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News, Views and Comments

Double Vision: Eye Findings in Twins Reared Apart/Twin Research: Perinatology and Conjoined Twins; Thoracopagus Twin Cattle; MZ Twins Discordant for Musical Training/In the News: College Benefits for Twin Parents; Octomom Revisited; Genetic Editing of Infant Twins; Quarternary Marriages; Unusual Twin Pregnancy

Nancy L. Segal
Department of Psychology, California State University, Fullerton, CA, USA

Abstract

Findings related to visual functioning, drawn from early reared-apart twin studies, are summarized. These data are supplemented by more recent research from similar investigations. This section is followed by a survey of findings and conclusions from a special issue of the journal *Seminars in Perinatology* concerning the challenges and management of conjoined twins. An early case report on thoracopagus-conjoined twin cattle is also presented, as are neuroanatomical findings from a study of monozygotic twins discordant for musical training. Items noted in the news include college benefits for twin parents, an update on octomom, claims of gene editing of infant twins, the nature of quarternary marriages and an unusual planned twin pregnancy.

Double Vision: Eye Findings in Twins Reared Apart

The impetus for this article on vision (ophthalmological findings) in twins reared apart comes mainly from my research on a rare case of two, doubly switched-at-birth monozygotic (MZ) male twin pairs from Colombia, South America (Segal & Montoya, 2018; Segal et al., 2017; Segal et al., 2018). Colleagues and I are currently analyzing data from a comprehensive study of the switched twins' visual functioning. As a prelude to that analysis, it is worth noting that a summary of relevant findings from early reared-apart twin studies has been completed (Farber, 1981). Furthermore, past and recent findings from the Minnesota Study of Twins Reared Apart (MISTRA), the only reared-apart twin project to include a formal ophthalmological component in the assessment battery, are available and add important information to that literature. I will focus on refraction, but reference other eye conditions as well.

Farber (1981) began her survey with reference to a 'remarkable book' on ophthalmological genetics by Sorssy (1970). Cited in the book is strong evidence of genetic influence on refraction, based on a study of 78 MZ twin pairs, 40 dizygotic (DZ) twin pairs and 48 control twin pairs. Refractive errors refer to optical deficiencies that prevent the eye from properly focusing light, causing blurred vision. The key refractive errors are nearsightedness (myopia), farsightedness (hyperopia) and astigmatism (blurred vision caused by light failing to find a single focus on the retina; Heiting, 2018). I was unable to obtain the original twin study (Sorsby et al., 1962), so the zygosity classification method is not known, but a subsequently published comment offers insight into the data analysis (Sorsby & Fraser, 1964). Specifically, correlations across the three pair types (MZ twins, DZ twins and controls), organized by refraction types, led Sorsby et al. (1962) to suggest a quantitative inheritance pattern consistent with additive genetic effects and no dominance — correlations for MZ twins were close to 1.0, correlations for DZ twins were close to .50, and correlations for the control pairs were close to 0. In later family studies, these investigators acknowledged that more than one mode of transmission for refraction errors was likely (Sorsby et al., 1966).

Ophthalmological data on 35 reared-apart MZ (MZA) twin pairs (from among the 121 pairs mentioned in the literature and assessed between 1922 and 1973) were available in the early studies. The data were recorded in various ways, including examinations and general statements. It was discovered that co-twins in 27/34 pairs (79%) were concordant for the absence or presence of visual problems, and that co-twins in 20/32 pairs (62.5%) were concordant for type of visual disturbance. Interestingly, concordance was the highest for nearsightedness, farsightedness and astigmatism. Also interesting is that some evidence of mirror-imaging effects was observed, such as two pairs in which the right-handed co-twin had strabismus in the left eye and the left-handed co-twin had strabismus in the right eye. Strabismus (exotropia) occurs when the visual axes are not parallel and the eyes seem to look in different directions (Grayson, 2004). However, a third twin pair concordant for right-handedness showed severe quint in opposite eyes.

