CHAPTER 4: HANDEDNESS IN TWINS

Summary

The incidence of left-handedness is the same in MZ twins, DZ twins, and singletons. The proportions of R-R, R-L and L-L pairs in MZ twins are not in a binomial distribution. Twins have not been shown to be subject to any special factors modifying their handedness and are thus suitable for genetic analysis.

4:1 Introduction

Twins, it is usually claimed, are more likely to be left-handed than are singletons, and monozygotic (MZ) twins are more likely to be left-handed than dizygotic (DZ) twins (Nagylaki and Levy, 1973; Corballis and Beale 1976). It is also claimed that the distribution of concordant and discordant MZ handedness pairs approximates to that of a binomial distribution (Collins, 1970). In this chapter I would like to suggest that none of these assertions is supported by adequate evidence, the published evidence being unsatisfactory. I shall consider the items in the reverse order to that just given.

4:2 The distribution of pair-types in MZ and DZ twins

Twin data have represented the Achilles heel of genetic models of handedness, the lack of any difference in concordance between MZ and DZ twins forcing Corballis and Beale (1976) to suggest, and Collins (1970) to directly claim, that R-R, R-L and L-L pairs, in both MZ and DZ twins, were present in binomial proportions, and hence to infer that there could be no genetic control over handedness. Similar conclusions have been made for the genetic control of hand-clasping (Martin, 1975), and have been shown to be false, since some genetic models predict very low degrees of concordance (see Chapters 7, 8 and 9).

Collins (1970) added together the results of several large studies of twin handedness and concluded that the twin pairs were present in binomial proportions. Nagylaki and Levy (1973) demonstrated that Collins' results were invalid, but in so doing they made a further error, of adding together data which are not capable of addition. It is not statistically valid to combine data from different studies unless the incidence of left-handedness is similar in the individual studies. Table 4.1 shows data on twin pairs from 19 studies of MZ twins, and 18 studies of DZ twins. There are highly significant differences in the incidence of left-handedness between studies, both for MZ twins ($X^2 = 73.26$, 18 df, $p < 0.001$) and for DZ twins ($X^2 = 53.32$, 17 df, $p < 0.001$). The differing incidence of left handedness in the separate studies implies that the criterion for left-handedness is different between studies: hence the data within a study cannot be regarded as strictly independent, and hence data from different studies may not be summated, although significance levels may be (Lewis and Burke, 1949.)

Differences between studies are partly due to an interesting difference between the large and small studies (a large study being defined as one in which there are both more than 60 MZ pairs and more than 60 DZ pairs). In both MZ and DZ twins there is a tendency for there to be more left-handers reported in small studies than in large studies, although this effect is only significant in MZ twins (MZ twins $p < 0.05$, Mann-Whitney U test). Nevertheless even when one considers only the large studies (n = 10) there are still differences in the proportions of left-handers in the different studies (MZ twins $X^2 = 35.0$, 9 df, $p < 0.001$; DZ twins $X^2 = 30.28$, 9 df, $p < 0.001$).

In order to test whether data are fitted by a binomial distribution it is therefore necessary to test each data set separately, and then to combine the X^2 goodness of fit values. Figure 4.1 shows data from the ten large MZ studies, showing the incidence of R-L and L-L pairs. In 9 of the 10 cases there are less R-L pairs than would be expected by a binomial distribution, and in the same cases there are more L-L pairs than would be expected by a chance distribution (exact binomial probability = 0.0107). Table 4.1 shows, in the columns marked X^2 Binom., for both MZ and DZ twins, the individual X^2 values for the goodness of fit of a binomial distribution. For MZ twins three of the studies are significantly different from a binomial distribution in their own right; together the 19 MZ studies have a X^2 value of 30.30, which with 18 df gives $p < 0.05$ for a binomial fit; for just the large studies $X^2 = 24.27$, with 10 df, for which P is less than 0.001. We may therefore accept Nagylaki and Levy's conclusion that MZ twin pairs do not occur in binomial proportions, even though their own evidence on this point was insufficient. Unlike MZ twins, the proportions of DZ pairs do not differ significantly from the predictions of a binomial distribution, the X^2 value for all the studies being 15.63 (17 df), and for the large studies alone being 11.26 (10 df, NS). A genetic explanation of handedness should not be ruled out merely because the DZ pairs do not differ significantly from binomial distributions; the genetic explanation merely has the constraint that for DZ twins its predictions should be close to those of a binomial distribution.

