The Validity of Weinberg's Differential Rule

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Evidence continues to accumulate that Weinberg's Differential Rule is a useful approximation. This is in spite of the fact that one of the premises he used in its derivation is almost certainly, to some extent, false. An explanation is offered here.

Let p be the probability that a dizygotic (DZ) twin birth is male. Then if p were equal and independent in all pairs of DZ twins, the frequencies of pairs with 2, 1, and 0 males would be in proportion to the binomial terms $p^2 : 2pq : q^2$, where $q = 1 - p$. And if p is close to the value .5, then the expected numbers of same-sex and opposite-sex DZ pairs will be approximately equal. This is the reasoning behind Weinberg's Differential Rule (Weinberg, 1901). The rule is important because it provides a method for estimating the proportions of monozygotic and DZ pairs in a sample of twins for which no genetic markers (other than sex) are available.

However, over the intervening years, evidence has accumulated that (in singletons at any rate), instead of being invariant, p varies appreciably within and across sibships. Since this would nullify one of Weinberg's premises, this evidence will first be summarised. Later it will be shown how, in spite of the fact that his premise is almost certainly false, his rule may nevertheless remain a close approximation to the truth.

Within-Sibship Variation of *p*

A short meta-analysis concluded that p, the probability that a birth will be male, varies substantially with the time of insemination across the fruitful maternal cycle (James, 2000); it also reportedly varies with the side of ovulation (James, 2001). Paternal sources of within-sibship variation may also be suspected, but they will not be considered here.

Between-Sibship Variation of *p*

Evidence has been adduced that offspring sex ratio reportedly varies with some viral conditions, some pregnancy-related conditions, and some male and female endocrine diseases: offspring sex ratios also reportedly vary with a number of paternal chemical and occupational exposures (James, 2006 a). It may be acknowledged that bias of various sorts may have entered this summary. But some of the cited data have been extensively replicated (e.g., those relating to adverse obstetric conditions, parental viral status, and chemical exposures). So there can be no reasonable doubt that (at least in regard to singletons), one of Weinberg's premises is, to some extent, false.

The Problem

Nevertheless, empirical research continues to suggest that Weinberg's Rule is 'rather robust and, that in spite of its simplicity, it gives reliable results, when official birth registers are analysed' (Fellman & Eriksson, 2007). What can be the explanation?

An Attempted Explanation

Two studies on very large samples (exceeding 500,000 and 800,000 births respectively) concluded that there is no appreciable correlation between the sexes within sibships (Maconochie and Roman 1997; Jacobsen et al., 1999). It follows that (in singletons), the within-sibship variance of p, and the between-sibship variance of p, counteract one another and are roughly equal.

If we make the assumption that the sexes of DZ twin zygotes are subject to the same sources of variation (across and within DZ twin pairs) as those of singletons (across and within sibships), then an explanation becomes apparent. Efforts to estimate the standard deviation of p across couples, using different methods, led to remarkable agreement, namely, .05 (Edwards, 1958), .045 (James, 1975), and .051 (Pickles et al., 1982). Using a value of .05 as the standard deviation of p (viz. a variance of .0025) both within and across samples of DZ twin pairs, one may construct a model which satisfies Weinberg's Rule, without assuming his premise of equality (see Table 1).

Comment

The empirical evidence suggests that Weinberg's Differential Rule is approximately correct, in spite of the falsity of the equality premise he used in its derivation. The explanation suggested here is that (in regard to DZ twin pairs, as is apparent in singletons within sibships), p has roughly equal within-pair and across-pair variances. Two consequences follow from this suggestion.

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Table 1

A Model Embodying Both Lexis and Poisson Variation and Yielding a Binomial Distribution of the Sexes Within Dizygotic Twin Pairs

	Values of *p*		Expected frequencies of sex combinations				
Subsample	Twin 1	Twin 2	MM	MF	FM	FF	Totals
A	.4	.5	20	20	30	30	100
B	.5	.4	20	30	20	30	100
C	.5	.6	30	20	30	20	100
D	.6	.5	30	30	20	20	100
			100	100	100	100	

Note: 1. The table was constructed by supposing that mothers of DZ twins are divided into four equal-sized subsamples, A, B, C, and D, with the given probability characteristics. The model is made simple to illustrate how Lexis and Poisson variation may counteract to yield a binomial distribution. As noted in the text, such simplification conceals the (likely) possibility that in some DZ twin pairs the probabilities p_1 and p_2 lie on opposite sides of the value .5 (thus providing difficulty for the conventional explanation for sex ratio variation [sex-related fetal wastage]).

2. The variance of the binomial is $n\,pq$. In the Lexis binomial, this value is augmented by: $n(n-1)(\text{sigma}_a)^2$, while in the Poisson binomial, this value is diminished by: $n(\text{sigma}_w)^2$, where n is the sample size, (2 in the case of DZ twin pairs), $(\text{sigma}_w)^2$ is the variance of p within samples, and $(\text{sigma}_a)^2$ is the variance of p across samples (e.g., Weatherburn, 1949, p. 115). If Poisson and Lexis variation were to coexist at the time of formation of the zygotes of DZ twins, then (since $n = 2$), the resulting variance would be binomial (as required by Weinberg's Rule) if the two variances were equal. In the above model, each takes the value of .0025 as suggested in the text.

3. For convenience, the mean value of p in the model is taken as .5. In practice, the mean value for (Caucasian) singletons is of the order of .514, but DZ twins (and their siblings) seem characterised by a slightly higher value than this (about .517; James, 1986).

First, as noted above, it enables one to reconcile the essential soundness of Weinberg's Rule with the false premise used in its derivation. Second, the conventional view of geneticists is that the variation of sex ratio at birth is dependent on sex-related nidation, and embryonic and fetal mortality (Boklage, 2005). In contrast, the present argument suggests that, in addition, there are preconceptional sources of variation of p (James, 2006b). This is so because it would seem that if the model embodied in Table 1 were to be endowed with a realistic degree of complexity, then some DZ twin pairs (like some women bearing singletons), would be characterised at the time of formation of the zygotes by p values that lie on either side of the value .5. In the absence of evidence that such variation (in DZ twin pairs and within sibships) is achieved by sex-related fetal wastage (of both males *and* females at different times within the same mother), the additional hypothesis of preconceptional determinants of sex seems tenable (James, 2006b). Geneticists may feel challenged by this.

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