Participants in the MISTRA underwent comprehensive eye examinations that lasted several hours. Twins were seen at the same

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time by a different ophthalmologist to avoid biased assessment. A paper reporting detailed findings for the first 26 pairs (18 MZA and 8 same-sex reared-apart DZ [DZA]) is available (Knobloch et al., 1985). Concordance for refractive errors was higher for MZA twin pairs (75%) than for DZA twin pairs (50%), consistent with the earlier data. Genetic influence on the C/D ratio (measure of optic nerve cupping) was also found, given 90% MZA twin concordance, relative to 50% DZA twin concordance; findings from this paper are further reviewed in Segal (2012). The sample size was small at this time in the study, but MZA twin concordance for wearing eyeglasses, age at wearing eyeglasses, presence of esotropia (turning in of one or both eyes; see American Association for Pediatric Ophthalmology & Strabismus, 2016) and strabismus surgery was observed in selected pairs.

In later years, some additional visual studies using a much larger number of reared-apart twin pairs were conducted by ophthalmologists working with the MISTRA. Comparison of 44 MZA twin pairs and 26 DZA twin pairs revealed genetic influence on various measures of the optic disc (Bitrian et al., 2014). The following year the same team produced evidence of genetic effects on selected vascular patterns, based on data from 66 MZA twin pairs and 40 DZA twin pairs (Tokarev et al., 2015).

It is unfortunate that the reared-apart twins' birth histories were generally unavailable, given that they might have offered insights into cases of discordance. Nevertheless, finding genetic influence on visual characteristics assists the understanding of why some individuals develop eye disorders, as well as identifying the proper management plan for individuals at risk.

Twin Research

Perinatology and Conjoined Twins

A 2018 series, *Seminars in Perinatology*, included an important introduction and overview followed by 10 very informative contributions concerning the perinatal and postnatal management of conjoined twins (Arnold et al., 2018a). Two of the papers (the introduction and a summary of the ethics of surgical separation) are summarized briefly below.

I am discussing the introduction because it provides an excellent survey of the challenges posed by the care of conjoined twins (Arnold et al., 2018b). The authors begin by noting that conjoined twins occur in 1.5/100,000 to 1/500,000 births, with females outnumbering males, 3:1. These twins are physically connected at birth, sharing a chorion, placenta and amniotic sac. Two theories proposed to explain their origins (delayed fission of fertilized egg and fusion of secondary embryos) are stated, but not evaluated; see Segal (2017) for discussion of this issue.

The 10 topics addressed in this issue are outlined and annotated. They include antenatal and delivery room management, simulation from delivery to discharge, nursing concerns, pharmaceutical dilemmas, nutritional considerations, therapy services/resources, radiological evaluation, ethical considerations, surgical separation and family support. It is explained that these topics were identified based on the literature and the nature of contributors' experiences in their respective centers.

The second paper addressing the unique ethical and care issues surrounding the surgical separation of conjoined twins is addressed in a sensitive and informative way (Thomas et al., 2018). Decisions are tailored toward different situations; for example, both twins will die if they remain conjoined (one twin will survive if the other twin is sacrificed), or both twins will survive if they remain conjoined. The nature and provision of family care is also closely examined. Helpful tables concern the ethical aspects of (1) pre- and post-surgical outcomes, (2) the doctrine of the double effect and its application to surgical separation decisions, and (3) palliative care with modifications to tenets offered by the World Health Organization.

In the paper, the doctrine of the double effect is discussed with specific reference to the sacrifice of one twin to save the other when both twins would otherwise not survive. According to this doctrine, it is sometimes permissible to cause harm as a side effect — a 'double effect' — of bringing about a favorable result even though it would not be permissible to cause such a harm as a means to bringing about the same good result (see McIntyre, 2018). Thomas et al. (2018) list various relevant criteria that must be fulfilled in order to justify the sacrifice of one twin; for example, the action must be good or morally indifferent; the agent must intend only good, not evil. The difficult and contentious nature of this situation is emphasized.

