

# Insulin Resistance and Hunger in Childhood Obesity: A Patient and Physician's Perspective

Wendy Scinta · Harold Bayes · Nicole Smith

Received: July 24, 2017 / Published online: September 7, 2017  
© The Author(s) 2017. This article is an open access publication

## ABSTRACT

This article is co-authored by the mother of a child with obesity and insulin resistance, who gives her perspective. It is also co-authored by the treating Obesity Medicine clinician and an investigator in obesity clinical research (both certified in Obesity Medicine), who give their perspectives. The discussion focuses upon the potential clinical use of metformin in managing young patients with obesity and insulin

**Enhanced content** To view enhanced content for this article go to <http://www.medengine.com/Redeem/23FBF0606851C005>.

W. Scinta (✉)  
Medical Weight Loss of NY, New York, USA  
e-mail: fatmd@weightlossny.com

W. Scinta  
BOUNCE Pediatric Obesity program, Fayetteville,  
NY, USA

W. Scinta  
Obesity Medicine Association, Denver, CO, USA

W. Scinta  
SUNY Upstate, Fayetteville, NY, USA

W. Scinta  
One Stone Technology, Fayetteville, NY, USA

H. Bayes  
Louisville Metabolic and Atherosclerosis Research  
Center, Louisville, KY, USA

N. Smith  
New York, USA

resistance. The article integrates what is scientifically known about the mechanisms of actions of metformin and how these mechanisms are reflected in the clinical response of young patients.

**Keywords:** Adiposopathy; Obesity; Metformin

## THE STORY OF GREGORY FROM MOTHER NICOLE

Gregory's weight has been a concern for us since he was about 4 years old. He was hungry all of the time. It did not matter what he ate, it was never fulfilling for him. Every year he would go to the doctor for his physical, and we would talk about my concerns with his weight. The doctor would send him for blood work to check his thyroid, etc., and everything would always come back fine. Gregory is a tall child and his height has always been off the charts. The weight gain has always been chalked up to him being tall. Repeatedly, we would hear, "He is just going to be a big boy." That wasn't a good enough reason for me, so I decided to take him to a nutritionist and see if her program would work for him. It didn't last very long because the poor kid was starving! I would pay attention to everything he would eat. I packed his lunches every day for school. We aren't a family that

would eat out a lot or eats junk all of the time. So, I just couldn't understand why he kept gaining weight. In addition, Gregory is also a very active child. He is always outside running around, playing basketball—just always on the go. He is not one to sit around and do nothing. He is probably the only kid I know who doesn't like to play video games!

Then one day I happened to be online reading the news and I saw an article on Dr. Scinta. The words from the article, "your child is telling you they are hungry and you say there is no way you can possibly be hungry," stuck in my head, and I thought I have to bring him to her (that statement was probably made in my house five times a day every day). So, I scheduled a consultation and learned about the possibility of insulin resistance. That is something that had never been mentioned to me by any doctor—or discussed that it could be an issue for him. In January, we started the program. Gregory had his blood work done, and the results from his bloodwork were that he was severely insulin resistant. Never in the 4 years that he struggled with his weight was he tested for this. He was put on metformin to help his insulin resistance. In addition, we met with the dietician to go over his diet. We only had to make a few minor changes with his diet because I already had him eating healthy. We had to add more protein to his diet and he definitely needed to drink more water.

Since Gregory has been on the medicine and worked with Dr. Scinta, he has lost 10 lb and grown an inch. He feels great about himself and has learned so much about food. He is no longer starving all of the time. The first time he didn't finish his dinner and said, "Mom I am full," I almost fell over! That had never happened before! In fact it was the opposite, it was, "Mom I am still hungry, can I have more?" When he goes for his follow-up visits, it is so helpful for him when he sees the charts with his progress. He has learned about water weight and how when he is gaining muscle and growing, the scale isn't going down but that he is still losing fat. He tried eating McDonald's once since he has been on the program, and it made him sick. He no longer asks to eat at fast food places because he has learned how bad it is for his

belly. In just 5 months, he is a whole new kid. He is happier; he feels better and can do little things now that he couldn't before, like bending over and tying his shoes or climbing into his dad's truck without anyone helping him. His favorite thing is when he shows us he can do a squat. He says, "Look! I couldn't do this before!"

