Serotonin and Leptin:
Hormonal processes in the brain as regulators of body weight.

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INTRODUCTION

In the last few years significant progress has been made in the study of pathophysiology due to the research of pleiotropic and hormonal interactions and their correlation with behavioral factors. Leptin produced in adipose tissue modulates the negative feedback system towards the Hypothalamus has become widely known as the “appetite” hormone. At the same time, the capability of serotonin transfer is correlated with cholesterol levels.

LEPTIN

- • In common obesity, leptin levels are proportional to the amount of fat, resulting in obesity related to hyperlipidemia and leptin resistance.
- • It has been shown that both normal and long-term recombinant leptin cannot be considered as important therapeutic agents for weight loss and hunger regulation.
- • After weight loss, blood levels of thyroxine, triidothyronine and leptin are decreased, and ghrelin is decreased resulting in hunger and a reduction in the metabolic rate.
- • At the same time, it has been observed that various metabolic and neurohormonal profiles of people who lost weight resemble those of leptin deficient individuals. In other words the state of weight loss can be considered leptin deficiency.
- • Replenishing this hormone promotes further fat loss by increasing the skeletal muscle functioning, sympathetic nervous system, metabolic hormones and T3 / T4 fraction in circulation
- • However, recent research has shown that leptin injection in women with significant weight loss after gastric bypass has no effect on weight, fat mass, energy expenditure, and cortisol and thyroid hormone levels.
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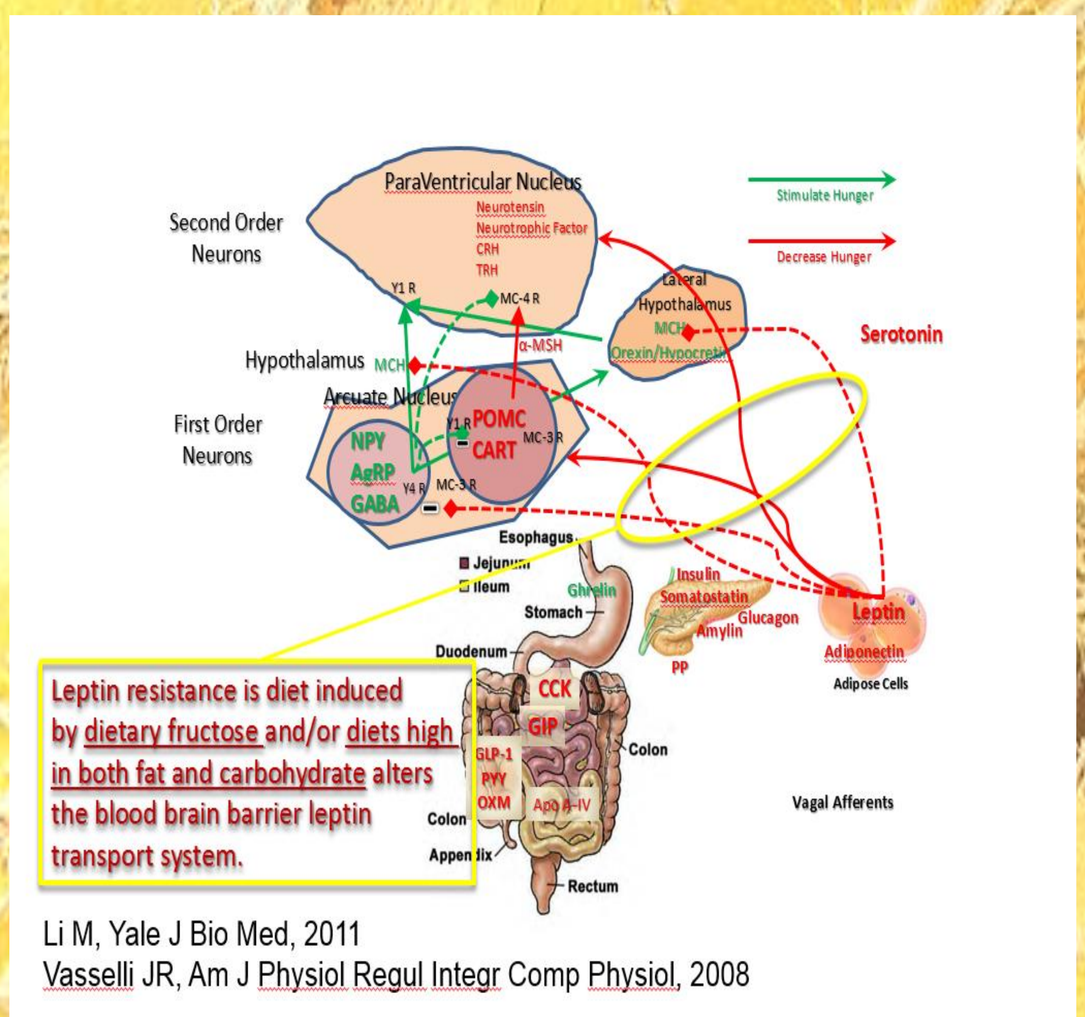
LEPTIN RESISTANCE

