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Sustained Up-regulated Autophagy (SUA) without Anorexia –Aetiology of Morbid Obesity and Anorexia Nervosa

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Abstract

Morbid obesity and anorexia nervosa (AN) are serious health problems with devastating consequences. Nevertheless, the aetiology of them is still elusive. By natural weight loss, one of the authors of this paper experienced a process from overweight to AN. And by adopting the anorexic Luigi Cornaro diet, he recovered from AN. Based on his unique experience, we hypothesize that the sustained up-regulated autophagy (SUA) without anorexia is the mechanism behind morbid obesity and AN. The main feature of a person with fully developed SUA without anorexia is that, starvation becomes anxiolytic, and normal eating is quite stressful. As SUA perpetually provides the host with plenty of recycled energy and nutrients from each cell of the body, daily regular restrictive eating becomes a natural requisite. Failing which and eating normally will lead to morbid obesity. At the other extreme, eating too less or long time fasting will result in atypical AN or AN. Patients with morbid obesity, atypical AN or AN are thus forced to adopt the Luigi Cornaro diet of eat-but-little. In this way, they can maintain or restore the homeostasis of their gut mucosa and healthy body weight, and lead an illness-free long life. As a precaution, we suggest that the attitude of a person towards normal eating and starvation should be a diagnosing criterion to determine the degree of a person in development of SUA in his body, and carry out early intervention if he is found to be prone to morbid obesity, AN or AAN.

Keywords: Autophagy; sustained up-regulated autophagy (SUA); Illness induced anorexia; Morbid obesity; Anorexia nervosa; Luigi cornaro diet; Anxiolytic; Gut mucosa homeostasis; Atrophy and dysfunction

Introduction

Overweight and obesity affect billions of people globally, and become a major health issue in recent decades, resulting in diseases include cardiovascular disease, Type II diabetes and certain types of cancer, which are the leading causes of preventable death [1]. On the other extreme, although relatively uncommon, anorexia nervosa (AN) represents a public health concern due to its severe physical and emotional consequences and high rate of recurrence, along with frequently under-treatment [2]. Despite the highly devastating consequences of obesity and AN, the aetiology of them is still elusive. It is suggested that a complex combination of biological, psychological and environmental factors contributes to the development of obesity and AN.

In a letter to the BMJ, We (BW and BX) have reported that, one of the authors of this paper (LG, hereafter refers as the patient) had developed plantar fasciitis due to overweight, and we designed a natural weight loss process by eating less and fasting which greatly relieve the plantar fasciitis of our patient [3]. As the benefit is so big and obvious, our patient had continued the fasting and eating less process, and accidently developed anorexia nervosa (AN). By adopting the Luigi Cornaro diet, he recovered from AN [4,5]. Since then, He has been following the Luigi Cornaro diet for more than one year, and he is able to maintain a normal body weight of around 50 to 52 kg. He is now extremely healthier than ever, and the good effects reported by Luigi Cornaro are gradually shown on him.

From this unique experience of our patient, we suspect that morbid obesity and AN have the same aetiology. We propose that the sustained up-regulated autophagy (SUA) without anorexia (loss of appetite) is the mechanism behind morbid obesity and anorexia nervosa (AN). To explain our hypothesis above, it is necessary to understand how up-regulated autophagy (UA) is triggered.

Up-regulated autophagy (UA) accompanied with Illness induced anorexia

Autophagy is an evolutionarily conserved catabolic process, which mediates the degradation of altered or dysfunctional proteins and organelles and the elimination of invading

microorganisms, and allows cells to reutilize the constituents of these degraded organelles for energy or protein synthesis when nutrients are scarce [6,7]. Autophagy occurs at low basal levels in virtually all cells to perform homeostatic functions such as protein and organelle turnover. Autophagy is rapidly up-regulated when intracellular nutrients and energy are needed for cells during starvation, growth factor withdrawal, oxidation, and pathogen invasion. During infection, up-regulated autophagy has a specific role in the capture and degradation of intracellular bacteria and viruses, a process termed as xenophagy [8-10].While infection up regulates autophagy, decreased food consumption (anorexia) is the most common sign of infection [11]. This illness induced anorexia is an active host defence strategy for pathogen elimination and health recovery [12-14]. During this up-regulated autophagy (illness induced anorexia) process the constituents of the pathogen and dysfunctional/damaged organelles in the cell are degraded, recycled and reused for energy or protein synthesis [15-18]. In this way, up-regulated autophagy as a catabolic process provides the host with plenty of energy and nutrients. To avoid over-nutrition, it seems that our body intentionally induced anorexia (loss of appetite) as a counter measure against up-regulated autophagy.

