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Clinical Review

Fighting Obesity with a Smile

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Understanding the Obesity

- Obesity is multifactorial
- Contributors to obesity:

Genetics, lifestyle and environment

Figure: 1

You mainly know about genetic factors and behavioral factors like (Eating, physical activity, Sleeping, smoking, drinking) that are responsible for obesity. Do you aware that stress also leads to obesity? The aim of this article is to elucidate how stress and obesity might be linked and discuss the cause/consequence relationship between the stress response and obesity. This article will enlighten you about the facts that stress increases the Glucocorticoid hormone, cortisol that fuels obesity.

The mechanistic link between stress and obesity is too complex. Most common reason that people associate is that stress tends to alter the pattern of food consumption and promotes craving of calorie-dense "comfort foods".

However, increased long term cortisol levels are strongly related to abdominal obesity. There are other numerous theories that provide insight to associate the connection of Cortisol with the functioning or pathway of other hormones that are linked to obesity. These insights may lead to more effective and individualized obesity treatment strategies.

Stress: one of environmental factor

Figure: 2

Types of stress

- Social (personal conflicts)
- Physiological/Biological (related to disease, pain, allergic reaction)
- Metabolic (exercise)
- Psychological/Emotional (death of loved ones/ financial crisis)
- Physical stress (long working hours, adjusting to different time zone for frequent travelers, insomnia)
- Chemical (low oxygen)
- Environmental stress (war, temperature, noise, crowd)

What is Stress?

Stress is a nonspecific response of the body to the real or perceived stimulus (by multiple systems in the body) to maintain the most optimal conditions for life.

Figure: 3

Short-term or acute stress is protective and has beneficial effects. A small amount of stress can be healthy and push us to perform efficiently. Stress indeed acts as a vital warning system in case of unknown threat in life. Our body's involuntary instant response protects us by releasing certain hormones that fuels our body with instant energy to deal with the treat. This kind of biological stress is activated for minutes to hours. The hypothalamic-pituitary-adrenal (HPA) axis and Autonomic Nervous system (ANS) play major role that respond to biological stress.

In contrast, ongoing repeated stress with insufficient time to return to a resting state fails the nature's fundamental surviving system and leads to chronic or long- term stress. The stress that lasts for months to years can have significant deleterious effects on health.

Stress fuels obesity

Development of obesity in individuals is not only about energy balance. It could be because of multiple factors viz unhealthy lifestyle behaviors or hormones or stress. These factors may act or interact with each other in such a way that leads to obesity. Figure: 4

Can you imagine stress stimulate weight gain? How many calories does stress have?

Stress may seem to have a small impact but it alters the biochemical profile of the body dramatically and interacts in a way that magnifies the problem of obesity. Stress impairs the functioning of Appetite hormones - Leptin (Satiety hormone) and Gherlin (Hunger hormone) forcing a preferential desire for sugar and fat meals affecting the Insulin response. Stress, when chronic and persistent, affects brain chemistry in a way that changes behavior. These behaviors are directly correlated to obesity and appear to be coming from more unconscious centers of the brain [1].

Response to acute stress

In response to unknown dangerous situation, nervous system sends messages to the adrenal glands atop the kidneys to pump out the hormone epinephrine (also known as adrenaline) and Cate-cholamines. This natural mechanism prepares and protects our body and helps us to cope up with the stress. The blood flow to kidneys, skin and digestive system is reduced that temporarily puts eating on hold in order to charge the body to tackle the sudden endanger. This kind of automotive reflex action is essential to save guard our body in unseen difficult episodes.

Response to chronic stress

Once the effects of adrenaline wear off, cortisol, known as the "stress hormone," hangs around during stress. Once a stressful episode is over, cortisol release from the adrenal cortex, followed by binding to glucocorticoid receptors (GR) in the brain. This signal stops the further release of the stress-induced cortisol and cortisol level decreases to normal. But in case of persistent stress, there is continuous flow of cortisol.

Figure: 5

Stress-induced signaling protein JNK was found to inhibit GR; consequently, this feedback normalization is blocked and cortisol content in blood of depressive patients is permanently high.

In response to stress, adaptogens release stress hormones (NPY and HSP72) into the blood circulating system that stimulate the FOXO protein to stabilize the physiological processes to maintain homeostasis.

