



Sylvia R. Karasu M.D.
The Gravity of Weight

Twin Studies: Determining the "Heritage of Corpulence"

Part 2: The contributions of heredity and environment on obesity.

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Vincent van Gogh's "Two Children," 1890, from Musee d' Orsay, Paris. van Gogh's children may not be actual twins, though they are dressed in similar clothing. Perhaps they are close enough in age and raised in the same family to be considered what researchers call "virtual twins." Source: Wikimedia Commons/Public Domain



Aldous Huxley (died 1963), English writer of the futuristic novel "Brave New World," that features identical twins produced "en mass." This photo is from a January 11, 1954 article in "Life Magazine." Source: Wikimedia Commons/Public Domain (no copyright on this photo)

"You get an average of nearly eleven thousand brothers and sisters in a hundred and fifty batches of identical twins, all within two years of the same age," (p. 9) wrote Aldous Huxley in the dystopia of *Brave New World* (1932) The year is 2495, and the principal elements of societal control are ectogenesis (babies bred in bottles), hypnopaedia (sleep teaching) and Pavlovian conditioning--and of course, Soma, the widely available drug that creates "happy smiles" of "universal benevolence" with no after effects. (p. 70)

"Nothing like oxygen-shortage for keeping an embryo below par," (p. 14) Huxley writes. Since the brain is the first organ to be affected, that's how someone becomes predestined to be an elite Alpha or a lowly subhuman Epsilon. While science had invented this

"Bokanovsky's Process" of creating "standard men and women; in uniform batches," (p. 8) science was seen as "potentially subversive," a "public danger" and something to be treated as "a possible enemy." (pp. 192; 193)

What about identical twins, who share 100% of their DNA, but who become discordant at some point during their lifetime for a trait or a behavior, somewhat (and loosely) analogous to what Huxley describes in his *Brave New World*?

For example, over time, researchers such as Allison and colleagues (Faith et al, *Behavior Genetics*, 1997) emphasized the "need to put more behavior into behavioral genetics" since obesity is multi-determined: at least, in some way, it depends not only on genetics--the *genetic architecture*--but also on behaviors such as eating and physical activity and the interaction of genes and environment, as evidenced, for example, by parenting styles, family dynamics, and even epigenetic effects that may lead to differences even between identical twins. (Musani et al, *American Journal of Clinical Nutrition*, 2008) Further, Heymsfield and colleagues (Allison et al, *Health Psychology*, 1994) note that although genes remain influential in determining weight, "genes make protein, not fat" and hence they have their effect indirectly through behaviors such as food intake and energy expenditure.

In an attempt to distinguish environmental effects from genetic effects, Segal and Allison (*International Journal of Obesity and Related Metabolic Disorders*, 2002; Segal et al, *International Journal of Obesity*, London, 2009) employed the unique design of "virtual twins." Virtual twins consist of one biological child and one same-aged (unrelated) adopted child (adopted within the first year of life) (or two adopted children of the same age) who are reared within the same family, with the hypothesis that "common environmental effects have been underestimated" by researchers previously. In other words, virtual

twins “replicate the twin situation but without the genetic link” and “improve on ordinary adoption designs” since these children are matched for age and placement history. (Segal et al, 2009) But even this model relies on certain assumptions, such as not being able to account for different environments prior to the adoption.



From the Children's Museum of Indianapolis, female ere ibeji twin figures, early 20th century, from the Yoruba of Nigeria. Reportedly, the Yoruba have the highest rate of twin births in the world, and twins have a special place in the Yoruba culture.
Source: Wikimedia Commons/licensed under the Creative Commons Attribution, Share Alike 3.0 unported.

Another difficulty (and some say major weakness) in twin studies, whether with the classic study of comparing dizygotic with monozygotic twins or with the co-twin study of comparing monozygotic twins with each other, is the *equal environment assumption*. (Eaves et al, *Twin Research*, 2003; Felson, *Social Science Research*, 2014) In other words, there may be subtle and not so subtle differences in the way twins are treated within a family (e.g. some parents dress their identical twins alike, give them rhyming names, and even send them to the same schools, etc., whereas others make efforts to distinguish the twins from each other); even the “emotional closeness” between twins and how they relate to each other can be a factor) (Felson, 2014), all of which may bias estimates of heritability.

