



NEWS, VIEWS & COMMENTS

Zygoty Assessment by Self-Report; Research Reports; Human Interest

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The research implications and personal perspectives associated with twins' and families' self-reports of zygoty are reviewed. This is followed by summaries of recent research reports including a possible first case of the freemartin effect in humans, twin-singleton comparisons of mental health in Japanese students and mechanisms associated with ART-induced monozygoty twinning. A look at twin stories in the media includes the extraordinary revival of an infant male twin, the career decision of a pair of MZ twin basketball players and the loss of a five-year-old triplet.

Zygoty Assessment by Self-Report: Research Implications

A number of monozygoty (MZ) twins fail to see the physical similarities between themselves and their co-twin, leading these twins to believe they are dizygoty (DZ). I have observed this phenomenon on many occasions, as have my colleagues. This situation was brought to my attention once again by recent correspondence from a 20-year-old female twin, Susan G., who believed that because she and her twin sister, Sarah, did not look exactly alike in every way they were most likely fraternal twins.

Susan's twin sister Sarah disagreed, perhaps the only point of contention between these close sisters. Sarah believed that she and Susan were identical twins because of their strong physical and behavioral similarities. She spoke only of 'small differences' between them, such as one twin being slightly tougher and the other twin being slightly stricter in personality.

Interestingly, when the twins were born, their parents had been told that they were fraternal twins because of their separate placentas, amnions and chorions. However, approximately one-third of identical twins have this placental arrangement so the family was misinformed.

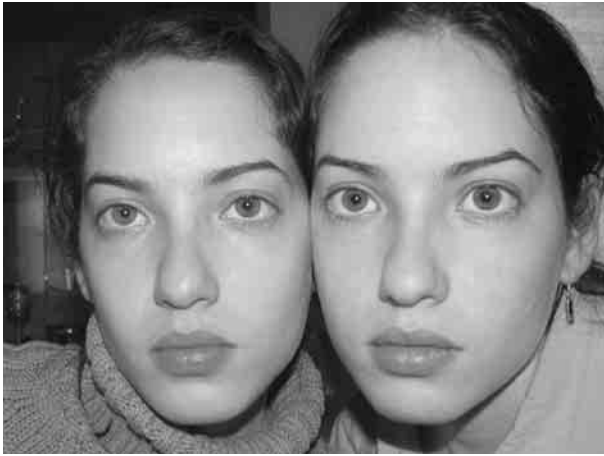
I examined a photograph of the twins and was struck by their extraordinary physical resemblance. I was certain

that they were MZ twins, recalling Race and Sanger's (1975) statement that, 'For many years, Mr James Shields of the Genetics Unit at the Maudsley Hospital has been sending us samples of blood from the twins. We find that the blood groups practically never contradict the opinion of such a skilled observer of twins.' A photograph of the twins appears in Figure 1.

Susan and Sarah were interested in undergoing DNA testing to learn the truth about their zygoty and I encouraged them to do so. Like many twins they lacked scientific proof of their twin type and wanted to respond with certainty to questions from family and friends.

Several weeks later I received the following message from Susan: 'We are both speechless to discover that we are in fact identical — honestly, it's like a NEW world. Now it's clear to us that the only reason we can combine pictures is because we are identical and not fraternal.' (Combining pictures meant cutting a photograph of each

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**FIGURE 1**

Twins Susan and Sarah G. Photo courtesy of the twins.

twin's face at the midline and joining one twin's left half with the other twin's right half.) By 'new world,' Susan explained that she now realized that she and her sister had originated from a single zygote — and had it not divided one of them would not have existed. She seemed awed by the immense chance associated with that event. The twins' similarities, social closeness and confusion by others became fully understandable to her in light of the DNA report. In contrast, Sarah who always believed they were identical was not surprised by the findings.

The twins' DNA test results are reproduced below in Table 1. The CSF1PO marker is missing for Twin 1 because the laboratory determined that her gene was weak, but the other markers matched, enabling their classification as monozygotic twins. The DNA laboratory indicated that the probability of this degree of match between two people chosen at random is 1 in 2.33×10^{16} .

