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Food addiction: Detox and abstinence reinterpreted?

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ABSTRACT

The senior patient and/or the geriatrician are confronted with a confusing literature describing how patients interested in combating metabolic syndrome, diabesity (diabetes plus obesity) or simple obesity might best proceed. The present paper gives a brief outline of the basic disease processes that underlie metabolic pro-inflammation, including how one might go about devising the most potent and practical detoxification from such metabolic compromise. The role that dietary restriction plays in pro-inflammatory detoxification (*detox*), including how a modified fast (selective food abstinence) is incorporated into this process, is developed. The unique aspects of geriatric bariatric medicine are elucidated, including the concepts of sarcopenia and the obesity paradox. Important caveats involving the senior seeking weight loss are offered. By the end of the paper, the reader will have a greater appreciation for the challenges and opportunities that lie ahead for geriatric patients who wish to overcome food addiction and reverse pro-inflammatory states of ill-heath. This includes the toxic metabolic processes that create obesity complicated by type 2 diabetes mellitus (T2DM) which collectively we call *diabesity*. In that regard, diabesity is often the central pathology that leads to the evolution of the metabolic syndrome. The paper also affords the reader a solid review of the neurometabolic processes that effectuate anorexigenic versus orexigenic inputs to obesity that drive food addiction. We argue that these processes lead to either weight gain or weight loss by a tripartite system involving metabolic, addictive and relational levels of organismal functioning. Recalibrating the way we negotiate these three levels of daily functioning often determines success or failure in terms of overcoming metabolic syndrome and food addiction.

1. Introduction

In substance addiction the concepts of detox (eliminating the substance from the body) and abstinence (desist using/taking the substance for a specified time) are well understood. In the controversial concept of food addiction, both complete detox and total abstinence from all food is not possible, so both terms must be redefined. In this article, we will briefly examine how food addiction plays a meaningful role in geriatric obesity/diabesity (again, where diabesity is defined as the combination of obesity and T2DM). Even though our focus is on seniors, the basic bariatric (i.e. weight) observations we make herein are essentially equally valid to other age groups as well. We will examine the role that fasting (in its various forms) may have on metabolic health and weight loss interventions to assist seniors afflicted with obesity/diabesity. The challenge will be to outline potential advantages that medically supervised dietary restriction (including fasting) might have on the management of obesity/diabesity, while simultaneously factoring-in the impact that food addictions may have on the outcome of such interventions. Hopefully, by cross calibrating the influences of both these entities (modified fasting [i.e. selective abstinence] and food addiction) we can better formulate more effective and durable treatments to serve both the obese and diabese (obese and diabetic) geriatric populations.

2. Geriatric obesity/diabesity

2.1. Magnitude of the problem

In terms of the definition and magnitude of the problem, Kyrou and Tsigos (2009) point out that geriatric obesity (like other forms of obesity in younger populations) is a growing worldwide problem. They offer that T2DM has evolved in tandem with the obesity epidemic creating unique challenges in the care and management of the diabese patient. Houston et al. (2009) argue there is a growing prevalence of obesity among older adults.

There is little argument that increased morbidity and mortality are associated with marked obesity; to be sure, there is even evidence that ideal longevity may be garnered from weights some 10% below the current US average (Manson et al. 1987). Similarly, diabetes (which is often complicated by obesity) is associated with increased morbidity and mortality in all age groups (Choudhary et al., 2012). The real challenge, however, is how to calibrate desired weight to mortality ratios since geriatric obesity is confounded by two important issues: 1) sarcopenia/sarcopenic obesity (Miller and Wolfe, 2008) which can be defined as the coexistence of diminished lean (i.e. muscle) mass and increased fat mass and 2) the obesity paradox

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of aging (Chapman, 2010). As Miller and Wolfe (2008) point out, it is hard to gauge the exact impact of weight on morbidity in aged populations since BMI (body mass index) may be a poor predictor of disease outcome. For example, these same researchers emphasize that BMI does *not* correlate as strongly with adverse health outcomes (e.g. cardiovascular disease) in the aged as it does in younger populations. In fact, weight loss and a low BMI are actually associated with increased mortality, at least in some seniors. Therefore, many experts in the field of geriatric bariatric medicine caution against caloric restriction in the elderly, even though weight loss is associated with increased mobility and improved daily functioning in many elderly persons.

