

The distributions of the combinations of the sexes in mammalian litters

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(Received 13 February 1975)

SUMMARY

There is subnormal dispersion in the distributions of the combinations of the sexes in some samples of litters of pigs, rabbits and mice. For instance, consider litters of exactly size 8. As contrasted with binomial expectation, there are too many with exactly 4 males and 4 females, and too few unisexual litters. It is argued that this supports the hypothesis (independently proposed by the author and by Guerrero) that P , the probability that a zygote will be male, varies with the time at which it is formed within the cycle. It is noted that data of Kaufman seem to support the hypothesis.

1. INTRODUCTION

It has been independently proposed on the basis of both direct data (Guerrero, 1970) and indirect data (James, 1971) that the probability P that a human zygote will be male varies with the time of insemination within the menstrual cycle. Further evidence on the point has been presented by Guerrero (1974) and by me (James, 1975*a, b*). It would seem odd if such a phenomenon were to be typical of man but of no other animal. The present study reports the results of a search for evidence of such a phenomenon in polytocous animals.

It is known that the zygotes within the litters of some species are not formed simultaneously (Austin & Braden 1954; Braden & Austin 1954) so it seemed reasonable to wonder whether P varied within litters with time. If it were so to vary, then the variation would constitute an example of Poisson variation (not to be confused with Poisson distributions). Now it is a standard result in probability theory that Poisson variation is associated with a lower variance than the binomial with the same mean (Edwards, 1960). In other words, if the hypothesis (that P varies systematically within litters with time) were true, then the distributions of the combinations of the sexes within litters should have subnormal variance because of the hypothesized Poisson variation of P . So I searched the literature for data on the distributions of the combinations of the sexes within litters of normally polytocous animals.

2. MATERIAL

All the volumes of the Science Citation Index were searched for citations of Parkes (1923), Gini (1951) and Brambell (1944) – three papers which I knew referred to the topic. I then combed the Index for citations of those references – and so on until all the references had been extracted. A second source of material was kindly released to me by Dr Douglas Grahn (of the Argonne National Laboratory) who allowed me access to the raw data underlying the paper of Verley *et al.* (1967).

3. METHODS

There are several methods for testing whether an observed distribution differs significantly in variance from that of the binomial of the same mean.

(1) One may calculate the expected binomial frequencies for the distribution, and then compare the observed and expected values in the central cell (n even) or central two cells (n odd). When there is subnormal dispersion, the observed will exceed the expected frequencies. In previous studies on the present topic, this method has usually been used. However its disadvantage is that it is not immediately obvious how to assess the statistical significance of a result: moreover the method is inefficient.

(2) Fisher (1963) has presented the standard error of the variance of a distribution. This statistic will not be used here because the method described below has the advantage that it may also be simultaneously applied to a number of different distributions to test for an overall tendency to depart from binomial variance.

(3) Robertson (1951), in his Simplified Maximum Likelihood Method, introduced the K -statistic. Each litter is assigned a score

$$K = \frac{1}{2} \left[\frac{f(f-1)}{q^2} + \frac{m(m-1)}{p^2} - \frac{2fm}{pq} \right],$$

where f is the number of females in a litter, m is the number of males in the litter, $n = f + m$, p is the proportion of males in the distribution as a whole, and $q = 1 - p$. Then for a sample of N litters each of size n , let us take

$$\Sigma I = \frac{Nn(n-1)}{2p^2q^2}.$$

Taking the sum of the N values of K as ΣK , Robertson has shown that $\Sigma K / \Sigma I$ is distributed normally with sampling variance $1 / \Sigma I$. For the present type of data, K is a particularly convenient statistic because $\Sigma \Sigma K / \Sigma \Sigma I$ is also distributed normally with sampling variance $1 / \Sigma \Sigma I$, where summation may be carried out over groups of litters of different size (and with different values of p and q). Hence one can test a whole range of material for a tendency towards over- or underdispersion.

4. RESULTS

Some of the data were not presented numerically, or were not presented in sufficient numerical detail to permit the use of Robertson's test. These data are summarized in Table 1. Table 2 gives the results of Robertson's test on the remaining data. The evidence for departures from binomial variance will now be discussed separately for the various species.