Sustained Up-regulated Autophagy (SUA) without anorexia and Weight Gain

Most of the dieters find that it is very difficult in maintaining their weight loss, and they regain their weight back in long term [19]. The common explanation for this yo-yo effect is that our body has a setting point for body weight, and any deviation to this point is not sustainable [20]. Nevertheless, the experience of our patient gives an exception for such explanation. By adopting the Luigi Cornaro diet, he successfully maintains a low healthy weight with a BMI around 20 after losing more than 20% of his initial body weight [4,5]. Moreover, the basal metabolism rate for our patient is above normal person, despite the extremely low amount of daily food intake of the anorexic Luigi Cornaro diet. As long as he eats a little more, his body weight will increase proportionally to the amount of excessive food. To explain this phenomenon, we suggest that the sustained up-regulated autophagy (SUA) without anorexia plays an import role in weight gain.

Historically, metabolic disorders like obesity have been viewed as lipid storage disorders because of over-nutrition. Recent research shows that chronic low-grade inflammation plays a decisive role in the initiation, propagation, and development of obesity, and may even precede and predispose to obesity [21-24]. As stated in section 2, during infection, illness induced anorexia (up-regulated autophagy) is triggered to eliminate pathogens. In normal healthy person, illness induced anorexia (up-regulated autophagy) is transit, and has no side effect. However, in certain persons, infection becomes chronic, and up-regulated autophagy is repeatedly triggered. Eventually up-regulated autophagy becomes sustained, and the accompanying illness induced anorexia (loss of appetite) vanishes. The bodies of these persons are thus able to remain in this sustained up-regulated autophagy (SUA) state after the elimination of the triggering illness or severe stress. When a person is born with weak constitution, he is more prone to chronic infection or other chronic illness in early childhood, up-regulated autophagy is triggered repeatedly, so that he has more chance to have fully developed SUA when he is in his childhood.

Infection is only one of the numerous triggers of up-regulated autophagy. Other triggers are also able to contribute to the development of SUA if the triggers become chronic, as shown in **Figure 1**.

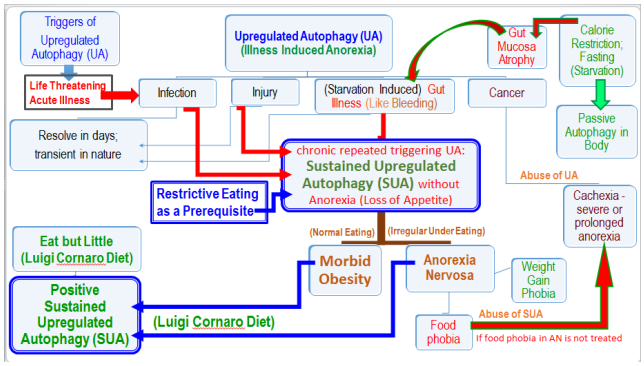

Figure 1: Development of SUA if the triggers become chronic.

Just as up-regulated autophagy is triggered in infection to eliminate pathogen, SUA is also developed to eliminate the chronic infection or other chronic diseases. The main feature of a person with fully developed SUA without anorexia in his body is that, starvation becomes anxiolytic. That is to say, he feels very energetic, calm and comfort when he is in fasting (empty stomach) state or eats very less, and normal eating becomes quite stressful although he may have a very good appetite [25-27]. This is because, SUA perpetually provides the host with plenty of recycled energy and nutrients from each cell in the body. Therefore, similar to the fact that UA is normally accompanied by illness induced anorexia, regular restrictive eating (i.e., only eating the right small amount of food, no more, no less) now becomes a natural requisite by SUA. By regular restrictive eating, SUA will naturally ward off the most common diseases, and a long and illness free life can be achieved. Yet, if SUA is fully developed without the self-awareness of the patients, serious health problem will occur. For them, normal eating creates too much nutrition and energy which leads to morbid obesity, and the anxiolytic nature of starvation makes them feel comfortable with irregular restrictive eating and long-time fasting, resulting in the atrophy and dysfunction of gut mucosa, which contributes to the development of atypical AN or AN, featured by food phobia [4,5].