It might be argued that the small difference between MZ and DZ twins is not good evidence for a genetic component in handedness. Far stronger evidence would be the incidence of the three types of handedness pair in MZ and DZ twins from parents of known handedness. There are no adequate data of this form in the literature, the only approximation being that of Rife (1950), which are shown in Table 4.2. There is a far higher proportion of L-L pairs amongst those MZ twins with a family history of left-handedness than in those without a history of left-handedness.

4:3 The difference in incidence of left-handedness between MZ and DZ twins

Nineteen studies in the literature have analysed the incidence of left-handedness in twins (including the study of Weitz (1924) who looked only at MZ twins). The study of Shields (1962) is difficult to interpret, since the author gives incomplete information regarding the six "ambidexters", and thus I have here only considered the overall proportions of right and left-handers and have omitted the twin-pair from the analysis.

Overall 15.09% of 5140 MZ twins showed left-handedness as compared with 12.80% of the 4436 DZ twins. It is not however permissible to combine data from studies in this way, since the incidence of left-handedness is clearly different between studies (see above). It is therefore necessary to look at each study separately, and to combine results only after analysis. Figure 4.2 shows the incidence of left-handedness in MZ and DZ twins in 18 studies. In only 11 of the 18 studies is the incidence greater in MZ twins than in DZ twins. Furthermore the correlation between MZ and DZ incidences is only 0.297, which is not significantly different from zero. If one excludes the eight 'small' studies (defined as above), the correlation is still only 0.333, which is also not significantly different from zero. Even if the differences in incidence in MZ and DZ twins were zero we might still expect a correlation between the two incidences. Since the value is not significant we may infer that there are systematic differences in measurement within studies as well as between them.

Table 4.1 shows, for each study, the incidence of left-handedness in MZ and DZ twins. In the column marked 'Difference' there is a '+' if the incidence is higher in MZ twins than in DZ twins, and '-' if the incidence is higher in DZ twins. Of the 18 studies, 7 found the MZ twins to have a lower incidence of left-handedness. The column marked 'X^2' gives the X^2 value for a homogeneity test for a difference between MZ and DZ pairs in either direction, the probabilities being given in the column marked 'Two-tailed'. Only 4 studies show significant differences, and one of these (Lauterbach, 1925) shows the difference in the opposite direction to that expected. Note also that all of the significant results were obtained before 1930 when we may assume that determination of zygosity was rudimentary, and when we know that both Newman (1928; 1940) and Dahlberg (1926) felt that symmetry reversal in twin pairs was actually pathognomic of monozygosity. The data of Table 4.1 may be combined to give an overall probability value for a difference between MZ and DZ twins. The column marked 'One-tailed' gives the probability of a significant difference in the direction of MZ twins having a higher incidence of left-handedness than DZ twins (calculated by taking the two-tailed probability, p_2, and calculating $p_1 = p_2/2$ if MZ is greater than DZ, or $p_1 = 1 - (p_2/2)$ if DZ is greater than MZ). These one-tailed probabilities may be combined using the method of Kendall (1951) (see also Jones and Fiske 1953 for further details). Overall the differences between MZ and DZ twins are significant ($X^2 = 70.28$, 36 df,

$p < 0.001$). However if one divides the data according to date of publication, then for studies produced up to and including 1930, the difference between MZ and DZ is highly significant ($X^2 = 34.86$, 12 df, $p < 0.001$), whilst for the periods 1931-1945, 1946-1960 and 1961-1976, the differences are not significant, either separately ($X^2 = 14.86$, 10 df, NS; $X^2 = 12.26$, 8 df, NS; and $X^2 = 8.30$, 6 df, NS respectively) or combined ($X^2 = 35.42$, 24 df, NS).

In summary the only evidence in favour of MZ twins having a higher incidence of left-handedness than DZ twins was obtained prior to 1930, when we may assume that classification of laterality was not entirely independent of zygosity determination, due to theoretical prior conceptions about the nature of mirror-imaging.

It should be noticed that the demonstration of differences between pre- and post-1930 studies does not invalidate earlier conclusions about the non-binomiality of MZ twins. Thus, in the post-1930 studies there is a significant departure from binomiality ($X^2 = 17.56$, 7 df, $p < 0.02$).