## PHYSICIAN'S PERSPECTIVE

Gregory is a classic example of a child with severe insulin resistance who cannot control his appetite. If a child can't achieve satiety, the meal plan and exercise regimen implemented become irrelevant.

In my 11 years of treating childhood obesity, I have found that there are two factors that are imperative for a child to achieve success. First: the family must be engaged and willing to make changes in the house in a united fashion. Let's look at the situation with Gregory's family. As Nicole indicated, Gregory was a very healthy eater in general. He didn't mind fruits and vegetables. His mother sent him to school with a healthy, packed lunch every day. Unlike most American families, they did not eat out very often. Mom was very careful not to have junk food in the house. She knew how to read nutrition labels and understood macronutrients and ingredients. Dinners were mostly home cooked, and they sat down regularly to eat dinner together as a family. Everyone was on board with healthy eating habits. To me, the most challenging family eating behaviors had already been addressed.

Second, a child's appetite must be controlled—something that is often overlooked, yet a critical part of the process. As I often heard from parents, Nicole told me that Gregory was a "bottomless pit." Gregory explained to me that he never felt full and often left the table after a couple of servings of dinner still wanting more. Gregory himself could not believe how much he was capable of eating in comparison to other kids.

Gregory had a classic case of insulin resistance. As Gregory's physical examination did reveal significant acanthosis nigricans, I was not at all surprised. Insulin is a gastrointestinal

peptide hormone secreted by pancreatic beta cells in response to increases in glucose levels, as occurs with the consumption, digestion, and absorption of carbohydrates. Insulin helps drive glucose into muscle to be stored as glycogen, stimulates lipogenesis, suppresses lipolysis in adipose tissue, and promotes both glycogen and fat deposition in the liver. Diagnostically, Gregory had elevated insulin levels. If he had elevated insulin levels with repeated low blood sugars, then one might have suspected an insulinoma. But Gregory did not have hypoglycemia. He had the more common presentation of high normal glucose in the face of elevated insulin levels. This is likely because when the activity of insulin is progressively

impaired, insulin levels increase, glucose levels increase, and the pancreatic beta cells further increase their (compensatory) secretion of insulin.

Given that both insulin and leptin (a hormone secreted by the fat cell or adipocyte) are thought to promote satiety, one might expect that the increase in insulin and leptin levels, common in patients with overweight and obesity, would serve as an effective counter-regulatory mechanism to reduce appetite and prevent overweight and obesity. But in our current obesity epidemic, these counter-regulatory mechanisms have proven to have limited efficacy. It is possible that other psychologic, environmental, hormonal or physiologic



**Fig. 1** Gregory before and after weight loss



factors overwhelm any potential decrease in appetite with hyperinsulinemia and hyperleptinemia. However, another proposed mechanism suggests the brain appetite centers may become “resistant” to insulin and leptin signaling. It is this (albeit unproven in humans) insulin and leptin resistance that may help explain why elevated insulin and leptin blood levels do not seem to reduce appetite in many overweight individuals. But why do overweight or obese individuals develop insulin resistance in the first place?

Some patients without obesity can develop insulin resistance via genetic abnormalities leading to deficiencies in insulin signaling. But for the more common presentations of patients

with overweight or obesity, limitations in the excessive energy storage in peripheral subcutaneous adipose tissue leads to adipocyte hypertrophy and subsequent intraorganelle dysfunction (e.g., mitochondrial and endoplasmic reticulum stress). The dysfunction of adipocytes and adipose tissue promotes adiposopathic endocrine and immune responses that contribute to metabolic disorders such as insulin resistance, elevated glucose, elevated blood pressure and dyslipidemia. Furthermore, adiposopathy-promoted limitations in excess energy storage also contribute to increased circulating free fatty acids, which may be “lipotoxic” to other body tissues, which again, may contribute to insulin resistance [1–3].