(i) *The pig*

There is overwhelming evidence for subnormal dispersion in some – though not all – samples of pigs. It is evident that there is heterogeneity between samples in this respect.

Table 1. *Data not presented in sufficient detail to be submitted to Robertson's test*

(a) Data in which numerical evidence is presented on the binomial expectations and observed frequencies in the central cell (n even) or central two cells (n odd)

Species	Author		Observed	Expected
Rabbit	Russo (1907)	Lecithin sample	82	58.4
		Untreated sample	84	62.6
Mouse	Schultze (1904)		85	98.7

(b) Data in which other evidence is offered on the variance of the distributions of the combinations of the sexes within litters

Species	Author	Evidence
Wild rabbit	Mills (1955)	Observed frequency in central cell (n even) or central two cells (n odd) stated to exceed binomial expectation
Rabbit	Boldrini	Observed frequency in central cell (n even) or central two cells (n odd) stated to exceed binomial expectation
Mouse	Boldrini	Observed frequency in central cell (n even) or central two cells (n odd) stated to exceed binomial expectation
	Howard <i>et al.</i> (1955)	Variance stated to be significantly less ($P < 0.02$) than expected.

(ii) *The mouse*

The application of Robertson's test to the data on mouse litters does not provide convincing evidence of subnormal dispersion (see Table 2). However when these data are considered in conjunction with those in Table 1, we may note two points:

(a) Of the five sets of data for which statistical assessment is available, one (Howard *et al.* 1955) suggests subnormal dispersion at the 2% level; and another (MacDowell & Lord, 1925) at the 3% level. If the null hypothesis were true, the probability of two (or more) such unusual events occurring in five trials may be calculated by reference to the binomial distribution. The sum of the first two

Table 2. *The results of Robertson's test*

Species	Source	Litter sizes	Total litters	Dispersion σ_p^2	z	P	Number of distributions with dispersion	
							Subnormal	supernormal
Mouse	Dr D. Grahn	2-11	10902	-0.0008	-1.33	0.2	31	20
	Copeman & Parsons (1904)	3-9	73	+0.0038	+0.53	0.6	3	4
	MacDowell & Lord (1925)	5-10	104	-0.0102	-2.21	0.03	6	0
Pig	Pankes (1923)	2-14	2020	-0.0055	-5.47	5×10^{-8}	10	3
	Döring (1955)	7-16	2414	-0.0005	-0.79	0.4	6	4
Wild rabbit	Peace data	7-16	4510	-0.0080	-16.4	2×10^{-60}	10	0
	Wartime data	2-11	972	-0.0019	-0.96	0.3	7	3
	Parker & Bullard (1913)	2-12	803	-0.0003	-0.21	0.8	7	4
Hare	McPhee (1927)	2-12	3082	-0.0047	-5.55	4×10^{-8}	9	2
	USDA data	2-10	197	-0.0009	-0.17	0.8	7	2
Cat	Watson (1957)	2-8	200	-0.0070	-1.27	0.2	5	2
	C.W. data	2-4	63	-0.0302	-1.57	0.1	2	1
Sheep	Flux (1967)	2-6	871	-0.0008	-0.24	0.8	4	1
	Robinson & Cox (1970)	3	146	+0.0055	+0.46	0.65	0	1
Farm mink	Wentworth (1914)	2-9	1539	+0.0002	+0.09	0.95	6	2
	Venge (1953)	2-15	21910	+0.0003	+9.1	2×10^{-14}	1	13
Dog	Winzenberger (1936)	2-6	1139	-0.0003	-0.1	0.9	2	3
	Sumner <i>et al.</i> (1922)							

In analysing Grahn's data, the parameters were calculated for the different mouse strains separately because the sex ratio varied significantly between strains. In these data, (because they are so numerous) analysis was only directed at distributions which totalled more than 100 litters.

'Dispersion', σ_p^2 (estimated here by $\Sigma K/\Sigma I$) is defined by

$$V = npq + n(n-1) \sigma_p^2,$$

where V is the observed variance, and npq is the binomial variance. When the dispersion is negative, it is referred to as 'subnormal'. z is the normalised deviate (viz. deviation/s.e.), and p is the associated two-tailed probability.