4:4 Handedness in twins and singletons

Nagylaki and Levy (1973) claim that the incidence of left-handedness in twins is higher than it is in singletons. Their evidence for this consists of a comparison between published studies of twins and singletons. However, in none of these cases is evidence quoted of twins and singletons assessed by the same criteria, in the same study, by the same investigators. In view of the wide differences in reported incidences of left-handedness in MZ twins, and also in DZ twins (See earlier) it is clearly fallacious to compare different studies in such a manner.

There are almost no studies in the literature in which twin and singleton handedness have been assessed by the same method. A notable exception is Zazzo (1960) who comments (p. 124) "Pour ma part, je n'ai jamais trouvé, dans mes multiple recherches sur les jumeaux, cet excès de gaucheurs dont parlent tous les auteurs", and he supports this statement with statistical evidence (his Table 8). Wilson and Jones (1932) found no difference in usage of the left hand for writing in twins or singletons, but did find a small difference in ball throwing.

In summary, there is no adequate evidence for the claim of Nagylaki and Levy. It is perhaps worth suggesting that any further studies on this topic should be carried out either by questionnaire, or preferably, by personal examination, with the experimenter blind to the twin status of each child, who should be examined individually not in pairs.

4:5 Handedness in twins: Secular trends

Despite the problems of twin data, we might expect that the handedness of twins has been rather more accurately determined than that of singletons in large population surveys. Thus, the probability of a true left-handed twin being recorded as a right-hander would be low, although the probability of a right-hander being recorded as a left-hander would be concomitantly higher, due to a tendency towards over-inclusive definitions of left-handedness (e.g. Newman et al, 1937, sometimes relied entirely on asymmetry of finger-tapping as evidence of left-handedness). Figure 4.3 shows the incidence of left-handedness in the 18 studies (MZ and DZ studies combined). Only the large studies have standard error bars. Note the tendency for small studies to have higher incidences of left-handedness than large studies (Mann-Whitney U test, $p < 0.05$). There is a hint that the incidence of left-handedness is increasing, although this trend is not significant. The relatively low value reported by Loehlin and Nichol (1976) might be a result of their use of a postal questionnaire rather than personal examination, as used by most of the other studies.

4:6 Discussion

Evidence submitted here suggests that the incidence of left-handedness in both MZ and DZ twins, is the same as that in singletons. This removes the objection of Nagylaki and Levy (1973) "that it is impossible to assess the heritability of a trait by using twin data if the frequency of the trait among twins differs from that among non-twins".

Nevertheless Nagylaki and Levy provide several other reasons why twins should have an increased incidence of left-handedness, and these must be considered, for if valid these reasons will put us in the awkward position of positing a true incidence of left-handedness which, if it were not for pathological factors, would be <u>lower</u> in twins than in singletons. Two main suggestions were made:-

" ... prenatal pathogenic factors are responsible for the high frequency of sinistrality in twins ..." There seems little doubt that twins, both MZ and DZ, suffer an increased intra-uterine mortality and morbidity, as well as increased perinatal death-rates (Anon, 1977, <u>passim</u>) and, as Nagylaki and Levy point out, this could be responsible for decreased IQ, and other mental sub-normalities. However these facts do not bear upon the main issue, since these associates have not been shown to relate <u>causally</u> to left-handedness,and until they have been, they need not concern us. The particular hypothesis of left-handedness being secondary to acute anoxia during delivery (Bakan, 1971) has received little further support (Hubbard, 1971; Schwartz, 1977; Hicks <u>et al</u>, 1978).

" ... some cases of handedness discordance in one-egg twins derive from asymmetry reversal". Asymmetry reversal, or mirror-imaging, has been proposed to account for the discordance of handedness, hair-whorling and dermatoglyphics. It is a much quoted concept for which there is no adequate published evidence. There would be little problem in demonstrating its existence if, say, all singletons were of phenotype R, and all MZ pairs were of type R-R or R-L, with none of type L-L, for then mirror-imaging would be indisputable. In the presence of a high singleton incidence of type L, and relatively high frequencies of L-L twin pairs, to demonstrate true mirror-imaging is a statistical problem of some complexity requiring rejection of a null hypothesis. This has never been done satisfactorily, Nagylaki and Levy (1973) quote Newman (1916) on the quadruplets of the nine-handed armadillo, as evidence of ectodermal mirror-imaging. However, Newman himself said that his data was so complex that he did not know how to analyse it, and he certainly gives no formal statistics, (Newman 1916). In the absence of a statement of chance probabilities his assertions of apparent mirror-imaging are difficult to assess.