2.2. The obesity paradox/sarcopenia further explained

Adding to the complexity and confusion of assessing the impact of diabesity and obesity in the elderly, Chapman (2010) has elaborated further on the obesity paradox. In the elderly, although being overweight is often associated with increased morbidity (e.g. risk of cardiovascular disease), it may be paradoxically associated with decreased mortality. The upshot of Chapman's recommendations has to do with not focusing entirely on weight loss in seniors, but equally focusing on limiting sarcopenia (see above) by emphasizing exercise and increased protein intake (to improve lean body mass, overall mobility and improved quality of life). More recently, Chang et al. (2012) have stressed that current clinical guidelines on healthy weight in the elderly should be reconfigured toward heavier weight acceptable targets.

Nonetheless, studies continue to reveal clear-cut association between abdominal obesity and insulin resistance (which includes the metabolic syndrome) with advancing age. As such, this gain in weight coupled with insulin resistance *does* have a dramatic adverse impact on the quality of life of geriatric patients (Sakurai et al., 2010).

3. Food addiction

3.1. Defining food addiction

The term “food addiction” has progressively evolved in the world literature with some of its core early development taking shape through the prescient work of Gold (Gold and Sternbach, 1984) and others (Liu et al., 2010). Elsewhere, Shriner has offered the following definition:

Food addiction represents a pervasive and enduring pattern of both food perception and food-related behavior (leading to either excessive food ingestion or aversion) whose dual valence (i.e. perception and behavior) biases interaction with food in harmful and unhealthy ways. Such a biasing and unhealthy valence toward food continues, despite knowledge of its harmful consequences. Food addicts usually present with both a tolerance (i.e. a need to increase participation in their harmful relationships with food over space and time) as well as a form of withdrawal (including anxiety, craving, depression or anger) when deprived of access to addictive foods. This latter emotional and behavioral reactivity must reliably occur during efforts to either alter or disrupt the food addict's harmful and maladaptive pattern of eating (Shriner and Gold, 2010).

3.2. Behavioral modeling

Although the above definition for food addiction is somewhat cumbersome, it follows the structure and criteria set forth for addiction in the DSM-IV-TR (APA, 2000). Expanding on this sort of DSM-like framework, researchers in food addiction (including Gearhardt et al., 2009), have greatly improved our understanding of this disease state. Such work seeks to offer both scientific and evidence-based data to support and define how food can create addictive behavior. Focusing on the neuroanatomical versus behavioral aspects of macronutrient intake (e.g. fat versus sugar), Hoebel et al. (2009) have made fundamental contributions to the science of food addiction. Using animal models, they have shown how specific types of macronutrient exposure cross indexed against different feeding schedules (continuous feeding versus intermittent), may create binge eating and explain, in part, how food addiction evolves. For example, rats fed cafeteria style rat chow (high in fat and high in sugar) tend to binge with much higher frequency than those fed standard chow. Alternatively, placing rats on intermittent feeding (episodic access to chow), increased binge eating whereas continuous access to food did not. These sorts of investigations have shed light on how humans indulging themselves on fast foods and then denying themselves access (perhaps out of guilt and shame) may be setting themselves up for binge eating down line. The bench lab science on rats and feeding behaviors would argue that patients should not feed/starve themselves when dieting, but rather eat rationally constructed non-cafeteria style foods throughout the day.

3.3. Neurometabolic neuroimaging links food to addiction and argues for changes in therapy

Moving from behavioral modeling of food macronutrient content and scheduling of feedings to actual neurometabolic process and neuroimaging, Wang et al. (2009) have verified how obese subjects (both animal and human) show the same neuroimaging of the brain we see in addictive disorders. These patterns of neurochemical changes seen for obesity and food addiction are the same patterns Gold has suggested are found for other substances that induce addictions such as cocaine, opioids, etc. (Gold and Sternbach, 1984). In other words, as we just suggested in the previous section, it appears that food (namely sugar) when eaten intermittently, may foster the same bingeing behaviors we see with other addictive substances such as alcohol, opioids, cocaine, etc. In continuity with this argument, Hoebel et al. (2009) have shown that sugar is a powerful addictive substance. Sugar (like other addictive substances) is able to stimulate the two key classic neurotransmitters of addiction: 1) dopamine and 2) mu-opioids. It then follows, since food is capable of eliciting addiction, including the same neuroanatomical and behavioral changes we see in alcoholism and drug addiction, obesity and its treatment might want to emulate programs that treat addiction, specifically—programs that help to foster food sobriety and support groups to maintain such sobriety over time. To date, however, most weight programs are strictly one on one interventions using chemicals or diets, and 95% of diets will fail over time.

In summary, as with other forms of addiction (e.g. alcoholism), overcoming food addiction and obesity is not just about counting calories or relieving stress, it's also about joining support groups and seeking validation through others, in order to achieve food sobriety over time. It involves dedicating one's life to a more resilient way of eating and exercising for a lifetime as has been shown in the National Weight Control Registry (Graham et al., 2011). Just like overcoming alcohol or any other addictive form of living, food sobriety requires constant work and commitment. Unfortunately, most insurance companies still fail to grasp the importance of addiction in obesity. Thus, they rarely cover (pay for) obesity support groups and/or the basic principles of recovery and/or relapse prevention.