Leptin resistance is roughly defined as the presence of elevated levels of the hormone, combined with absence of its physiological biological effect.

- Limited blood-brain barrier permeability, reduced functionality of leptin receptors as well as presence of inflammatory agents have been suggested as potential causes.
- Obesity initiates low-intensity inflammatory processes with CRP, TNF-α and LPS inflammatory mediators, to induce leptin production. High leptin levels in turn induce down-regulation of its respective receptors.
- A high-lipid diet is implicated to induce leptin resistance due to the interaction of the latter with the dietary factor SOC3.
- At the same time, there is a possibility of alteration of the normal microbial flora on the grounds of leptin resistance.



Li M, Yale J Bio Med, 2011
Vasselli JR, Am J Physiol Regul Integr Comp Physiol, 2008

MATERIALS AND METHODS

Review of valid online database (Pubmed, Elsevier). With the use of keywords (microglia, obesity, POMC, brain, serotonin, cholesterol), articles were selected from reliable journals whose results were examined and summed up.

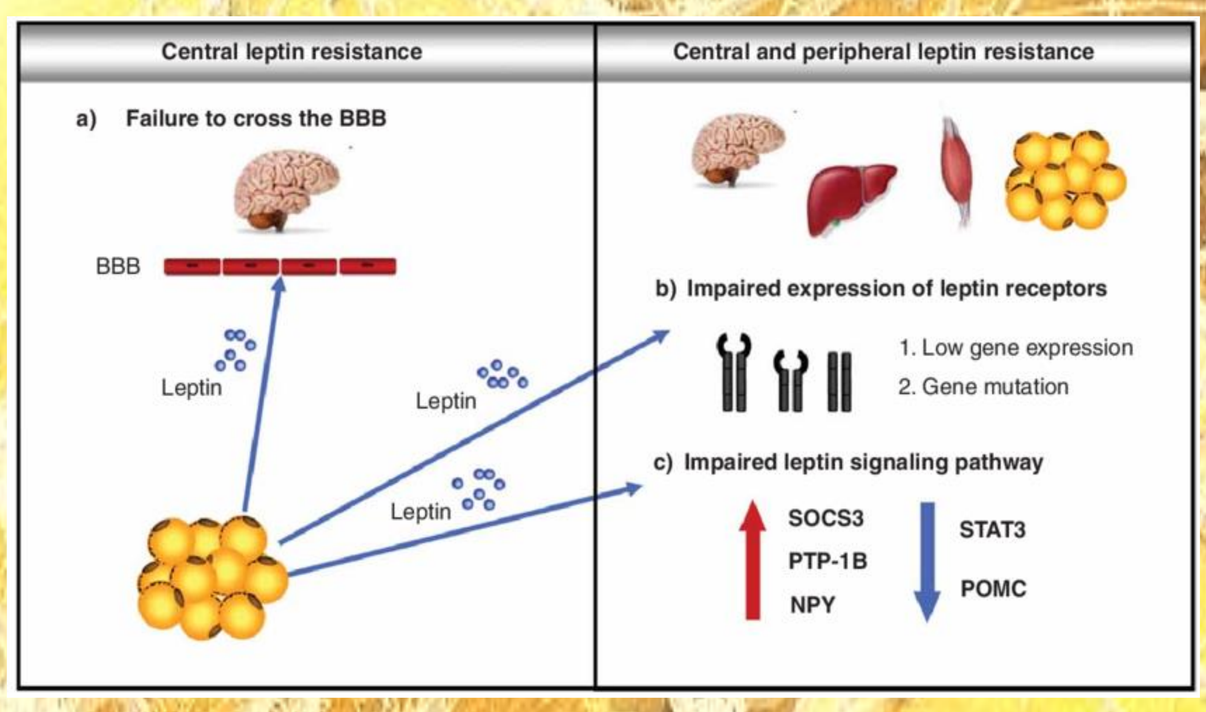
PURPOSE

The aim of this study is to investigate the contribution of the brain to weight control. We focus on the role of leptin and serotonin.

THERAPEUTIC INTERVENTION

- Administration of recombinant human leptin has contributed in:

1. A significant decrease of the body weight and fatty tissue.
2. Restoration of insulin’s effect, Diabetes Mellitus type II and hyperlipidemia treatment
3. CD4+ T cells proliferation and regulation of cytokines production.
4. Treatment of hypothyroidism and Hypogonadotropic hypogonadism.



SEROTONIN

There is a significant correlation between 5HTTLPR polymorphism and lipid levels in all ages. The connection between cholesterol and serotonin was demonstrated in human embryonic cell cultures, where depletion of the former brought up 5-HTT transporter deactivation. In addition, decreased cholesterol levels affect cell membrane fluidity and consequently reduce serotonin uptake.