Thoracopagus Twin Cattle

MZ twins occur in about 10% of national cattle populations (Echternkamp & Gregory, 2002). An early case of fairly equal conjoined twin cattle was documented by researchers in South Africa (Petersen & de Boom, 1970). Observation of dystokia (abnormal labor) alerted staff to this unusual pregnancy.

The twins, both female, were delivered alive by cesarean section. As thoracopagus twins, they were joined along the sternum and showed fusion of their livers. However, two separate hearts of approximately equal size were present. One twin survived for only 2 min, while the other twin survived for 10 min. The shorter-lived twin's slight deformed head and forelimbs were attributed to intrauterine pressure caused by the restricted space. This twin also showed some lung reversal in that the left lung showed the form of the right lung, and vice versa. However, other than the joining of their livers, no other external distortions were noted.

As with human twinning, reduced gestation length and lower birth weights are of concern when it comes to cattle (Nephawe, 2002). The physical reversal of an organ in one of the conjoined twins is also a typical manifestation of conjoined twinning in humans (see Segal, 2017).

MZ Twins Discordant for Musical Training

An ongoing controversy within the musical field is the origin of associations between skill level and brain anatomy. The specific issue is whether expert musicians are born with particular brain characteristics or if they are acquired over the course of practice and learning. A fresh approach to this question was taken by de Manzano and Ullén (2018) in a study of MZ twins discordant for musical training. Their design controlled for genetic differences, thereby highlighting the effects of practice.

The participants included nine MZ twin pairs drawn from an initial cohort of 1211 twins who were part of a large web-based survey associated with the Swedish twin registry. The larger group was reduced to 83 pairs in which only one twin was playing keyboard and the twins had a total within-pair practice difference of 1000 or more h. The final nine pairs (five female and four male) were those who agreed to travel to Stockholm to participate; a tenth set had agreed, but an equipment malfunction caused the loss of their data. The twins ranged in age from 31 to 47 years. Their zygosity was variously assessed via standard questionnaires and genotyping, as explained in an earlier related study (see Eriksson et al., 2017).

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Both structural (sMRI) and functional magnetic resonance imaging (fMRI) were used to obtain information on the brain characteristics of interest. sMRI outlines the sizes and shapes of the brain's subregions (Stigler & McDougle, 2013), whereas fMRI measures and maps brain activity (Center for Functional MRI, 2019). Key findings were that (1) more musically active co-twins showed greater cortical thickness in the auditory-motor network of the left hemisphere, and (2) the more musically active twins had more developed white matter microstructure in the relevant areas of corpus callosum and in both hemispheres. It was suggested that this study offers the first compelling evidence that training is largely responsible for differences in the anatomical brain characteristics of expert and nonexpert musicians. I agree, yet the small sample size and lack of baseline data (i.e., brain anatomy based on examination prior to the twins' musical training) urge cautious interpretation and further study.

In the News

College Benefits for Twins

The increasing financial burden of supporting children's college education is well recognized. A worry is that mothers and fathers will do little advance planning simply out of fear; fortunately, a recent guide that can assist families manage these challenges is available (Bernard, 2018). Interestingly, parents are advised to 'ask the fertility gods to grant you twins or children close enough in age that they'll attend college at the same time'. The reasoning is that this situation increases the chances of obtaining financial aid based on need, as well as grants that do not need to be paid back.

Unfortunately, Bernard failed to note that having two or more children at the same time creates financial burdens from birth onwards, long before college attendance is a consideration. (Some companies do offer multiple birth parent discounts on clothing and other items, but it seems unlikely that the many child-rearing costs would be sufficiently offset; see Multiples Illuminated, 2019). In addition, she failed to note that some colleges offer two-for-one college scholarships to twins, such as Lake Erie College in Ohio and Wilson College in Pennsylvania (College Scholarships, 2018).