4. Fasting/caloric restriction

4.1. Caloric restriction as a component of fasting

The concept that caloric restriction may be associated with greater longevity was first suggested by the pioneering work of Clive McCay as outlined by Kemnitz in his recent paper on caloric restriction in nonhuman primates (Kemnitz, 2011). This paper argues that caloric

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restriction results in lower fat, lower rates of T2DM, lower incidence of neoplasia, improved insulin sensitivity, etc., in rhesus monkeys. In other words, these primates may live longer. We should note, however, more recently, Mattison et al. (2012) have challenged this idea, presenting recent data that may refute Kemnitz's longevity claim. Obviously, more research in this area needs to be done.

Regardless, caloric restriction (CR) does have therapeutic effects on insulin resistance (Kemnitz, 2011) and pro-inflammation, thus, fasting or modified abstinence might play a role in healthy geriatric weight modification. Within this framework of discussion, Trepanowski and Bloomer (2010) have defined fasting as, "a partial or total abstention from all foods, or a select abstention from prohibited foods." In terms of this paper, this includes liquids (especially liquids that constitute calorie rich colas) since they represent a type of liquid food. In general, liquid foods would include such things as high fructose colas, protein shakes, alcohol, etc., but would not include water.

4.2. Three basic types of fasting

Trepanowski and Bloomer (2010) have highlighted some interesting insights regarding fasting, outlining 3 basic forms of a fast: 1) CR (caloric restriction), 2) ADF (alternate-day fasting), and 3) DR (dietary restriction). CR (in agreement with Kemnitz's observations above) results in overall improvements in global health. This includes a decrease in fasting glucose, insulin level, increased insulin sensitivity, decrease in body fat and lower overall incidence of diabetes (Trepanowski and Bloomer, 2010). On the other hand, ADF fasts improve insulin sensitivity only in men but actually cause impaired glucose tolerance in women. Finally, DR fasts show no increase in longevity (with either carbohydrate or fat restriction), but protein restriction improves longevity by 20% (these results were only given for animal not human subjects).

4.3. Fundamental metabolic toxicity

Elsewhere, Horne (2011) has suggested that caloric deprivation may favor the genomic expression of FOXA (PHA-4) in worms which leads to greater longevity. This FOXA gene is implicated in humans to regulate glucose homeostasis. It is important that the reader remember this, since (as we will argue below) carbohydrates may be the initiator of destructive fatty oxidation of tissues (called glucolipotoxicity.) That said, Horne goes on to argue that human growth hormone (HGH) is increased during fasting and has an antagonistic effect on insulin as well as a direct effect on the induction of lipolysis. He also stresses that research has proven an associated lower risk of coronary artery disease (CAD) in humans who fast.

Summarizing, Horne speculates that fasting in humans might have positive effects on health and longevity by creating biological changes that decrease adipose tissue (via lipolysis), reduce insulin resistance, and have ameliorative effects on cardiovascular risk (Horne et al., 2008). More recently, Horne et al. (2012), have published more definitive work on periodic fasting and diabetes mellitus showing that periodic fasting was associated with lower prevalence of diabetes mellitus in patients undergoing coronary angiography.

5. Detox/receptor "reset"

5.1. Pro-inflammation: the common denominator

When we reflect on a common denominator that underscores the pathological impact of obesity/diabesity on humans (including the elderly), Shriner (2011) and others (Vgontzas et al., 2000; Xu et al., 2003) have pointed out that pro-inflammation lies at the center of this entire issue. In terms of metabolic receptors that either cause or prevent obesity or diabesity (e.g. the insulin receptor), when such receptors become dysfunctional because of inflammation, we can speak of a need to reset such receptors in order to reapproximate a state of health. This often involves detoxifying the organism from those environmental agents that are fostering the development of inflammation. An example might be detoxifying children from the pro-inflammatory effects of high fructose sugar colas.

Obesity and diabetes, together with hyperlipidemia and hypertension, contribute to the profound disease state of pro-inflammation we call the metabolic syndrome. This syndrome now threatens large populations of humans across the world. The geriatric patient is neither immune nor invulnerable to the wrath of metabolic syndrome, nor to the pro-inflammatory processes it promulgates. It can now be argued that future medical interventions that lead to a cure of the metabolic syndrome will need to involve detoxifying patients from pro-inflammatory foods that are threatening the healthy integrity of important metabolic receptors. For example, this involves in the case of diabesity the *reset* of pathologically inflamed insulin receptors, transforming them from a state of pro-inflammation back to a de novo state of non-inflammation whenever possible.