In the case of hair-whorling, Morgan (1976) has demonstrated that the work of Bernstein (1925) is dubious, and therefore Rife's observations of a binomial distribution of hair-whorling in twins actually refutes the possibility of mirror-imaging, since binomiality is surely the null hypothesis to be rejected in such a case. Collins (1977) has shown there to be no evidence for hair-whorling mirror-imaging in twins.

There is no adequate evidence for mirror-imaging in dermatoglyphics (Newman 1930; Rife and Cummins, 1943); neither is there evidence for mirror-imaging in tooth cusps, another ectodermal derivative (Staley and Green, 1974; Potter and Nance, 1976).

Nagylaki and Levy (1973) accept that there is no evidence for mirror-imaging of the viscera, or other non-ectodermal structures.

One may only concur with Bulmer (1970) who commented that mirror-imaging "does not occur more frequently than would be expected by chance".

We may conclude, in the absence of other evidence, that MZ and DZ twins are suitable for testing genetic models of handedness, not being subject to any special influences which may be demonstrated statistically. An important consequence of this conclusion is that any genetic model has to explain a significant but non-binomial degree of discordance in MZ twins. As Corballis and Beale (1976) have clearly shown, the model of Nagylaki and Levy (1972) cannot cope with such a possibility, and it must therefore be regarded as inadequate.

TABLE 4.1

Study	Size designation	N_{MZ}	$\%L_{MZ}$	N_{DZ}	$\%L_{DZ}$	Difference	X^2_{MZ-DZ}	Two-tailed	One-tailed	X^2 [illegible] MZ	DZ
Siemens (1924)	Small	37	16.21	31	27.41	-	2.52	0.108	0.946	0.00	0.09
Weitz (1924)	Small	18	25.00							0.02	-
Lauterbach (1925)	Large	75	5.33	126	12.69	-	5.69	0.016	0.991	0.24	0.00
Dahlberg (1926)	Large	69	14.49	128	7.03	+	5.72	0.015	0.992	6.14	0.25
Verschuer (1927)	Large	244	20.28	278	14.04	+	5.51	0.018	0.009	0.14	7.77
Newman (1928)	Small	50	31.00	50	17.00	+	5.37	0.019	0.009	0.62	0.31
Hirsch (1930)	Small	43	20.93	58	6.03	+	2.90	0.084	0.042	3.01	0.24
Wilson & Jones (1932)	Large	70	10.71	123	11.38	-	0.04	0.832	0.583	0.06	0.13
Stocks (1933)	Small	42	9.52	94	10.63	-	0.08	0.776	0.611	1.23	1.03
Newman *et al* (1937)	Small	50	19.00	50	11.00	+	2.51	0.108	0.054	1.21	0.76
Bouterwek (1938)	Small	122	18.85	35	17.14	+	0.105	0.744	0.372	0.04	1.50
Rife (1940)	Large	223	11.88	146	15.41	-	1.91	0.163	0.918	3.32	0.09
Thyss (1946)	Large	103	18.44	86	16.27	+	0.305	0.587	0.293	5.24	0.05
Rife (1950)	Large	343	12.82	211	11.61	+	0.356	0.557	0.278	0.03	0.32
Dechaume (1957)	Small	33	24.24	33	19.69	+	0.397	0.535	0.267	0.00	0.44
Zazzo (1960)	Large	259	13.32	335	10.89	+	1.63	0.198	0.099	5.62	1.24
Shields (1962)	Small	88	10.23	25	12.00	-	0.129	0.720	0.639	-	-
Carter-Saltzmann (1976) *et al.*	Large	187	17.11	176	19.31	-	0.59	0.552	0.723	3.30	0.04
Loehlin & Nichols (1976)	Large	514	14.10	333	11.11	+	3.21	0.069	0.034	0.08	1.37
Total		2570	15.09	2218	12.80						