Although the underlying mechanism has not yet been elucidated, it has been suggested that the lipid bilayers dysfunction could be a potential etiologic factor factor.

Serum levels of total, HDL and LDL cholesterol by serotonin transporter gene linked promoter region (5-HTTLPR) polymorphism in different age groups during a longitudinal study.

	l/l genotype	l/s genotype	s/s genotype	l allele effect (F value)
9 year old				
Total cholesterol	0.071 ± 0.063	−0.047 ± 0.063	−0.092 ± 0.121	0.655, p = 0.419
HDL cholesterol	−0.039 ± 0.063	0.034 ± 0.064	0.020 ± 0.121	0.030, p = 0.862
LDL cholesterol	0.096 ± 0.062	−0.068 ± 0.063	−0.107 ± 0.121	0.887, p = 0.346
15 year old				
Total cholesterol	0.041 ± 0.046	0.004 ± 0.046	−0.158 ± 0.082	4.132, p = 0.042
HDL cholesterol	−0.016 ± 0.046	0.032 ± 0.046	−0.051 ± 0.083	0.218, p = 0.640
LDL cholesterol	0.053 ± 0.046	−0.008 ± 0.046	−0.160 ± 0.082	4.231, p = 0.040
18 year old				
Total cholesterol	0.058 ± 0.051	−0.011 ± 0.050	−0.151 ± 0.093	2.979, p = 0.085
HDL cholesterol	0.006 ± 0.052	−0.003 ± 0.051	−0.007 ± 0.094	0.007, p = 0.932
LDL cholesterol	0.005 ± 0.050	0.054 ± 0.052	−0.194 ± 0.093	4.932, p = 0.026
25 year old				
Total cholesterol	0.067 ± 0.070	−0.026 ± 0.066	−0.098 ± 0.114	0.880, p = 0.348
HDL cholesterol	−0.098 ± 0.070	0.015 ± 0.066	0.213 ± 0.113	4.142, p = 0.042
LDL cholesterol	0.105 ± 0.070	−0.034 ± 0.066	−0.175 ± 0.114	2.802, p = 0.095

Total, HDL and LDL cholesterol levels expressed as mean ± SD. Z-scores stand for cohort adjusted value. In comparison of s/s vs s/l and l/l ANOVA F statistic is presented.

CONCLUSION

Hormonal pathways appear to affect human psychology by controlling the human weight in a biochemical and a behavioral way. This approach seems to complicate our understanding of the mechanisms associated with obesity. However, various data enable the development of new biomarkers and therapeutical approaches.

References

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