5.2. High fructose corn syrup and glucolipotoxicity

In terms of receptor pro-inflammatory detoxification and resets, a critical scientific argument on the impact of high fructose corn syrup (HFCS) on hepatic function was recently offered by Lustig (2010). This argument maintains that HFCS may have a pivotal toxic influence on metabolic receptors that determine insulin sensitivity and T2DM expression. HFCS causes the liver to become a more thermodynamically selfish organ. This change in hepatic functioning induced by HFCS causes the liver to extract over 400% more energy equivalents, resulting in increased hepatic fatty deposition within the liver parenchyma. This includes skewing oxidative over reductive processes within the liver causing hepatic hyperlipidemia. Ensuing hepatic oxidative damage occurs both locally (within the liver) and more distally (at the level of insulin receptors located in peripheral tissues). Again, this toxic cascade of oxidation and dyslipidemia can be traced back to the initial upsetting impact that HFCS has on hepatic function. Lustig's metabolic arguments give us a clear example of how carbohydrates (HFCS) interacting with fats (dyslipidemia) can effectuate oxidative destruction of liver tissue (called necrosis). Altogether, we call this sugar + fat = oxidative destruction of tissue—*glucolipotoxicity*.

Here are some of the essential elements of the toxic cascade of HFCS glucolipotoxicity:

- HFCS increases fructose-1-P which causes hepatic insulin resistance.
- HFCS creates excess potential reducing equivalents of pyruvate which stimulates hepatic dyslipidemia over time.
- HFCS (by inducing dyslipidemia) contributes to muscle insulin resistance.
- HFCS's increased induction of fructose-1-P induces PPAR-gamma that stimulates de novo lipogenesis and another aggravation of dyslipidemia.
- HFCS's impact on fructose-1-P/fructose chemistry indirectly increases Foxo1 which then goes on to stimulate hepatic gluconeogenesis, which aggravates hyperglycemia and ultimately insulin secretion and insulin resistance over time.
- HFCS's impact on fructose-1-P/fructose chemistry also inhibits NO which blocks vascular muscular relaxation contributing to the hypertension.
- HFCS's capacity to stimulate net hyperinsulinemia (from the processes outlined above) results in leptin resistance which stimulates hyperphagia, further aggravating the relentless progression to metabolic syndrome including the possibility of emerging T2DM, and even worse, the patient's eventual matriculation into T1DM.

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5.3. Communication: digestive/metabolic organs communicate with the brain

Lustig (2008) has outlined a persuasive neurometabolic argument. He shows a clear-cut impact that HFCS (a food stuff) can have on various metabolic and neurometabolic receptors within organ tissues (stomach, small intestine, pancreas, liver, etc.) via specific endocrines released by these same metabolic tissues. In other words, these metabolic organs are actually endocrine organs (including the adipocyte or fat cell) which are capable of producing endocrine-like chemicals called gut peptides, adipokines, etc. Using these "endometabolic" chemical messengers, the brain is, in turn, signaled or made aware of the quality and quantity of energy coming from various food stuffs (e.g. fats versus carbohydrates versus proteins). Reciprocally, the brain responds to these endometabolic messengers by producing its own neuroendocrine messengers (called neurotransmitters) to communicate back to these same digestive/metabolic organs. In this way, an energy communication or messaging loop has evolved that allows the body to control the ebb and tide of energy creation and storage throughout in the body.

5.4. Communication: the brain communicates with the digestive/metabolic organs

The key neurotransmitters that talk back to the digestive/metabolic organs form two classes of neuroanatomic circuitry (the sympathetic and the parasympathetic nervous system). Via these two circuits, the brain exerts its control over all thermodynamic processes that surround the metabolism of food. This includes the thermodynamic energy influences coming from carbohydrate, fat or protein and translating that energy flow into either anorexigenic (eat less) versus orexigenic (eat more) messages. If sympathetic signals coming from the brain prevail after a foodstuff is digested, this favors anorexigenic processes and we often lose weight (via "FOX" or fatty acid oxidation). If parasympathetic signals prevail, this favors orexigenic processes and we often gain weight (via "FAS" or fatty acid synthesis) (Lustig, 2008). For example, cocaine and/or stimulants like methamphetamine stimulate sympathetic traffic over parasympathetic, causing FOX and, hence, weight loss (e.g. phentermine, a popular appetite suppressant, works this way). On the other hand, sugar ingestion will tend to stimulate parasympathetic traffic, which stimulates insulin, which favors FAS and causes ensuing weight gain.