Figure: 6

Sustained stress interferes with our body's ability to manage a normal life, affecting the metabolism. It can cause or exacerbate many serious health problems. Cortisol hormone released for long -term stress cause higher insulin levels, your blood sugar drops and you crave sugary, fatty foods. Insulin set the stage for the body to store fat and to gain weight [2].

Influence of cortisol on glucose metabolism

Figure: 7

During stress, HPA axis stimulate the release of Cortisol (by Adrenal cortex) and Catechol-amines (by adrenal medulla). These two catalyzes Glucose metabolism and stimulates glycogenolysis and gluco-neogenesis and this results in high blood sugar levels necessary for fast energy. The higher sugar level consequently stimulates the release of insulin, which leads to an appetite increase.

These processes can cause cravings for "comfort foods," that are high in fat and sugar such as a bag of potato chips or a tub of ice cream that result in obesity. Ongoing stress leads to abdominal obesity, insulin resistance that is responsible for vicious cycle of obesity.

Influence of cortisol on lipid metabolism

In response to stress, Mitochondria swiftly satisfy the enhanced energy demand. Cortisol, the major glucocorticoids increase circulating glucose levels by acting simultaneously on the liver, skeletal muscle and adipose tissue (White and Brown Adipose Tissue (Magomedova and Cummins, 2016).

During stress or starvation, the increased mobilization of fats, combined with increased oxidation of fatty acids in the cells, helps shift the metabolic systems of the cells from utilization of glucose for energy to utilization of fatty acids. Cortisol stimulates lipolysis causing insulin resistance via an increase in circulating FFAs. The insulin resistance is responsible for obesity.

Figure: 8

 $https://www.researchgate.net/figure/Schematic-view-of-the-\\role-of-GCs-in-lipid-metabolism-in-the-liver-white-adipose-\\tissue_fig2_275587013$

Mechanism underlying the exacerbation of obesity due to mental stress

Mental stress induces two kinds of responses: physiological and behavioural responses. In terms of physiological responses, the sympathetic nervous system and HPA axis are activated. Under the activation of these two major systems, a wide variety of cellular events are involved that explain the pathogenesis of insulin resistance, dyslipidaemia, atherosclerosis and obesity.

Figure: 9

 $https://www.researchgate.net/figure/Mechanisms-underlying-the-exacerbation-of-cardiovascular-disease-due-to-mental-stress_fig2_260374112$

HPA axis suppresses with Thyroid function

During chronic stress, the cortisol is released by adrenals. The elevated cortisol depresses the functioning of HPA axis through negative feedback loop. Too much cortisol, stimulate the thyroid to work harder to create sufficient amounts of thyroid hormone.

Secondly, High levels of cortisol decrease the liver's ability to clear excess estrogen from the blood, that in turn increases the level of TBG protein. These TBG protein binds with thyroid hormone turning it inactive and cannot activate cellular receptors resulting in drop of free T3 and T4.

Since, Thyroid gland is the master gland that controls most of our organ's functionality. Eventually metabolism will be slow that leads to obesity.

Figure: 10

 $https://www.researchgate.net/figure/effect-of-stress-on-HPA-and-HPT-axis-CRH-corticotrophin-releasing-hormone_\\fig1_30330765\red{7}$

Stress affects leptin and ghrelin signaling

Leptin, the Satiety hormone produced by adipose tissue regulates both our appetite and metabolism.

During stress, there is problem in leptin signaling cascade. Because of this it cannot perform its job that way it is supposed to. That leads to increase appetite contributing to weight gain.

Leptin levels affect the Ghrelin level. Since during stress, leptin signaling is impaired, ghrelin's response gets affected and we tend to overeat

Figure: 11

Stress elevates Neuropeptide Y

NPY is one of the chemicals released by HPA axis which regulates flight or fight response. Release of NPY and activation of NPY2R (its Y2 receptor) stimulates the proliferation and differentiation of pre-adipocytes to new adipocytes, fat angiogenesis (the development of new blood vessels), macrophage infiltration, (responsible for the production of Inflammatory cytokines that have been shown to suppress thyroid receptor site sensitivity and causes insulin resistance resulting in abdominal obesity and a metabolic syndrome-like condition.