TABLE 4.2

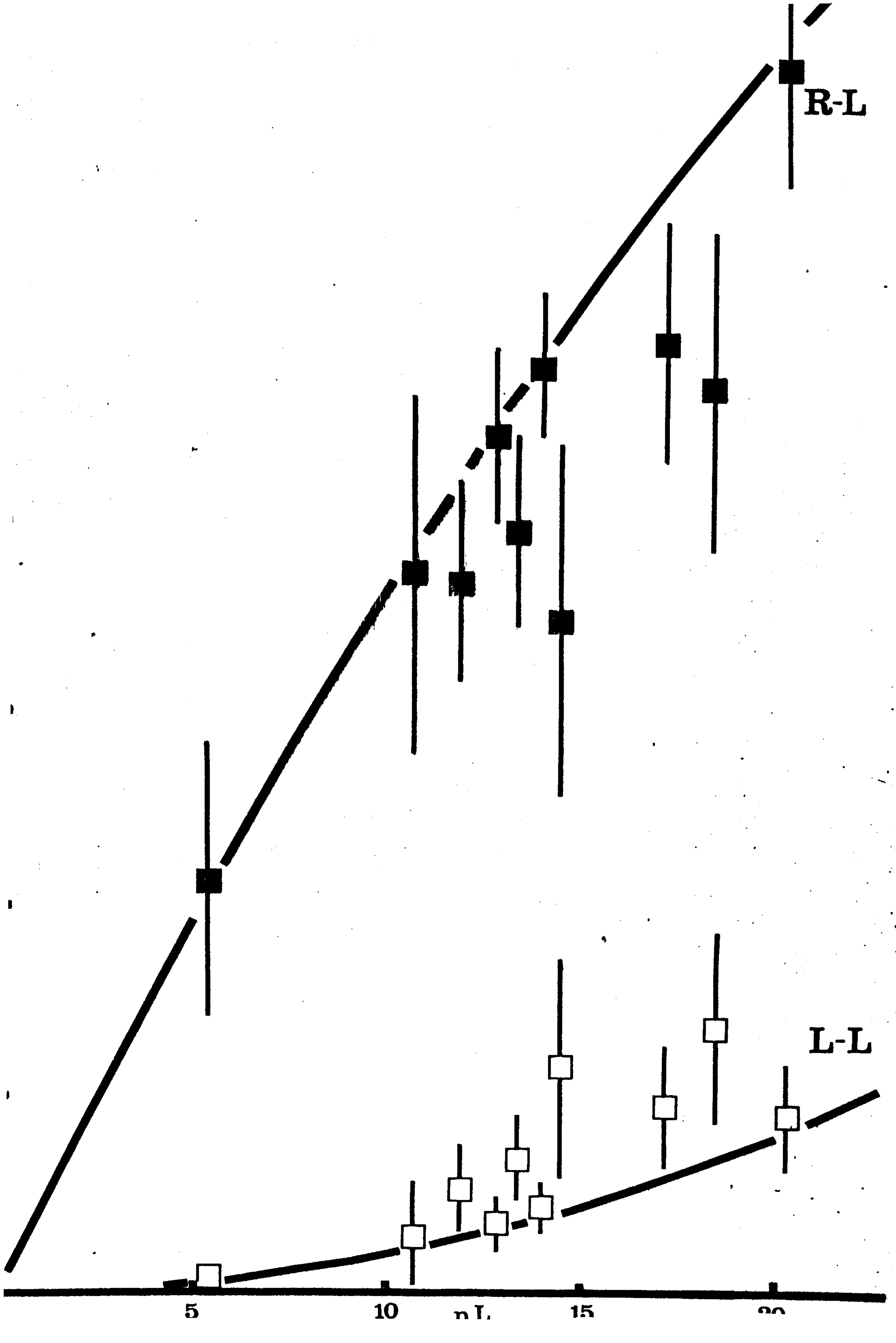
Data of Rife (1950) showing the effect of a family history of left-handedness upon the handedness pairs of MZ and DZ twins.

Twin type	Family History	R-R	R-L	L-L	n(pairs)
MZ	+	56.41	41.02	2.56	78
MZ	-	81.88	16.60	1.50	265
DZ	+	54.16	43.75	2.08	48
DZ	-	84.66	14.72	0.61	163

$\underline{X}^2$ MZ: $X^2 = 21.74$, 2 df, $p < 0.01$

DZ: $X^2 = 17.28$, 2 df, $p < 0.01$

Figure 4.1 Shows, for the ten large studies of monozygotic twins, the percentage of pairs that were L-L (open squares), and the percentage that were R-L (solid squares). All points are ± 1 standard error. The abscissa shows the overall proportion of left-handers in the sample. The solid lines indicate the expected values under a binomial hypothesis.