5.5. How sugars and fats are addictive and pro-inflammatory

If the body is overwhelmed with enough sugar (e.g. high carb colas) and fats (e.g. fast foods) this will favor parasympathetic neurometabolic states, glucolipotoxicity (i.e. colas = glucose and sugar + fast food = lipids or fat), resulting in insulin resistance (especially if we are consuming HFCS) which hypothetically leads to insulin insensitivity and/or possible beta cell exhaustion (i.e. necrosis) and ensuing diabetes. In other words, there exists (at least conceptually) a direct pathway from sugar to insulin to FAS to obesity to glucolipotoxicity to insulin resistance and then on to diabetes. Indeed, each step inevitably creates a process that melds obesity and diabetes toward a fateful dance with one another. The end result is often the most toxic dance of all, metabolic syndrome.

Poitout et al. (2010) have shown how glucolipotoxicity creates the fertile environment that ultimately leads to necrosis (oxidative destruction of cells) including the cellular decline of the Islets of Langerhans (pancreatic beta cells) facilitating the evolution of diabetes. This entire pro-inflammatory dance that unfolds between sugar and fat called glucolipotoxicity can also affect other receptors and organs of the body, including the brain. This often leads to neuropsychiatric disturbances that can affect human relationships. Finally, food (especially sugar), being able to stimulate both dopamine and mu-opioids, can be addicting (Hoebel et al., 2009) which helps to drive a vicious cycle of sugar induced glucolipotoxic metabolic inflammation. Therefore, we are beginning to see how glucolipotoxicity (hence, diabesity itself) may influence metabolic (insulin resistance), addictive (mu-opioid and dopamine pathological stimulation) and relationship (aggravation of pathological neuropsychiatric states) functioning, all in complex and inflammatory ways. We will develop this tripartite concept involving metabolism, addiction and human relationship function next.

At this point, however, at least one thing appears evident, metabolic inflammation is fueled by the addictive drive of sugars leading to more obesity (especially if that sugar is HFCS). Such obesity may then lead to profound psychic disturbance (such as low self-esteem) and anger (Shriner, 2011). These stressful psychic distillates may then lead to a need for more "comfort food," which is often high in sugar, further aggravating more metabolic inflammation. This sugar–inflammation–obesity–stress–more sugar cycle is well known to both obesity experts and bariatric clinicians, alike, since they are constantly required to deal with its consequences. It is a cycle that has created a toxic feeding frenzy driving the current globesity (global obesity) epidemic we see unfolding across the world.

5.6. Treating metabolic, addictive, and relationship levels simultaneously

Shriner and Gold (2012) has outlined three levels of bariatric medicine (metabolic, addictive and relational) which attempts to calibrate the three inflamed levels of neurometabolic dysfunction we just alluded to: 1) metabolic (glucolipotoxicity), 2) addictive (the power of sugar to stimulate dopamine and mu-opioids) and 3) relationship (the neuropsychiatric impact of diabesity and excessive inflammation). This tripartite model gives the bariatric clinician, perhaps for the first time, the opportunity to co-factor these three simultaneous levels of neurometabolic dysfunction in a continuous and dynamic way (Shriner and Gold, 2012). Such a dynamic continuum gives the clinician the ability to cross calibrate the contributions of metabolism (including dietary induced pro-inflammatory changes) with addictive inputs (including a consideration for those foods that inflame addictive dysfunctional eating patterns) alongside ensuing inflamed human relationships. Shriner argues that this is exactly why 95% of diets fail; they fail to calibrate and/or deal with the total input coming from all of these three levels.

In this way, you may gain initial control over, say, the metabolic level of bariatric health (by eating less French fries, pizzas or chocolate), but if you do not simultaneously learn how to deal with the relationship level (say, by failing to consider the way your sister's comments on your weight can aggravate you) it will only come back to derail your diet. How? The ensuing anger coming from your sister's comments will act via the relationship level to trigger a response on the addictive level causing you to turn to your favorite food addiction: enter chocolate comfort food. This, in turn, re-aggravates the metabolic level of your diet.

It now becomes rather obvious, failing to deal simultaneously with all three levels of bariatric health (metabolic, addictive and relational) will ultimately cause you to yo-yo between sojourns into sugar abstinence, relationship frustration and then sugar indulgence. However, as Hoebel et al. (2009) have previously argued, this abstinence, indulgence, abstinence cycle of intermittent feeding will only increase the chances of eventual sugar bingeing behavior. We all have experienced these frustrating and stress-inducing sorties into dieting, ones that ultimately lead to a 95% confidence that we will fail with our diet over time.