Figure: 12

http://www.scielo.br/scielo.php?script=sci_arttext&pid =S0104-42302014000100084 https://www.frontiersin.org/files/Articles/136821/fncel-09-00085-HTML/image_m/fncel-09-00085-g001.jpg

Cortisol: the villain in metabolic syndrome

Chronic stress, mainly through HPA axis dysregulation, promotes the accumulation of visceral fat. VAT can cause alterations in fatty acid metabolism. Visceral obesity results in an increase in interleukin (IL)-6, and other adipokines, which in turn result in in-

sulin resistance. VAT also induces increased lipolysis and free fatty acids, which also cause insulin resistance. IR is one of the major factors that leads to metabolic syndrome.

Figure: 13

http://www.scielo.br/scielo.php?script=sci_arttext&pid =\$0104-42302014000100084

Chronic Stress and obesity: Insulin link

The stress act as stimulus that activates HPA and cortisol is released as a result of physiological adaptation. Cortisol directs insulin to restrict glucose uptake in peripheral tissues in order to meet increased energy requirement to face the challenge. Cortisol might also influence glucose metabolism, possibly by stimulating gluconeogenesis in the liver, leading to increased plasma glucose.

After responding to fight or flee mechanism, insulin rebalances blood glucose levels and glucose are welcomed back into the cells. Whereas During prolonged stress, the signaling switch gets impaired and cells become insensitive to insulin, consequences leading to weight gain and obesity.

Figure: 14

https://www.researchgate.net/post/Chronic_Stress_and_Obesity

Stress and binge eating: vicious cycle

This is common in the events of emotional stress.

Stress increases cortisol. This in turn enhances the craving for comfort foods (sugar and fat foods like muffins, ice-creams) - feel good hormone released- temporarily feel better. Cortisol wears off the serotonin and dopamine. Guilt/shame/Anger leads to stress and cycle goes on.

Figure: 15

https://www.cambridge.org/core/journals/the-british-journalof-psychiatry/article/cortisol-serotonin-and-depression-allstressed-out/766A58A46F537EA85FB5CB9AEDF33552

Cortisol affects metabolism

Cortisol is a steroid hormone that regulates a wide range of vital processes throughout the body. It helps in controlling the body's blood sugar levels during stressed condition by gluconeogenesis. For the uptake of increased glucose, insulin is released. The high levels of cortisol, on the other hand, blocks the uptake of glucose by muscles via the GLUT4 transporter.

Cortisol affects metabolism as it is intimately related to thyroid function. During stressful condition, high cortisol levels decrease the conversion of thyroxine (T4) to triiodothyronine (T3) this means lower thyroid function, hence poor metabolism and weight gain.

Figure: 16 www.ncbi.nlm.nih.gov/books/NBK26/#A460

Stress/Sleep merry go round

Worry is a major cause of insomnia. Our minds are overactive and won't switch off. Stress is both a cause and consequence of eating disorder. Stress also activates HPA axis, that stimulates the release of more cortisol that impairs sleep and causes insulin resistance.

Lack of sleep may disrupt the functioning of ghrelin and leptin—chemicals that control appetite. More appetite means more food intake that leads to weight gain.

Figure: 17 http://sleepscience.org.br/details/236

Coping with stress

It is not easy to cope with stress but following few relaxation techniques to deal with stress is essential for overall health.

Practice meditation, Gardening, yoga, tai chi, controlled breathing, listening to music, reading a good book, progressive muscle relaxation, playing with a pet, taking a nap, massage therapy, aromatherapy, reducing caffeine intake, writing, walking, join group laughter club, and connection with friends and family.

Change the perception

By reframing the thought (you cannot change a person or situation, but you can change the way you think.)

The way we perceive and interpret life impacts our health.

Beliefs, thoughts and emotions create the chemical reactions that affects every cell. Our cells are constantly processing and metabolizing our experiences according to our personal views.

Just think you can walk with comfortable shoes even on the pebbles. whereas it's difficult to walk on a smooth road if there is a pebble inside your shoe. The one pebble inside our shoe is the negative attitude that makes our life terrible, not the external challenges. How you experience every situation is you (unpleasantness is happening from within you).

How to overcome negative attitude practice self-awareness, forgiveness, start counting the blessings and by reframing the thought.

Figure: 19

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