While monozygotic twins, which occur in 1 in 250 births in the U.S., share 100% of their DNA and are genetically identical, they are not necessarily completely “identical” phenotypically. Over the course of life, sometimes they become less so. (Fraga et al, *Proceedings of the National Academy of Sciences, USA*, 2005; Bouchard, *Obesity, Supplement*, 2008) In other words, they may become discordant for traits, behaviors, and even susceptibility to disease. These differences can stem from epigenetic factors (differences in DNA methylation and histone acetylation) that can occur even in utero (e.g. differences in the placenta, vascularization, or amniotic sac) or due much later to the

effects of differences in smoking, diet, exercise, (Fraga et al, 2005) or even in space flight, as in the study now of identical twin brother astronauts, Scott, who had spent a year in space, and his brother Mark Kelly, who had not.



American artist, Albert Henry Mauer's "Two Heads," c. 1928, private collection. Even though identical (monozygotic) twins are genetically alike, they may differ phenotypically, particularly over time and differ in traits, behaviors, and susceptibility to disorders.
Source: Alamy stock photos, used with permission.

As a result of discordant features or discrepant behaviors in MZ twins, many investigators have relied on a co-twin monozygotic design to demonstrate how genetic and environmental contributions interface with each other, including for hormone replacement therapy (Ahtiainen et al, *Menopause*, 2012); risk of myocardial infarction, death and diabetes (Nordström et al, *JAMA Internal Medicine*, 2016); leisure time and fat accumulation (Rottensteiner et al, *Obesity*, 2016); chronic back pain (Suri et al, *The Spine Journal*, 2017); hip osteoarthritis (Magnusson et al, *Epidemiology*, 2018) or even PTSD and obesity (Mitchell et al, *Psychological Medicine*, 2018) Other researchers have used the co-twin monozygotic design to confirm the strong influence of genetics, as, for example, on very low-calorie diets (Hainer et al, *International Journal of Obesity and Related Metabolic Disorders*, 2000) or metabolic efficiency. (Hainer et al, *International Journal of Obesity and Related Metabolic Disorders*, 2001.)

Bottom Line: Twins have fascinated the human imagination throughout history and have even featured prominently in Huxley's futuristic dystopia in *Brave New World*. In an attempt to separate out genetic from environmental contributions to obesity, researchers have

turned from the classic twin design of comparing and contrasting monozygotic and dizygotic twins, either reared together or reared apart (e.g. adoption studies) to the co-twin design in which monozygotic twins, discordant for a particular trait or behavior, are compared. Despite years of research and creative research designs (e.g. use of virtual twins), investigators still have difficulty, because of the need to rely on certain assumptions that cannot be proven, in delineating the contributions of nature as distinguished from those of nurture.



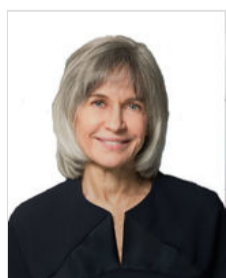
Saints Cosmos and Damian were reportedly twin physicians and early Christian martyrs, 3rd century A.D. They did not accept payment from their patients. Depicted here (16th century art), assisted by angels in transplanting a leg. Stuttgart. Photographer: Andreas Praefcke, 2006. Source: Wikimedia Commons/Public Domain

Note: For the writing of Parts I and II of this blog on twins, special thanks and appreciation go to Dean David B. Allison, PhD, for suggesting the topic of co-twin design and for his phrase *genetic architecture* that I used in my original subtitle; Dr. Robert Michels for alerting me to the existence of photos he had remembered from years ago of monozygotic and dizygotic twins (and to his assistant Mr. Russell Scholl for his prodigious efforts in tracking down a version of the photos); to Weill Cornell librarian Mr. Kevin Pain, for his own detective work; to Dr. Steven Heymsfield for his contacting Drs. Claude Bouchard and George A. Bray to enlist their help in finding the source of the images, and especially to Dr. Bray, who was the one who actually remembered the 1976 Börjeson reference in which the images of the twins (both photos reproduced in Part I of this blog) first appeared and who called my attention to his book *The Battle of the Bulge* that provided me with my title, *The Heritage of Corpulence*; and to Ms. Lee Dion and John Wiley and Sons, who expeditiously facilitated my obtaining permission to use these two copyrighted images.



Danish painter (mid-19th-early 20th century) Bertha Wegmann, "A Young Woman Breastfeeding her Twins in a Cornfield." Source: Alamy Stock Images, used with permission.

About the Author



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