5.7. Stress management patient information tools to the rescue

At the University of Florida, in our *Living with Food Program*, we have developed patient stress management information tools that help to

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identify which of 5 distinct sub-types of stress management (called IGS-rooms™) a patient uses. The term IGS stands for "Information Gathering and Sharing." This information technology (IGS-IT™) allows the patient (and the clinician) to discover the patient's stress management cognition room, so they can better tailor a personalized bariatric intervention specific to a given patient. Here is how it works. The patient plays a simple game (The Flow Game™) which allows them to discover and share with others how they tend to bias information gathering and sharing under stress. Then, we are able to teach the patient how to work around such biases so they can learn to better navigate all three levels of bariatric health (metabolic, addiction and relationship) in a more resilient way.

As we just mentioned, using this Flow Game technique, we are able to personalize the patient's bariatric intervention. This includes patient-personalized translational medicine which deals with four distinct challenges: 1) how patients "think about food" (called food cognitions or perceptions), 2) how they engage in maladaptive eating patterns that foster disordered eating (uncontrolled eating), 3) how they eat to offset powerful emotions (e.g. emotional eating [note: each of the 5 IGS-room information personality types favors one of 5 powerful emotions]), and 4) how they handle stress (e.g. IGS-room 5 creates its own stress/solution issues).

We have found that after a patient discovers their "home room" (i.e. the IGS-room they turn to under stress) they have increased weight loss success. This is engineered by asking patients to participate in a 10 session group learning experience, which teaches them how to integrate their home room assets with the other 4 IGS-rooms (and their attendant assets) by constructing a set of contracts that will determine how they access specific types of foods using the tripartite model we described above. These contracts allow patients to learn how to quit certain toxic foods, hold on to healthier foods and/or change or modify their relationships with still other foods. This ultimately improves the chances for weight loss success (e.g. learning how to modify the amount and presentation of chocolate in their diet). By the end of this group learning and sharing process, all participants learn how incorporate "all 5 IGS-rooms, all the time." This fosters both metabolic, addictive and relationship resiliency and health over space and time. It also helps to mitigate metabolic, addictive and relationship pro-inflammatory influences that would otherwise sabotage weight loss success. Finally, that which is learned in these 10 session groups is then practiced and perfected through patient run aftercare groups that are sustained via either face to face interactions or virtual social networking over the internet (Shriner and Gold, 2012).

Supporting our line of research and clinical intervention, Porter and Johnson (2011) have recently shown that obesity in older adults is more strongly associated with inappropriate eating behaviors than mental health per se. Specifically, their studies show that the elderly patient's 1) cognitive restraint, 2) uncontrolled eating (disordered eating), 3) emotional eating, and 4) stress—showed a higher correlation with obesity than anxiety or depression. At the University of Florida, Living with Food Program, we are investigating the hypothesis that stressed human relationships coupled with food addiction and metabolically toxic diets collectively work to create the metabolic receptor toxicities that must be reset in order to overcome diabesity.

Again, we are researching how food perceptions can be altered with group based behavioral modifications and information theory in order to drive the adoption of healthier food choices. In turn, these healthier choices can assist in detoxifying or resetting those neurometabolic receptors and processes that create and sustain obesity. To date, our investigations have shown that one of the most viable dietary interventions may include low carbohydrate/high vegetable (or whey) protein diets (with reasonable medium chain fat supplements). It is this sort of diet that may assist in the pro-inflammatory reset of our patients suffering from obesity/diabesity (Shriner and Gold, 2012). In addition, we are in the process of formally examining the efficacy of patient education regarding the resilient integration of all 5 IGS-food perception types, with specific diets and exercise regimens to see how this may effectuate the improvement of pro-inflammatory changes in metabolic health (i.e. to include changes in pro-inflammatory marker analysis, improvements in pre and post intervention weight, decreases in insulin resistance, etc.).

6. The processes underlying the fasting reset

6.1. Fatty acid mobilization is fundamental

The key to the transitioning from obese to overweight to healthy (or "eubaric") weight is the realization that fatty acid mobilization is paramount and integral to the entire process. In other words, fatty acid mobilization, far from being pathological, is integral and to be expected in individuals that are truly mobilizing excess fat from the adipocyte to energy hungry tissues such as muscle, liver, heart, brain, etc. During such a metabolic state, one would expect highly visible levels of plasma fats (triglycerides) to be present in rapidly turning over tissues that are under sympathetically driven FOX (fatty acid oxidation). Again, as Shriner (Shriner and Gold, 2012) and others (Poitout et al., 2010) have argued, the reset of excess weight must involve the mobilization of fat by way of its transport via triglycerides extruded from adipocytes. Therefore, high normal triglycerides in the blood stream would be expected in patients transitioning from obesity to less toxic weight. Perhaps this is also the case in elderly who have preserved cognitive functioning and resilient metabolic functioning. To this end, Yin et al. (2012) reported that high normal plasma triglycerides were associated with preserved cognitive function in their test subjects.