TABLE 1

DNA Analysis of MZ Twins Who Believed They Were DZ

DNA Locus	Twin 1 (Susan)		Twin 2 (Sarah)		Matching probability (n-1)
D8S1179	13	16	13	16	61.76
D21S11	29		29		15.73
D7S820	10	11	10	11	07.61
CSF1PO	12		12	14	10.40
D3S1358	14	16	14	16	17.84
TH01	06		06		17.33
D13S317	11	12	11	12	05.65
D16S539	08	11	08	11	91.57
D19S433	14	15	14	15	09.20
vWA	18		18		22.05
TPOX	08		08		03.38
D18S51	13	14	13	14	22.89
D5S818	12		12		06.57
FGA	20	22	20	22	18.38
AMELOGENIN	X		X		

The scientific literature on twins lacks a satisfactory explanation for why some MZ twins are either confident that they are DZ or are uncertain as to whether or not they are MZ. It has been generally assumed by the scientific community that MZ twins focus on the slight differences between themselves, leading them to believe they are not identical, but this explanation may be one of several. The popular literature does hold some clues that may explain the self-misclassification of some MZ twin pairs. For example, celebrity twins and actresses Mary-Kate and Ashley Olsen, who look very much alike, have been described as fraternal twins because they claim to be. Twins who look alike may refer to this well-known pair as an example of how similar twins can look and still be DZ; however, I am certain that the Olsen twins are MZ, based on their physical resemblance. Of course, there are similar-looking DZ twins just as there are very similar looking non-twin siblings, but such sets are relatively rare. A photograph of a very similar-looking DZ female twin pair is included in my 2000 book *Entwined Lives*. When I studied these twins my first impression was that they were MZ, but blood-testing proved otherwise. Nevertheless, such sets are not common and deserve comment.

I explored the situation of how and why MZ co-twins misperceive their resemblance with Susan and Sarah. It turned out that the assumption that some MZ twins focus on their differences, even magnifying them, was true in their case. Susan detected small variations in the shape of the nose and mouth, which to her were evidence of dizygosity. Both twins draw, but their approach to producing art is different — Sarah observed that Susan draws from imagination, while she sketches objects that are in front of her. Susan has explained what she considered her lack of artistic talent by referring to her 'different genes,' but admits she can no longer use that excuse.

Most researchers rely on DNA analysis to document the zygosity of the twin pairs they study. However, some investigators outside twin research who encounter interesting twin cases often rely on the twins' or families' self-report for assigning zygosity. Some attorneys managing twins' wrongful death, injury and custody cases do the same unless advised by expert witnesses that DNA testing is the most reliable and accurate methodology for classifying twins. Interpretations of case study findings and life history information can change significantly depending on the zygosity of the twin pair in question. Thus, DNA testing which is now a simple and relatively inexpensive procedure should be considered mandatory in case study reports.

It is striking that twins' and parents' misclassifications of twin type tend to be in the direction of labeling true MZ twins as DZ, rather than the reverse. This may have two underlying causes. First, people may assume (incorrectly) that identical twins must be identical in every way and if they are not they must be fraternal. Such reasoning

would reflect misinformation on the part of the public, as well as provide support for abandoning the term identical in favor of monozygotic. It is well known among scientists that monozygotic twins can differ across virtually every behavioral and physical trait, including intelligence, personality, height and weight. Perhaps these observations need to be communicated more clearly outside the research community.

A second explanation as to why MZ twins are more often misjudged as DZ than the reverse is that individual differences in appearance and behavior are highly celebrated in most societies. Thus, the concept of genetically identical individuals may be disturbing to some twins and their families who suspect that MZ twins will struggle over issues of identity and selfhood. Several identical twins who

participated in the Minnesota Study of Twins Reared Apart had such concerns prior to meeting their co-twins, but their worries proved unfounded upon reunion when they realized that they and their co-twins were not exactly alike in every measured trait.

It is important that parents of same-sex twins be informed of their children's twin type soon after their birth. This information can help parents and ultimately teachers, family members, friends and twins themselves to understand their similarities, differences, preferences and predispositions. DNA testing should be a routine part of twin deliveries and needs to be covered by health insurance plans.

I am grateful to Susan and Sarah for sharing their story with me and allowing me to share it with readers of TRHG.

