notable initiators in living cells are reactive oxygen species (ROS), such as OH• and HO2, which combines with a hydrogen atom to make water and a fatty acid radical.

Propagation [edit]

The fatty acid radical is not a very stable molecule, so it reacts readily with molecular oxygen, thereby creating a peroxy-fatty acid radical. This radical is also an unstable species that reacts with another free fatty acid, producing a different fatty acid radical and a lipid peroxide, or a cyclic peroxide if it had reacted with itself. This cycle continues, as the new fatty acid radical reacts in the same way.[1]

Termination [edit]

When a radical reacts with a non-radical, it always produces another radical, which is why the process is called a "chain reaction mechanism". The radical reaction stops when two radicals react and produce a non-radical species. This happens only when the concentration of radical species is high enough for there to be a high probability of collision of two radicals. Living organisms have different molecules that speed up termination by catching free radicals and, therefore, protecting the cell membrane. One important such antioxidant is vitamin E. Other anti-oxidants made within the body include the enzymes superoxide dismutase, catalase, and peroxidase.
Beck et al., 2012- macronutrient-dependent or caloric-related? Unnecessarily enriched nutrition imprints hypothalamic Feeding example: comparing maternal high-fat, high carbohydrate diet resulted in lower arcuate nucleus POMC expression.

(This encodes at this site appetite curbing hormone alpha melanocyte-stimulating- hormone, alpha MSH) and higher paraventricular nucleus NPY and orexin peptide concentrations in their young adult rat offspring)
A decrease in sleep leads to an increase in neuronal activity when presented with food.

Interestingly enough, obesity negatively affects sleep and as a result makes the individual more hungry so they want to eat more.

Rats who had their circadian rhythms affected grew gradually in weight. They also exhibited diminished memory and inflammation mechanisms.
Cognitive performance declines with decrease physical activity and aerobic fitness. (Donnelly et al., 2009)

In more existing studies weight loss may result in improvement of cognitive functions (Gunstad et al., 2011; Siervo et al., 2011) and metabolic control (Ryan et al., 2006)

Both peripheral inflammation and central inflammatory processes may affect the brain in the obese state: it is well accepted that expression of inflammatory cytokine can be induced in brain cells, which then leads to neuronal apoptosis and impaired cognition (Gemma and Bickford., 2007)
Leptin improves cognitive impairment and helps the protective mechanisms in obese individuals.

GLP-1, a hormone obese individuals have a decrease amount of, increases insulin release and helps improve learning.

GLP-1 has also had a beneficial effect against Parkinsons and Alzheimers since it has been linked to decreasing neurodegeneration.

Glucagon-like peptide-1 (GLP-1) is an incretin derived from the transcription product of the proglucagon gene. The major source of GLP-1 in the body is the intestinal L cell that secretes GLP-1 as a gut hormone.
Over-nutrition → Obesity

Hyper-GLP-1

GLP-1 dysfunction?

Hyper-insulinemia

Insulin resistance

↑ Glucagon
↑ Gluconeogenesis
↑ Triglycerides
↓ HDL cholesterol
↑ Adrenal catecholamine
↑ Peripheral vascular resistance
↑ Inflammation

Metabolic syndrome

↑ Appetite
↑ Gastric emptying
↓ Insulin sensitivity
↑ β-cell apoptosis
↑ Gluconeogenesis

Cardiovascular Disease

↑ Cardiac hypertrophy
↓ Cardiac output
↓ Vascular endothelial function
The process an individual goes through when they are obese puts them at risk for diabetes, hypertension, dysglycemia, and metabolic syndrome. There are two ideas which try to classify obesity as a brain disease.

The first one claims that there is an anomaly which deregulates the individual’s diet.

Chronic brain damage evolves secondary to obesity.
Overeating causes hypothalamic inflammation causing there to be a problem with homeostasis regarding energy and insulin.

The structural changes they create further facilitate the anomaly the body is going through.

Much of the problems from obesity can be attributed to genetics and an imbalance of hormones.