

The First “Classical” Twin Study? Analysis of Refractive Error Using Monozygotic and
Dizygotic Twins Published in 1922

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Abstract:

The first classical twin studies, recognizing the potential of comparing findings in identical twins, have previously been reported to be those by Siemens and by Merriman, both published in 1924. However, we would like to bring to attention a study performed by Walter Jablonski, two years earlier, investigating the contribution of heredity to refraction in human eyes. Jablonski examined the eyes of 52 twin pairs and by comparing the size of within pair differences between identical and nonidentical twins was able to infer the heritability of a trait. Therefore, this is likely to be the first reported classical twin study.

Twin studies have been described as “the perfect natural experiment to separate familial resemblance from genetic influence” (Martin et al., 1997). A “classical” twin study uses the similarities or concordances of a trait or disease within monozygotic (MZ) twin pairs compared to dizygotic (DZ) twin pairs to judge the relative importance of genetic and environmental factors. It is assumed that both MZ and DZ twins share roughly the same common family environment and therefore any greater concordances among the MZ twins compared to DZ twins can be attributed to greater sharing of genetic factors.

The first scientist to recognize the potential of twins to study nature versus nurture is generally thought to be Galton in London in 1874 (Galton, 1874) who stated “There are twins of the same sex so alike in body and mind that not even their own mothers can distinguish them.....This close resemblance necessarily gives way under the gradually accumulated influences of differences in nurture, but it often lasts until manhood”. However, it is not clear whether Galton realized the full potential of using the two distinct types of twins, as the biology of twinning was not fully understood at that time.

Spector has cited in his review (Spector, 2000) that the first reported classical twin studies were in 1924 by two independent researchers. Hermann Siemens, a German dermatologist, examined naevi in twins (Siemens, 1924) and published a book on twins in which he states, “With the help of twin pathology we found a way to judge hereditary factors on the features under

investigation....The assessment is based on the comparison of the findings in identical and nonidentical twins”. In the same year Merriman in the United States published a study examining IQ using psychological monographs. Compared to the total twin population, identical twins were found to have a much higher correlation (88-98%) and he states, “The duplicate of the one egg origin should show a very much higher degree of resemblance than the fraternal because each member of the pair develops from substantially the same arrangement of the factors for heredity in the germ cells” (Merriman, 1924).

However, Walter Jablonski, an ophthalmologist working in an eye clinic in Frankfurt, published a pioneering twin eye study two years earlier in 1922. His manuscript, published in German in *Archiv für Augenheilkunde* was entitled “Ein Beitrag zur Vererbung der Refraktion menschlicher Augen” (English translation: A contribution to the heredity of refraction in human eyes). He used both MZ and DZ twins to examine refractive error (Jablonski, 1922). Fifty-two twin pairs of the same sex underwent an ophthalmological examination; 40 were identical and 12 pairs were nonidentical twins. Total refraction and total astigmatism were measured by cyclopegic objective refraction using skiascopy. Corneal refraction and degree of astigmatism were measured using a Javal Ophthalmometer.

It is clear from his paper that Jablonski realized that there are phenotypic differences within twins but that the differences in a genetic trait would be less in identical twins compared to nonidentical twins. The principle of this comparison is the methodological basis of the classical twin study.

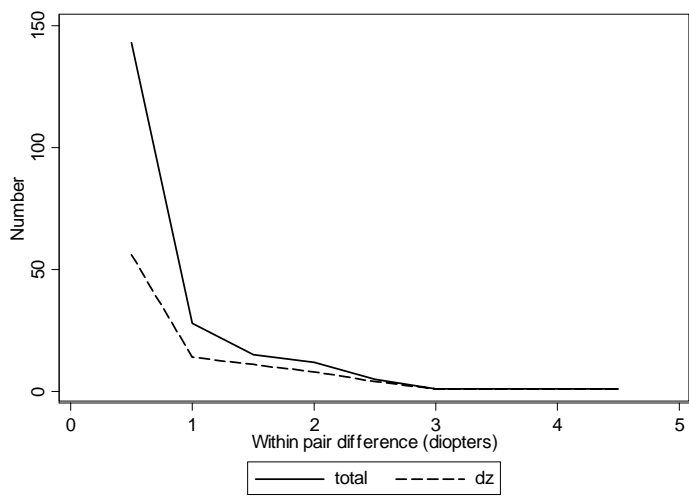
For each of the four parameters of interest investigated, the size of the within-pair differences was calculated. For MZ twins, you would expect a smaller or narrower within-pair difference in the parameter of interest (e.g., 0.5 diopters) to occur more frequently than larger within-pair differences (e.g., 3 diopters). Jablonski states in this paper “the smaller differences are seen in the majority of monozygotic cases, while larger differences occur in dizygotic cases” (English translation).

These results were plotted on graphs named ‘modification curves’. Figure 1 shows a reproduction of the figure in Jablonski’s paper for total refraction. One curve displayed the number of all twins (MZ and DZ combined) while another dashed line curve on the same graph represented DZ twins only. The number of individuals was plotted on the vertical axis and the size of the within-pair difference, the measurement of interest, was plotted on the horizontal axis. At the point where the two curves met, a ‘modification width’ was calculated. Jablonski assumed that at this point, the degree of refraction or astigmatism was due to other nongenetic influences. For total refraction, the author found that the curves met at 2.5 diopters, resulting in a modification width of approximately 2 diopters. This rather small or narrow modification width of refraction is interpreted by Jablonski to imply that hereditary factors have a great influence on the development of refraction. Although Jablonski’s use and interpretation of these modification curves may have some flaws, it is clear that he understood the importance of using within-pair differences of MZ and DZ twins.

More recent classical twin studies have now confirmed Jablonski's finding that genetic factors are of major importance in refraction with a heritability of approximately 85% (Hammond et al., 2001; Lyhne et al., 2001).

This study was pioneering as it used both MZ and DZ twins to analyze a phenotype by comparing the size of their within-pair differences to infer the heritability of a trait. To our knowledge, therefore, this is likely to be the first classical twin study reported.

Fig.1 Total Refraction



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