Octomom Revisited

Nadya Suleman of southern California became famous in 2009 with the birth of octuplets. The six boys and two girls represent only the second set of octuplets to be successfully born in the United States; the first set was born to the Chukwu family in 1998, although one of the multiples passed away at 1 week of age (Keminications Media/PR, 2009). Among Suleman's eight babies are two sets of identical twins. In an earlier issue of *Twin Research and Human Genetics*, I presented an analysis of the number of identical and fraternal twin pairs that could be generated by this set, co-authored with Altowaiji and Ihara (Segal, 2009).

Late last year, a newspaper reporter visited Suleman, now aged 43, and her 14 children (Popescu, 2018). In addition to the octuplets, Suleman has six other children, including a set of fraternal twins, also conceived by in-vitro fertilization. Note that the mother's name is Nadya, not Natalie, as indicated in the newspaper article. There is also the implication that 12 embryos were implanted, but that is incorrect as stated. It is correct that six embryos remained after her previous pregnancies and all were implanted; two apparently divided to produce two identical twin pairs.

The octuplets are described as being small for 10 years of age, but healthy, polite and studious. However, one child (presumably one of the octuplets) is severely autistic and another child shows autistic symptoms. It is well known that twins and other multiples are more likely to be born prematurely and to suffer physical complications than nontwin children (Segal, 2017).

Suleman works full-time as a counselor, but also relies on government assistance. She is working on a book that she hopes will present a truthful picture of her life.

Gene Editing of Infant Twins

In November 2018, Chinese researcher He Jiankui, at the Southern University of Science and Technology in Shenzhen, claimed to have performed gene editing on newborn female twin infants. The claim was that the twins, known as 'Nana' and 'Lulu', had their DNA modified to prevent them from contracting HIV; the gene in question is called *CCR5*. This work was not sanctioned by He's institution, whose administrators are launching an investigation. Many experts in the genetics field reacted very negatively to the claims, citing dangers that could result from the procedure and the fact that HIV can be controlled with drugs, preventing its transmission from parents to newborns. Some experts called the claim questionable (Roberts, 2018).

Quarternary Marriages

The only study of identical twins married to identical twins, conducted by Taylor (1971), is well known, but other perhaps less formal research has been performed. One year later, psychologist Robert Ravioli (1972/2018) published an article on this topic in the *New York Times* that was reprinted in the newspaper in 2018. This work has great relevance for one of the news items that follows.

Ravioli developed a two-person interaction task to identify and analyze patterns in families with different structural characteristics. Impressed with the success of these quarternary marriages, he explained them with reference to two effects, namely economic and child-rearing. He argued that economic challenges are less acute in what he terms 'natural communes'. Twins married to twins often share a home, reducing the size of taxes and mortgages. When it comes to child-rearing, wives often work outside the home, but arrange their hours so that one mother is usually home to care for their children. In my own work I have observed similar features that I also believe explain the success of these arrangements (Segal, 2007). In addition, I agree with Ravioli that these families can serve as marital models from which nontwin families can learn to improve their lives.

Interestingly, Ravioli indicated that quarternary marriages include three kinds of couples: two husband–wife pairs, two identical twin pairs and one pair of marriages. (I am unclear as to the meaning of the last pairing.) I would say that the third pair is the in-laws, namely the twins who form part of the foursome, but are not married to each other.

Unusual Twin Pregnancy

In December 2018, identical Australian twin sisters, Anna and Lucy DeCinque, appeared on FOX TV to announce their plan to each become pregnant with the child of their common boyfriend, Ben Byrne. They also noted that they would like to change the law in order for both to legally marry Byrne. Heeding their mother's advice, they hope to conceive naturally, rather than by in-vitro fertilization (Bartiromo, 2018).

The children resulting from these two unions would be genetically equivalent to full siblings, sharing 50% of their genes on average,

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by descent. That is because the mothers would be genetically identical and the same father would be used. Of course, the children would also be legal first cousins, and each twin would be both an aunt and a 'mother' to their nieces and nephews. There have been cases of identical twins married to identical twins whose children are also considered to be genetic full siblings (see Segal & Montoya, 2018), but the proposed situation described above may be a first.

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