In order to understand how fasting or modified abstinence might be associated with a similar process of mild hypertriglyceridemia (at least during mobilization of excess fat from adipocyte stores), we need to examine how the body reacts to food restriction or CR type diets. Again, CR stands for caloric restriction. Maughan et al. (2010) have reported how fasting affects metabolism. As basic biochemistry teaches us, the body goes through a normal but predictable progression from expenditure of plasma carbohydrate stores (plasma glucose) to total expenditure of liver glucose stores (via breakdown of liver glycogen to glucose [hepatic glycogenolysis]) to the release of free fatty acids (from triglyceride degradation via adipocyte fatty oxidation) to then steady state hepatic gluconeogenesis (the latter to ensure glucose is available as a nutrient resource to the brain) along with ketone formation to serve as a general four carbon source of energy that sustains life when all sugar resources have been expended. Over time, after all fat reserves have been exhausted, there remains only amino acids from remaining protein tissue substrate as a fuel source. Since such a process requires 1.75 g of protein to net 1 g of glucose (via hepatic gluconeogenesis) eventually this zero sum metabolic process leads to thermodynamic bankruptcy and death during the last agonal phases of starvation (Maughan et al., 2010).

6.2. CR fasting and ketosis

The important point is that the intermediate phase of starvation (the onset of ketosis) will take place in about 48 to 72 hours after the removal of all caloric resources (except water) during CR fasting (if no exogenous carbohydrates are consumed) and after all liver glycogen has been expended. Since the average liver stores of glycogen is somewhere between 60 and 80 g, restrictive diets that stay below the 60 g figure may be expected over time to awaken ketosis by turning-on FOX (fatty acid oxidation) as net glucagon to insulin ratios favor FOX. Thus, a diet less than 60 g carbohydrate is particularly fat mobilizing, especially in the face of reasonably high protein

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(Shriner and Gold, 2012). As Shriner and Gold (2012) has argued, an ideal fat mobilizing diet would:

- tend to not induce tolerance, addiction or withdrawal.
- tend to be administrated on a continuous, instead of intermittent, schedule to prevent binge eating-like behavior (see Hoebel et al., 2009).
- need to be administered within a therapeutic environment that mitigates stress in order to prevent disordered eating.
- need to be administered within a program of exercise to insure fatty acid oxidation by muscle tissues that maximizes (sensitizes) adequate muscle glucose receptor functionality.
- need to be one that maximizes evolutionary adaptations that keep the organism's thermodynamics net energy negative by fostering early satiety (e.g. protein's ability to improve satiety).

Summarizing, Shriner and Gold (2012) has suggested that such an ideal diet would consist of a low-carbohydrate/moderate fat/relatively high-protein, minimally salty diet which is fully integrated into an interactive social networking stress management platform. One of the fastest ways to catalyze this diet would be to consider a CR/DR fast (i.e. modified abstinence) that limited carbohydrates to around a 40 to 60 g per day, while liberalizing daily protein to at or above 80 g per day. Our own research has shown that such diets, especially if episodically "re-primed" by occasional high protein and essentially zero carbohydrate fasts, will assist in keeping net glucagon to insulin ratios less than unity, mobilizing fat and helping to preserve weight loss and proper metabolic health over time. Such diets would allow for fat (ideally unsaturated) to substitute for carbohydrate sources of calories, to make up for residual needed calories to fulfill the desired total calorie per day target. These sorts of reasonably low carbohydrate diets may even be palatable to diabetic patients if carefully monitored and supervised by both physician and dietician (Shriner and Gold, 2012). Obviously, these are only theoretical conclusions and *not treatment recommendations* and all diets that involve any nuance of fasting (especially in seniors or medically compromised patients) should be carefully prescribed and supervised by a physician and dietician.

7. Is there a role for fasting in geriatric obesity management?

7.1. Pros and cons

This is an intriguing question. Surely in younger populations (as argued in the research cited in this paper), periodic fasting may, in fact, result in improved risk offsets that lessen the chance of these same patients contracting diabetes, at least in the cardiac patients so identified. But as was also suggested, the geriatric bariatric (obese) patient is perhaps somewhat insulated from the ravages of mild obesity (at least when compared to younger patient populations). Unlike younger patients, however, seniors are especially vulnerable to lean body mass decline (sarcopenia) and this requires calibrating-in sufficient protein and exercise to maintain this lean mass during any attempt at losing weight. Geriatric obesity is certainly associated with increased morbidity whether that be in the form of increased diabetes, hypertension, weight associated arthritis, cancer, chronic pain, potential neuropsychiatric distress, etc. In this regard, any weight intervention that can assist in allowing the senior patient to lose even a small amount of weight if they are frankly obese (BMI > 30), and certainly if they are morbidly obese [BMI > 40], would seem to be reasonable. Whether this requires fasting is assuredly controversial.