Research Reports

Blood Chimerism and Possible Freemartin Effect in Opposite-Sex Twins

The frequency of blood chimerism in dizygotic (DZ) twins has been of great interest to twin researchers. In 1996, van Dijk et al. reported that members of 8% of DZ twin pairs and 21% of DZ triplet sets showed foreign fetal blood, demonstrating that blood chimerism in DZ twins is more frequent than had been supposed. In 2010, an extraordinary case study of a 2 1/2-year-old male–female twin pair was reported by Bogdanova and colleagues in Germany. The twins, conceived by ovarian stimulation and intrauterine insemination, were born to a healthy 32-year-old mother. Fetal ultrasound revealed a monochorionic diamniotic placenta, although this arrangement was not confirmed after birth. It is rare for DZ twins to have a single chorion, but this placental arrangement has been observed previously. Cytogenetic and molecular genetic analyses of the twins indicated blood chimerism in the fibroblasts (cells in connective tissue) of the female twin (46, XY and 47 XX) who was also diagnosed with Down syndrome or trisomy 21.

The most remarkable clinical feature of the female co-twin in this pair was that despite the presence of normal female genitalia, she showed aplasia (developmental failure) of the uterus and Fallopian tubes. The researchers speculated that the female twin's sexual development was caused by the effects of Mullerian Inhibiting Substance (MIS), transmitted by her male co-twin during gestation. If so, this would lead to regression of the Mullerian ducts that give rise to females' sexual anatomy. The process by which female twins' sexual development is curtailed by exposure to male hormone from the co-twin is known as the freemartin effect, and has been documented in opposite-sex cattle. In fact, female co-twins in male–female cattle pairs are typically sterile. The freemartin effect has

not been observed in people, but based on their observations the investigators suggested that they have identified the first case of freemartinism in humans.

Mental Health of Japanese Twins and Non-Twins

Many people assume that twins are more highly represented among populations of individuals with mental difficulties, but the findings are actually mixed in this regard. A 2010 study by Japanese investigator Oshima and colleagues added important information to this question. The researchers identified 353 high school students in grades 7, 9 and 11, a group that comprised 66 twins and 287 non-twins. Fifteen twin pairs were MZ, four twin pairs were opposite-sex and fourteen twin pairs were unclassified. Three twins were unavailable on the day of testing. The high school is unique in that each year 10–20 pairs of twins are specially recruited. I believe that many ISTS members visited this school during the 1992 International Twin Congress held in Tokyo.

The researchers hypothesized that the twins would show poorer mental health status relative to the non-twins, given their less favorable intrauterine environment. In order to test this hypothesis students were requested to complete four questions concerning psychotic like experiences (PLEs); for example, 'Have other people ever read your mind? Have you ever heard voices other people cannot hear?' Students also completed the Japanese version of the 12-item General Health Questionnaire (GHQ-12). Interestingly, the twins showed more favorable mental health status than the non-twins. GHQ-12 scores were significantly lower in twins than in non-twins, and PLEs were less frequent among female twins than non-twins. Modest tendencies along these lines were observed for the GHQ-12 in females and the PLEs in males. It was

suggested that twinship provides a positive developmental environment for twins, an explanation strengthened by the finding that more singletons than twins indicated that they had no one in whom to confide.

The authors noted that their findings may be limited by the possible exclusion of twins with mental difficulties, due to these twins not having taken the school entrance examination. In addition, the self-report format and modest sample size may have restricted the reliability and/or accuracy of the data. Nevertheless, this study contributes to existing knowledge of twins' mental status, a question that will always be important to twins, families, therapists and researchers.

MZ Twinning and Assisted Reproductive Technology

The mechanisms by which monozygotic (MZ) twinning occur have yet to be fully elucidated. A comprehensive review of this subject by Aston and colleagues from the University of Utah School of Medicine in Salt Lake City provides an informative overview of what is known, what is unknown and why, with reference to the etiology of MZ twinning. In contrast, much more is known about factors affecting DZ twinning, such as genetic factors and advanced maternal age.

The authors noted that the lack of animal models poses a limitation for understanding human MZ twinning. The only natural MZ twinning in a non-human mammal occurs in the nine-banded armadillo, an animal that regularly produces MZ quadruplets. One explanation for this phenomenon has been delayed post-fertilization implan-

tation. Delayed implantation may not account for all cases of human twinning, but might be related to some cases of conjoined twins. Experimental lowering of temperature and reducing oxygen availability have also been linked to induced MZ twinning in fish and in rabbits.