Historical persons with fully developed SUA in their bodies - Luigi Cornaro and Angus Barbieri

As chronic illnesses are very common in population, especially for people with weak bodies, and the chance of a person having chronic illness grows with growing age, the prevalence of fully developed SUA in population might be very high. All AN patients have fully developed SUA inside their bodies. That is why

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although they eat very less, they always feel energetic, and tend to over-exercises. Ordinary people have some degree of SUA developed in their body with the degrees in between that of normal healthy persons and that of morbid-obesity/AN persons.

People with morbid obesity also have fully developed SUA, here we give two examples. Luigi Cornaro is one of them. Luigi Cornaro was born in Venice in 1464 into the noble Cornaro family. One can find his story in detail in his book [28]. The special feature of his body is that he was quite comfortable with eating very less. In his Discourse he wrote: "The consequence was that in a few days I began to perceive that such a course (to live a strictly sober and regular life) agreed well with me". This is a strong indicator that because of his "weak constitution" and chronic illness in childhood, he had fully triggered SUA in his body before he embarks on the restrictive eating, or even before he became morbidly obese. He was very lucky to find that the regular restrictive eating was the only suitable lifestyle for his body condition, so that he lived a long, happy and illness free life with the protection of fully developed SUA. Another person who was also very comfortable with eating very less was Angus Barbieri [29]. His 382-day fasting sets a world record. Yet, he was not aware that he had fully developed SUA in his body, and regular restrictive eating was necessary for his body condition. He had obviously developed atypical anorexia nervosa after the long fasting. This was reflected by the fact that, five years later after the fasting, he had only regained 16 pounds (7.3 kg) [29]. which is quite unusual, indicating that he could not resume normal eating after the fasting, and had eaten irregularly and fasting occasionally. If he ate normally after the long fasting, he would have regained his weight back in these five years [19]. Angus Barbieri tragically died in September 1990 at the premature age of 51-year-old [30]. If he was aware that his body was in SUA condition, and adopted the Luigi Cornaro diet after his long fasting, he would be still healthily living now at the age of 81, and might continue to live beyond the age of 100 like Luigi Cornaro.

Gut protection as the most important issue for health

The tragedy of Angus Barbieri shows that regular eating is very important for our health, especially for persons have fully developed SUA, and are forced to eat very little. This is because, by regular eating, we are protecting our gut mucosa from atrophy and dysfunction. We all think that our stomach is inside of our body. Yet, the most important part of our stomach, the gut mucosa, is actually separating itself and the content of our stomach (the eaten food) from our main body [31,32]. The gut mucosa forms a strong barrier between itself and our main body. Because of this barrier, the nutrition for our stomach mucosa cannot be obtained from our main body, and is solely relaying on the food we eat. Short duration (<18 h) fasting is good for resting gut mucosa and recovering it from any minor injury during food digestion. Yet, long duration fasting (fasting longer than 24 h) will result in gut mucosa atrophy and dysfunction, and may lead to bacteria translocation and sepsis [33,34]. So in order to maintain the homeostasis of the gut mucosa, frequent food intake during the day is necessary.

Conclusion

Based on the unique experience of our patient on weight loss and weight management, we hypothesize that sustained up-regulated autophagy (SUA) without anorexia is the cause for morbid obesity and anorexia nervosa. As chronic illness induced fully-developed SUA perpetually provides the host with plenty of recycled energy and nutrients, daily regular restrictive eating (i.e., only eating the right small amount of food, no more, no less) become a natural requisite. Normal eating creates too much nutrition and energy which leads to morbid obesity and the anxiolytic nature of starvation makes these persons feel comfortable with long time fasting or irregular eating, resulting in the atrophy and dysfunction of gut mucosa, which contributes to the development of atypical anorexia nervosa (AAN) or anorexia nervosa (AN). Patients with morbid obesity, AN or AAN are thus forced to adopt the anorexic Luigi Cornaro diet of eat-but-little. In this way, they can maintain or restore the homeostasis of their gut mucosa by the small amount of food they eat and avoid over-nutrition or under-nutrition at the same time, and lead a healthy, happy and long life. As a precaution, we suggest that the attitude of a person towards normal eating and starvation should be a diagnosing criterion to determine whether a person has fully developed SUA without anorexia in his body or not, thus to predict the proneness of a person in developing morbid obesity, AN or AAN, and carry out early intervention.

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