R-L
L-L
5
10
15
20

Figure 4.2 Shows, for 18 separate studies, the percentage of left-handers in dizygotic twins (abscissa), and in monozygotic twins (ordinate). Solid circles are the 10 'large' studies, and open circles are the eight 'small' studies. The dotted line at 45 degrees represents the point of equality for MZ and DZ twins.

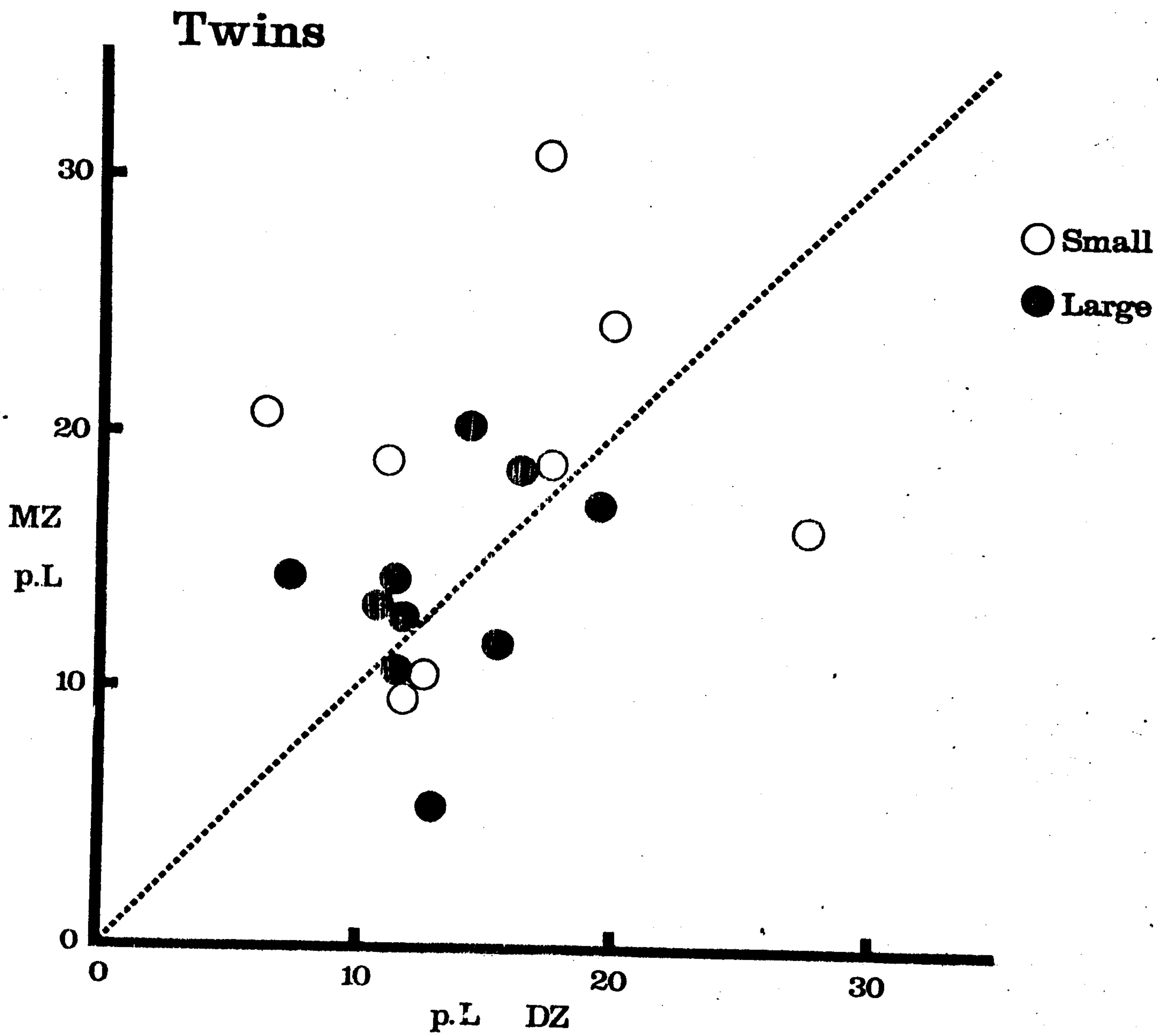
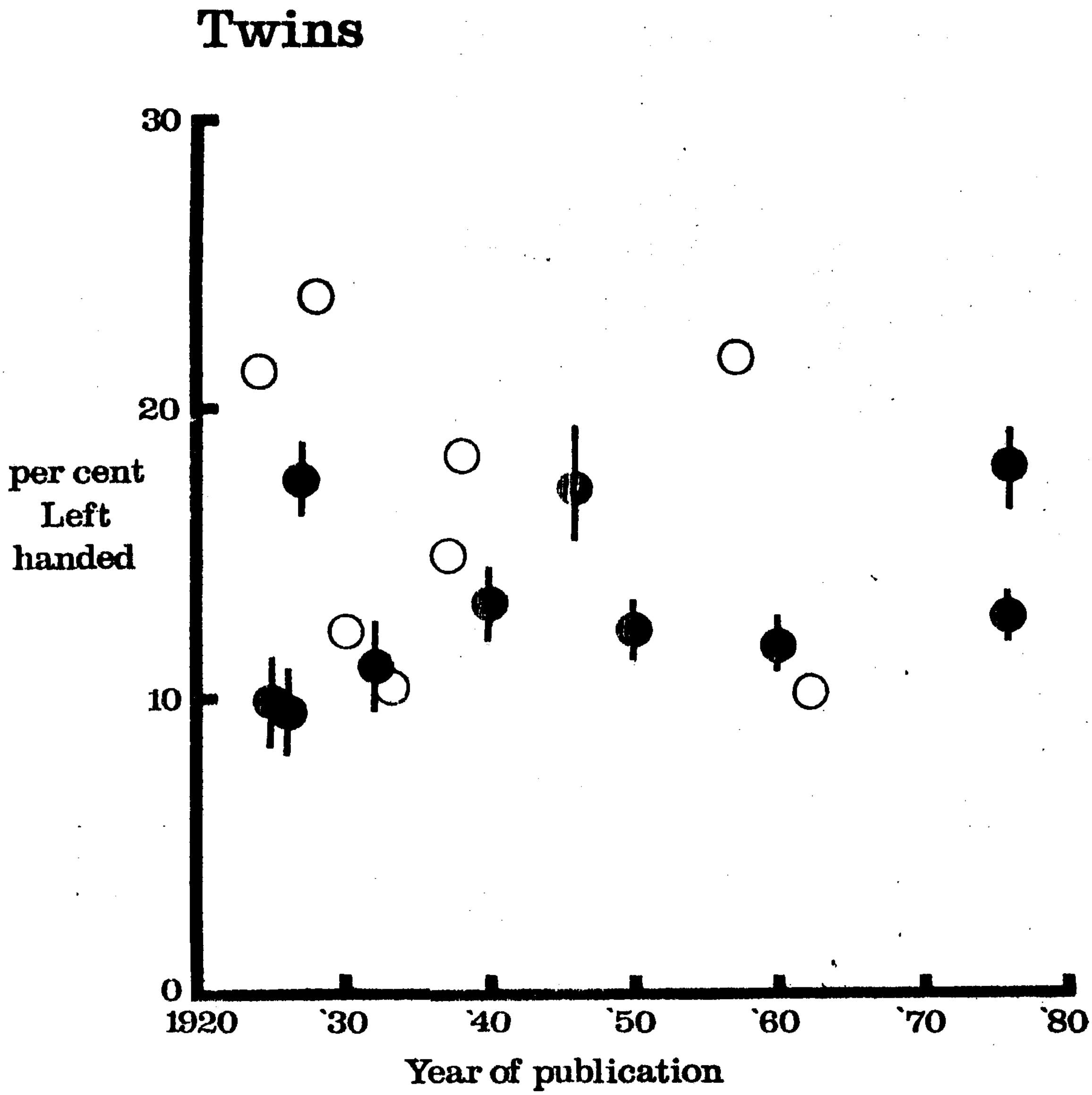

Twins
30
20
10
0
MZ
p.L
0
10
20
30
p.L DZ
Small
Large

Figure 4.3 Shows the overall incidence of left-handedness in eighteen different twin studies (MZ and DZ twins combined), plotted against the date of publication of each study. Solid circles represent the ten 'large' studies, and open circles the eight 'small' studies. Only the large studies have bars, which represent ± one standard error.


Twins
30
20
10
0
per cent
Left
handed
1920
`30
`40
`50
`60
`70
`80
Year of publication