In addition, Hoebel et al. (2009) have shown that episodic food restriction (especially carbohydrates) in rats has increased the chances of compensatory food bingeing behavior over time. Thus, it could be argued, dieters who intermittently suspend access to chocolate will only resume eating chocolate (perhaps in the form of chocolate bingeing) at a later phase in the diet cycle. This has led many researchers in the field of bariatrics to reconsider the advisability of periodic suspensions in food access (i.e. DR fasting), especially in terms of carbohydrates, since rebound bingeing might be expected to eventually thwart the success of the diet. Curiously, Hoebel et al. (2009) were able to show that unlike carbohydrates, fats seldom cause withdrawal-like behaviors in rats, as one might expect from a truly addictive substance. Hence, carbohydrates and cafeteria foods (i.e. foods high in both carbs and fats) are probably the most addicting, at least in terms of causing rebound bingeing if the test subject tries to periodically totally withhold such foods from their diet.

Collectively, the data presented herein would seem to argue that perhaps the most effective diet would be one that mimicked a fixed schedule modified fast (modified abstinence) from carbohydrates, without a total cessation of access from them altogether. Such a diet would probably keep the total carbohydrate load down somewhere below 60 g for reasons we just cited above (i.e. to maintain overall metabolic mechanisms in the body that favor fatty acid oxidation over fatty acid synthesis). Pending stability in weight, if the dieter found him or herself regaining weight, a periodic lower carb/higher protein priming fast might then be employed to reset the "set point" weight. By "set point" we mean the weight the patient tends to want to settle in at over time.

8. Conclusion

It becomes obvious that the geriatric patient wishing to work with his or her physician to lose weight has several challenges. These are:

- Seniors likely have a different metabolic state than that seen in younger patients, which requires careful calibration and recognition for sarcopenia and the obesity paradox.
- Like all patient populations, seniors need to keep in mind that "not all foods are equal," especially in terms of their addictive potential (with sugar and cafeteria style foods, foods often readily available during retirement, leading the way).
- Seniors have far less tolerances for caloric restriction and because of loss of lean body mass need more exercise incorporated in their dieting programs.

The geriatric patient looking to reset their body and life from a state of metabolic inflammation needs to keep in mind that such a reset will involve adjustments and changes on more than one level (see Shriner's tripartite model for bariatric health, described above). Given the caveats we just outlined, this transition out of a state of metabolic toxicity to metabolic resiliency (i.e. wherein less inflammation prevails) may need to involve a modified CR fast or modified sugar/cafeteria style food abstinence, but only under the careful supervision of his or her physician, dietician and fitness trainer. In fact, this diet is probably more accurately a CR/DR hybrid with the dietary restrictions taking the form of no HFCS, less than 60 g of carbs per day, generous protein, emphasis on unsaturated fats, at least 30 minutes of aerobic exercise (as was suggested in the STRRIDE Study outlined in Shriner's (2011) earlier paper) and some form of group bariatric social network and information sharing exchange. The latter is necessary since obesity is an addiction, and like all addictions (e.g. alcoholism) is something we need to work at, one day at a time. The importance of group fellowship and outside support is vital to long-term weight loss success. In fact, it may well be the most important element.

The geriatric obese patient, as the literature argues, may benefit from the obesity paradox, wherein slightly heavier weights are tolerated without increased mortality, at least in comparison to younger populations. Still, excess weight during the geriatric period of life WILL lead to excessive morbidity (e.g. diabetes, hypertension, chronic pain, sexual dysfunction, etc.). It is true that this excessive morbidity and the misery it brings may not lead to immediate mortality, but it sure makes life a bitter pill to swallow. Therefore, general increased

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quality of life is still granted to those geriatric patients (even decagenarians!) who are able to keep their weight within a range that prevents diabesity or other forms of obesity associated states of ill-health. We may see in the future that reasonably low carbohydrate, relatively high protein intake (assuming no advanced renal disease), coupled with regular exercise, may be the most ideal "detoxifying" diet yet devised for the geriatric patient. Only time and further research will tell. In the meantime, we hope some of the information provided in this paper assists practitioners in their clinical interventions with patients, taking them from a state of metabolic toxicity to one of greater metabolic resiliency and health.

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