McPhee's data are based on two separate sources:

- (i) records of experimental herds maintained by the U.S. Department of Agriculture, and
- (ii) records of the Chester White Swine Association.

terms (corresponding to no event and 1 event) of the binomial $(0.97 + 0.03)^5$ is more than 0.99. In other words there is less than one chance in 100 of such an unusual combination of results being due to chance.

(b) If the null hypothesis were true, the two totals in the right-hand columns of Table 2 ought to be roughly equal; indeed one would suppose the extreme right-hand column total ought to be the larger one, bearing in mind the suspected heterogeneity in sex ratio, and the known MZ twinning in mice (Grüneberg, 1952). The disparity between these totals suggests that the null hypothesis is false.

It seems reasonable to conclude that there are causes of subnormal dispersion in some samples of mouse litters.

(iii) *The rabbit*

Again, the evidence provided by Robertson's test is weak. However when all six sets of data are considered together, there is certainly a suggestion of subnormal dispersion:

(a) All six sets of rabbit data are consistent in suggesting subnormal dispersion, and

(b) In the data of Watson and of Brambell (the only data for which the evidence is available), there are 12 distributions with subnormal dispersion and only 4 with supernormal dispersion.

The suggestion of subnormal dispersion here seems to be too strong to be wholly attributable to chance.

(iv) *The hare*

There is some suggestion ($P \approx 0.1$) of subnormal dispersion in the litters of this animal.

(v) *The dog*

There is overwhelming evidence of supernormal dispersion in litters of puppies. Presumably this is due to heterogeneity in sex ratio and to monozygotic twinning.

(vi) *Cat, sheep, farm mink and deer-mouse*

There is no suggestion of sub- or of super-normal dispersion in the litters of these animals.

5. DISCUSSION

It may be useful to consider briefly the circumstances under which subnormal dispersion and supernormal dispersion arise. Edwards (1960) reviewed two modifications of the binomial distribution:

(a) that described by Lexis in which P remains constant for the n trials of an experiment, but varies among several experiments. In the present case, Lexis variation would occur if P (the probability of a male birth) were constant within litters, but varied from one dam to another. Lexis variation is associated with a variance larger than that of the binomial with the same mean.

(b) that described by Poisson in which P takes the value P_i at the i th trial

in each experiment. In the present case, Poisson variation would occur if P varied systematically within litters. Poisson variation is associated with a variance less than that of the binomial with the same mean.

In the case where both Lexis and Poisson variation co-exist, then the observed variance is more or less than that of the binomial with the same mean, according to whether the Lexis or the Poisson variation is the more powerful.

Returning to the present data, the important point is not that evidence for subnormal dispersion is negative in some samples, but that it should be so strong in others. The mysterious thing is not that the dispersions of these distributions are sometimes normal or supernormal (that would be easy to explain as will now be shown) but that they are ever subnormal.

Subnormal dispersion has occurred in some of the present data in spite of the (presumed) existence of two causes of Lexis variation and thus of supernormal dispersion, viz.

(1) variation between individual dams in the propensity to produce male pups, and

(2) occasional monozygotic twins, which apparently occur in pigs (Hughes, 1927; Selby *et al.* 1973) and in mice (Grüneberg, 1952).

The cause, whatever it is, of this subnormal dispersion has overwhelmed these causes of supernormal dispersion. What can it be?

Subnormal dispersion is most unusual in Nature: Gini (1951) commented that the present type of data 'furnishes the unique examples so far known of a subnormal dispersion in statistical series'. So it is perhaps not surprising that though the phenomenon has been known for more than 50 years, there has been no agreement on its cause.

I wish to propose an explanation which, as far as I know, was first mentioned (though not in the present context) as a possibility by Edwards (1960).