**Fig. 2** Gregory and Nicole before and after weight loss

I treated Gregory's insulin resistance with metformin 1000 mg po bid. Metformin reduces hepatic glucose production (gluconeogenesis), but this is not its only mechanism of action [4]. Metformin increases insulin sensitivity and decreases appetite. Some data suggests metformin may improve insulin sensitivity by insulin receptor activation [5]. The reduction in appetite with metformin appears to be multifactorial. Metformin may improve leptin sensitivity, reduce neuropeptide Y levels and increase glucagon like peptide-1 (GLP-1) activity (i.e., increased GLP-1 levels and receptors) [6]. The improvement of insulin sensitivity and reduction in appetite by metformin's various mechanisms have clinical implications. It is true that when exogenous administration of insulin causes low blood sugars then this can increase appetite. However, the physiologic effect of insulin itself on the brain is to increase satiety. As before, if the central nervous system becomes resistant to the effects of insulin, then improving central nervous system insulin resistance may decrease appetite. The potential for metformin to reduce central nervous system insulin resistance is further supported by the finding that metformin may penetrate the blood-brain barrier [7]. Finally, it is with interest that chronic hyperinsulinemia and hyperleptinemia in obesity may impair insulin sensitivity in liver, skeletal muscle, adipose tissue and the brain [8]. This may contribute to a pathologic cycle that may ultimately lead to diabetes mellitus, a cycle that may be broken by weight reduction and theoretically broken by administration of metformin.

The above may help explain the nature of Gregory's hunger and why it was so difficult for him to achieve fullness despite how much he ate. It may also help explain his beneficial response to metformin. My plan with Gregory involved both nutritional and medical management to help gain control of his hunger. From a nutritional standpoint, I wanted to decrease hunger by increasing the macronutrients that improve satiety: lean proteins and healthy fats. To decrease inflammation, cravings and lipogenesis, I decreased his sugar and starchy carbohydrates in his diet, which would further promote satiety. This helped to a degree,

but wasn't enough to control his hunger. My next step was to start metformin 500 mg and work up to 1000 mg twice a day with food. Gregory was incredibly responsive to this regimen and compliant with his medications. Although we have only worked together for 5 months, Gregory has already lost 9% of his body weight. His mother, who became a patient to support her son, has already lost 25 lb in this same time and is close to her goal (Figs. 1, 2).

The Obesity Medicine Society has published a pediatric algorithm that addresses medical management of hunger, nutrition and behavioral modification in children with obesity. The algorithm is free to download and can be found at <https://obesitymedicine.org/childhood-obesity>.

## ACKNOWLEDGEMENTS

The authors are fully responsible for all content and editorial decisions and received no financial support or other form of compensation related to the development of this manuscript. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published. The opinions expressed in the manuscript are those of the authors.

**Disclosures.** Wendy Scinta: Speaker/PAB for Novo Nordisk, PAB for Nestle/Optifast, Founder/Medical Director for One Stone Health Technology. Harold Bayes and Nicole Smith have nothing to disclose.

**Compliance with Ethics Guidelines.** This article does not contain any new studies with human or animal subjects performed by any of the authors. Permission was granted from the parent for use of the figures in this article.

**Open Access.** This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (<http://creativecommons.org/licenses/by-nc/4.0/>), which permits any

noncommercial use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

## REFERENCES

1. Bays HE, Seger JC, Primack C, et al. Obesity Algorithm 2017, presented by the American Society of Bariatric Physicians. 2016–2017. [www.obesityalgorithm.org](http://www.obesityalgorithm.org). Accessed Jan 2, 2017.
2. Bays H, Scinta W. Adiposopathy and epigenetics: an introduction to obesity as a transgenerational disease. *Curr Med Res Opin.* 2015;31:2059–69.
3. Bays H. Adiposopathy, “sick fat,” Ockham’s razor, and resolution of the obesity paradox. *Curr Atheroscler Rep.* 2014;16:409.
4. Rena G, Hardie DG and Pearson ER. The mechanisms of action of metformin. *Diabetologia.* 2017. [Epub ahead of print].
5. Gunton JE, Delhanty PJ, Takahashi S, Baxter RC. Metformin rapidly increases insulin receptor activation in human liver and signals preferentially through insulin-receptor substrate-2. *J Clin Endocrinol Metab.* 2003;88:1323–32.
6. Adeyemo MA, McDuffie JR, Kozlosky M, et al. Effects of metformin on energy intake and satiety in obese children. *Diabetes Obes Metab.* 2015;17:363–70.
7. Labuzek K, Suchy D, Gabryel B, et al. Quantification of metformin by the HPLC method in brain regions, cerebrospinal fluid and plasma of rats treated with lipopolysaccharide. *Pharmacol Rep.* 2010;62:956–65.
8. Chen W, Balland E, Cowley MA. Hypothalamic insulin resistance in obesity: effects on glucose homeostasis. *Neuroendocrinology.* 2017;104:364–81.