The increased use of artificial reproductive technology (ART) has led to an unexpected increase in MZ twinning, albeit to a lesser degree than the increase in DZ twinning. The authors point out that the various placental arrangements shown by ART MZ twins suggest that a variety of mechanisms — alone or in combination — may explain ART-associated MZ twinning. These mechanisms include delays in fertilization, embryo development or implantation, mechanical disruption of the early embryo and alterations in culture conditions. Interestingly, an increase in maternal age (usually associated with DZ twinning) has also been linked to MZ twinning. Findings in this area are mixed, but increased maternal age may be a function of the fact that older mothers are the ones likely to seek ART to overcome infertility.

Given the relative rarity of MZ twinning in the human population, efforts toward identifying the important causal factors underlying ART-related MZ twinning are hampered. The larger studies do show that the most important factors include ovarian stimulation and extended embryo culture, combined with blastocyst transfer. The importance of understanding these processes is underlined by the elevated frequency of neonatal complications among twins compared to non-twins. Knowledge of what causes MZ twinning could potentially lead to improved management of multiple birth pregnancies and better treatment of newborn twins.

Human Interest

Newborn Twin Revived

Opposite-sex twins, Emily and Jamie Ogg, were born prematurely at 27 weeks to an Australian couple, Kate and David Ogg, in Spring 2010 (Inbar, 2010). Emily survived, but her twin brother Jamie was declared deceased after physicians failed to restore his breathing after a 20-minute interval. It was decided to place Jamie on his mother's chest so she and her husband could come to terms with his death. Within five minutes the newborn started making short startled movements, but doctors informed his parents that these behaviors were simply reflexive. However, Jamie's movements continued over the next several hours until he finally opened his eyes. He began to accept breast milk from his mother who placed the milk on her finger and brought it to his lips. He also began grabbing his mother and father's fingers.

The parents' efforts to obtain the attention of their doctor failed until they relayed the message that they had

come to terms with their baby's death. When the doctor arrived, he examined the newborn in disbelief. Dr. Lisa Eiland of New York's Cornell Medical Center commented that the mother's warmth and heartbeat most likely provided the stimulation needed to revive the infant. The couple had practiced kangaroo care, in which newborns are immediately placed on their mother's chest to regain the body warmth and heartbeat sounds available in the womb. This process is analogous to what take place in the case of newborn kangaroos that receive these benefits from being in their mother's pouch. Kangaroo care is practiced in many locations throughout the world and is especially helpful in places where incubators are unavailable.

The Oggs, Jamie and his twin sister Emily appeared on NBC's Today Show in September 3, 2010 when they were 5 months old. I was fortunate to have seen this moving and informative televised segment.

UCLA Twin Basketball Recruits

Identical twin brothers, David and Travis Wear, will be leaving the University of North Carolina (UNC) to play basketball for the UCLA Bruins (Gold, 2010). The twins are 6 feet, 10 inches tall, and were McDonald's All-Americans in high school. They are originally from Huntington Beach, California and will have the opportunity to play with some former teammates (Markazi & Leung, 2010).

Their decision to leave UNC after one year is not clear, but it seemed that the program there was not as good a fit as the twins would have liked. They also noted that several universities offered a place for just one of the twins, but they were not interested in being apart from one another. The twins say that they are comfortable playing together, something they have done all their lives. According to Travis, 'It was a given that we'd go to the same place.' In choosing the same colleges, David and Travis join other basketball twins, such as Robin and Brook Lopez who recently played for Stanford University before being drafted by different professional teams in 2008. These twins exemplify the genetically based physical skills and achievement motivation necessary for unusual athletic success. Identical twins have the added advantage of a close relationship that enables frequent practice sessions with a well-matched partner and provides the social support essential to great performance.

Loss of a Triplet

Five-year-old Florida triplet, Delaney Rossman, was killed by an out of control car on November 5, 2010, while playing in a neighbor's yard with her two co-triplet sisters, an older sister and a friend. One of the other triplets, Gabrielle, was badly injured, but is recovering, while the older sister and third triplet escaped injury. Delaney's friend sustained some injuries in the accident. The triplets appear to be fraternal from the photograph displayed in the newspaper articles about the loss.

The funeral of the young triplet attracted many friends and neighbors. One of them, a mother of twins, com-

mented that she could not imagine losing a twin or triplet child because of their special connection.

The effects of losing a twin in childhood have not been studied as extensively as have the effects of losing a twin in adulthood. However, the cases I have come across indicate that losing a twin in childhood is a devastating event with lasting emotional consequences. Grief counselors were available at the triplets' school to assist Delaney's classmates in coping with the loss.

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