

## **The Thrifty Gene**

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**Abstract:**

Based on James V. Neel's theory of the thrifty gene proposed in 1962, this gene was said to help individuals efficiently use fat stores during periods of famine. In contrast, in today's modern society with abundance of food, the 'thrifty gene' has been shown to be a disadvantage. Neel hypothesized that this gene is responsible for the increase in metabolic syndrome; however, some do not believe this is the case and have developed alternate hypotheses to justify the rise in obesity, diabetes and metabolic syndrome.

**Introduction:**

In 1962 a genetic epidemiologist, James V. Neel, proposed in the *American Journal of Human Genetics*, that diabetes was a single gene disorder characterized by a metabolic abnormality from birth. He argued that this abnormality ultimately resulted in faster and more efficient insulin function. This would cause a minor but useful advantage to heterozygote carriers of the gene, but would also cause type 1 diabetes in homozygotes. The gene would exist in balanced polymorphism in the gene pool, creating a selective advantage for heterozygotes that counteracted the mortality in homozygotes. The gene was named the 'thrifty gene' (Gale, 2014). Thrifty implies some degree of prosperity deriving from earlier frugality and careful management of resources (Wells, 2015). Neel hypothesized that this genotype helped our hunter and gatherer predecessors efficiently use fat stores to survive cycles of feast and famine. Neel stated that "during the first 99 percent or more of man's life on earth, while he existed as a hunter and gatherer, it was often feast or famine" (Ayub, 2014). However, today in the food abundant environment, the "thrifty gene" may be responsible for elevated insulin resistance and obesity (Graham, 2014). Neel's theory was based upon Native Americans who were seen to have high incidence of obesity, hypertension, hyperglycemia, type 2 diabetes and heart disease (Richards,

2006). Specifically, in Pima Indians about one half of the population has diabetes and 95% of those are overweight (Richards, 2006).

Despite the fact that the ‘thrifty gene’ coincides with the principles of natural selection, there has been a great deal of debate and controversy over the topic (Dani, 2015). Many of which involve the failure to identify major thrift genes. Instead, in a broader sense, there is a thrifty genome that represents the interactions of hundreds of genes capable of influencing adaptations to feast and famine (Gale, 2014). There is also controversy regarding how influential this ‘thrifty gene’ is on obesity, and as a result, type 2 diabetes. Genetic scientists today argue that this throwback to starvation is not the overriding influence, but instead, thrifty genes (if they exist), are just a small part of the intricate genetic picture that contributes to the obesity epidemic (Beil, 2014).

#### **Nutrition and metabolic function review:**

Metabolically, the concept of the ‘thrifty gene’ is based off of the feast-famine cycle. This cycle claims that the thrifty gene allows people to store fat after heavy meals in order to survive periods of famine. Supposedly, skeletal muscle glucose is replenished and excess glucose is more efficiently stored in adipose tissue during thrifty storage. During famine and activity, the stored glycogen is depleted and thrifty gene stores are significantly reduced. The cycle then states that contracting skeletal muscle increases due to the combination of the GLUT4, the insulin related glucose transporter, and AMPK. Then after successful physical activity, an intake of glucose and fat restarts the cycle and causes storage once again (Chakravarthy, 3-10). The theory is not based on ‘nutritious’ eating persay, it is more so focused on general periods of feast and famine, regarding any food source that is available to the person.

#### **Introduction of metabolic significance:**

Studies have been completed to investigate obese versus non-obese individuals to understand how their lifestyle factors such as overeating, and people's tendency to have a sedentary lifestyle has affected their metabolism to ultimately store body fat instead of burning it (CDC, 2013). Especially in western countries it has shown that low socioeconomic status in childhood is one of the strongest predictors for adult obesity and found that the 'thrifty gene' mechanism was likely to contribute to general obesity (Levitan, 2013). It has been thought that America has a weight loss problem because human metabolism run on genes that are not adequate for the amount that we consume. It is believed that the diet of hunters and gathers which is defined as heavy on protein and light on carbohydrate is reflected on the current paleo diet (Beil, 2014). To better understand how this is a modern issues, when we have unlimited food supply and no exercise this results in triglyceride storages that are not decreased and the GLUT 4 and AMPK levels are not increased. When Americans feast they intake high amounts of glucose and fat, and when there is no physical activity, the thrifty gene results in high storage of energy within the body and we never experience famine due to the constant supply of resources (Chakravarthy, 7). In this cycle of consumption, to thrifty storage, and to famine, and physical activity, we see a stop in the cycle which results is metabolic syndrome resulting in low skeletal muscle and results in high blood pressure, insulin and therefore resulting in insulin resistance (Chakravarthy, 7).

**Current research areas of the topic:**

Genomic regions related to signaling pathways, sensitivity, production, response, and regulation are apparent candidate for thrifty gene research. A recent sequence that has been of particular interest is the insulin variable number of tandem repeats (INS-VTNR). This microsatellite, a short segment of DNA that has repeated sequences, is found in the insulin gene promoter region. Non-African populations show only three variations of this sequence; whereas African

populations display over 2. The variation between African and non-African populations supports the characteristics of the thrifty gene and may explain the higher incidence of diabetes in specific populations (Graham 2014). In addition, a second genomic region has been recently claimed to have 'thrifty gene' qualities. The gene encoding for ApoE, the main lipoprotein incorporated into the chylomicron surface, has shown great variation between populations. ApoE2 is seen in Mediterranean populations, but ApoE4 which is associated with increased risk of cardiovascular disease, is seen in Aborigines and Native Americans (Graham, 2014). It is argued that the ApoE gene is thrifty because certain variations improve fertility by producing steroid production. However, research replicating of the thrifty nature of these two genes has either been unsuccessful or very limited.

In 1992, Nicholas Hale and David Barker contradicted the 'thrifty gene' theory by re-naming it a 'thrifty phenotype'. They suggested that an individual's environmental cues during the early periods of life opposed to their genetic composition. The study that tested the phenotype hypothesis was done in Gambia. Gambia has experienced significant food shortages and malnourishment during fetal development proved to be a positive adaptation. However, when the situation changed and individuals from Gambia moved from a rural environment to an urban one with more abundant food sources, they were more likely to develop metabolic disorders at a higher rate than those who were not born into malnourishment and their counterparts that stayed in rural areas (Graham, 2014).

### **The movement in business and society over the issue:**

It has been found that the cause of obesity is related to diet, lifestyle and genetic predisposition, which all contribute to increase in obesity. It has been hypothesized that the thrifty gene implies that because of the potentially scarcity of nutrients are higher in Native Americans compared to

non-Native Americans, due to their hunter and gatherer lifestyle (Richards, 2006). The common patterns of the Native American diet has shifted from high-protein, high-fiber and complex carbohydrate, to a diet that is high in saturated fat and sugar and low in complex carbohydrates and fiber (Richards, 2006). Based upon the study completed in 2001 on a Native American reserve in Arizona, it was found that there is a concern for the amount of money families are spending on their food sources. Additionally, protein values are relatively high in Native American supermarkets and therefore. they are substituting their diets with fat and carbohydrate based foods which ultimately are less expensive.

**Conclusion:**

In conclusion, the research provided displays that the topic of the 'thrifty gene' needs to be more heavily researched in order to prove the numerous hypotheses stated above. Although the topic is cited in many arguments and theories today, all of this information still under debate and a more precise definition needs to be established before this theory is seriously incorporated into healthy and medicine today. The controversy involves the genotype, phenotype and environmental factors and how they relate to the thrifty gene.

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