First though, let us consider other possible explanations:

(a) In the past, efforts to explain variation in the secondary sex ratio have invoked variation in prenatal mortality. In the present instance we have to consider the possibility that prenatal mortality differentially affects the sex which predominates in a litter (regardless of whether that sex happens to be male or female). Döring (1955) supposed such a phenomenon to occur as a result of dietary deprivation; and indeed only his war-time data show subnormal dispersion. However, of the other data showing strongly subnormal dispersion, though those of Parkes (1923) seem to relate to farrowings in 1918–19, those of McPhee (1927) relate to farrowings during peace-time. So though one would not doubt that the various samples of pigs vary in regard to the magnitude of this dispersion, it seems unlikely that Döring has identified the source of the difference (and indeed it is not clear why dietary deprivation should have such an effect). Moreover, consider all the other samples with subnormal dispersion in Tables 1 and 2: it seems difficult to suppose that they were all undernourished. Brambell (1944) writes of differential foetal mortality (by the predominating sex within a litter) as a cause of the subnormal dispersion in the distributions of the combi-

nations of the sexes in litters in wild rabbits: '. . . this selective mortality of litters tending to unisexuality would have to occur at a stage in development considerably before the gonads have differentiated. Since this appears highly improbable, it is difficult to see how the observed distribution can be explained in terms of differential mortality.'

The last point to make against this suggestion is that there seems to be subnormal dispersion in the data of MacDowell and Lord (1925): yet litters suffering foetal wastage (detected by counting corpora lutea) had been eliminated from these data.

(b) Gini (1951) has noted that in spermatogenesis (in species in which the male is the heterogametic sex), individual male-producing and female-producing sperms have a common origin. He proposed that male- and female-producing sperms may not get the chance to distribute themselves randomly in space, but that individual sperms with a common origin remain spatially associated with one another. As far as I know, there is no evidence for such a process.

(c) McPhee (1927) suggested that herdbook data are subject to defective reporting. He thought that subnormal dispersion is somehow a result of this. However, McPhee does not offer a direct explanation of how reporting error would yield the subnormal dispersion: he falls back on the fallibility of human memory without specifying how this might yield such a result. Lastly, McPhee's explanation cannot deal with the subnormal dispersion characteristic of some samples which were not recorded in herdbooks (e.g. the data on mice and rabbits).

THE PRESENT HYPOTHESIS

Since the above hypotheses seem unlikely, I propose the following hypothesis: there is Poisson variation, within litters, of P , the probability of a male zygote; i.e. P varies systematically from one zygote to another in an individual litter (Edwards, 1960).

The merits of this explanation are that

- (a) it explains the subnormal dispersion described above, and
- (b) it would suggest that other animals are characterized by a phenomenon for which evidence exists in man (Guerrero, 1970, 1974; James, 1971, 1975*a, b*) and
- (c) it seems to be supported by data of Kaufman as will now be described.

If there were Poisson variation of P within litters, then (in principle) P could vary with some variable other than time (e.g. uterine site). So if there were Poisson variation, it is important to know what P varies with within litters. An analysis of data provided by Kaufman (1973) suggest that this variable is time. Kaufman examined litters of mice at varying times after fertilization. In some of the litters a minority of the eggs had entered the first cleavage division and were showing sexable metaphase plates, while the majority were still in the one-cell stage. In other litters examined rather later, the majority of eggs were in the 2-cell stage, but a few were still in metaphase of the first cleavage division.

Let us assume that those eggs which developed sooner were the ones in the litter which had been fertilized earlier. Then, if I am correct, the sex ratio of the sexable

zygotes should vary with time of examination. Kaufman gives the distributions of 62 male and 61 female zygotes by time after administration of the hormone HCG. If I am correct, these two distributions should differ. Their means are almost identical, but their variances are 1.50 (males) and 1.08 (females). The ratio of these two values is 1.4. This is the 10% point of the F -ratio for samples of 60 and 60. Since I would have predicted, on the basis of human data presented by Guerrero (1970) that the male variance would be greater, it seems reasonable to suggest that Kaufman's data support the hypothesis at the 5% level.

I am supported by the Medical Research Council and the Population Council of New York.

For helpful suggestions made in the course of conversation and correspondence, I am grateful to Professor H. Grüneberg, Dr A. R. Jonckheere, Professor H. Kalmus, Dr Anne McLaren and Professor C. A. B. Smith (all of University College London); Sir Alan Parkes (Galton Foundation); Mr J. D. Turton (Commonwealth Bureau of Animal Breeding and Genetics) and to an anonymous reviewer. Lastly, I am grateful to Dr Douglas Grahn (Argonne National Laboratory) for access to his data.

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