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Annett's theory that individuals heterozygous for the right shift gene are intellectually advantaged: Theoretical and empirical problems

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Annett & Manning (1989; 1990*a*,*b*) have proposed that left-handedness is maintained by a balanced polymorphism, whereby the *rs*+/− heterozygote manifests increased intellectual ability compared with the *rs*−/− and *rs*+/+ homozygotes. In this paper we demonstrate that Annett's method of dividing subjects into putative genotypes does not allow the *rs*+/− genotype to be compared with the *rs*−/− genotype within handedness groups. Our alternative method does allow heterozygous right-handers to be compared both with *rs*+/+ and *rs*−/− homozygotes. Using this method in undergraduates we find no evidence that supposed heterozygotes are relatively more intellectually able than homozygotes on tests of verbal IQ, spatial IQ, diagrammatic IQ or vocabulary.

Theoretical analysis of the balanced polymorphism hypothesis reveals additional limitations. Although estimation of the size of the heterozygote advantage suggests that it must be very large (21 or 45 IQ points) to explain the effects found by Annett & Manning, it nevertheless must be very small (3.4 IQ points) to be compatible with the known differences between right- and left-handers in social class and intelligence. Moreover power analysis shows that the latter effect size is too small for Annett & Manning to have found effects in their studies. Additional power analyses show that studies looking for effects in groups of high intellectual ability, such as university students, are incapable of finding significant results, despite Annett claiming such effects.

If the Annett & Manning paradigm does demonstrate differences in intellectual ability related to skill asymmetry then those differences are unlikely to result from a balanced polymorphism, but instead probably reflect motivational or other differences between right-handers of high and low degrees of laterality.

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In the past few years, Marian Annett and her colleagues have published several papers relating handedness to cognitive ability (Annett, 1991*a*; Annett & Manning, 1989; 1990*a*, *b*). In these studies, Annett has shown that strongly right-handed individuals, as measured by her peg-moving task (Annett, 1985), perform more poorly than do less strongly right-handed people. She has used these data to support her genetic model of handedness, and to argue for a balanced polymorphism with a heterozygote advantage (Annett, 1985).

Annett's (1985) model of the genetics of handedness is one of the most widely accepted models extant (but see McManus & Bryden, 1992). Simply put, her model postulates two alleles at a single locus, one leading to a 'right shift' (*rs*+) and one leading to a randomly determined lateralization (*rs*−), with a mean shift of zero, equal numbers of individuals being lateralized to left or right. This provides for three genotypes, *rs*+/+, *rs*+/− and *rs*−/−. According to the model, *rs*−/− individuals are equally likely to be more skilled with the left hand as with the right hand, and to be either left hemispheric or right hemispheric dominant for language, by random determination. In contrast, *rs*+/− and *rs*+/+ individuals are generally more skilled at using their right hand, are right-handed by preference, and left hemisphere dominant for language, although normal distributions of skill asymmetry mean that small numbers of such individuals will be more skilled with their left hand. In her present model, Annett argues for a 'balanced polymorphism', with each of the two alleles having similar frequencies. By analogy with sickle-cell anaemia, in which a deleterious gene is kept in the gene pool because the heterozygote is protected against malaria, Annett has argued for a heterozygote advantage of *rs*+/− individuals over both *rs*−/− and *rs*+/+ people. We believe that Annett has misunderstood some of the fundamental principles of population genetics in developing her arguments. Since her model is becoming increasingly accepted (e.g. Corballis, 1991) it is important to clarify the implications of the model before further misunderstandings are generated.

Annett's studies (e.g. Annett, 1991*c*) also require and apparently demonstrate a relation between handedness and cognitive ability that has hitherto been unnoticed. Hardyck, Petrinovich & Goldman (1976), in their review of left-handedness, concluded that there was no consistent relation between handedness and ability. A similar conclusion was reached by Porac & Coren (1981). By drawing a distinction between two groups of right-handed individuals, Annett has provided a somewhat different way of looking at the relation between handedness and ability. If replicable then Annett's studies would provide the first convincing evidence for an association between handedness and cognitive ability. The second purpose of this report is therefore to examine the replicability of the Annett findings.

Firstly we will consider the problems inherent in Annett's genetic arguments.

(i) *Balanced polymorphisms, it is claimed, require equal frequencies of the two alleles.* Annett seems to suggest that a balanced polymorphism leads to a situation in which the two alleles are of equal frequency (Annett, 1985, p. 338), since she uses gene frequencies approximating 0.5 to argue for a balanced polymorphism (see also Corballis, 1991). Annett is undoubtedly correct in asserting that handedness is indeed maintained by a balanced polymorphism, in the sense that it involves more than one allele and those alleles seem to be at an equilibrium in the population; and it is quite probable that the equilibrium is maintained by heterozygote advantage, although there are other potential mechanisms for maintaining a balanced polymorphism (Cavalli-Sforza & Bodmer, 1971, p. 178). However the gene frequencies in a balanced polymorphism need not approach 0.5, since the polymorphism is balanced 'when the heterozygote is at an advantage over both homozygotes, (and) a situation results in which both alleles tend to remain at substantial frequencies in the population' (Bodmer & Cavalli-Sforza, 1976, p. 307). In such a case the stable incidence of the two alleles depends entirely on the relative costs of the two homozygotes. More precisely, if three genotypes, *PP*, *PQ* and *QQ*, have relative fitnesses of $(1-s)$, 1 and $(1\text{-}t)$, where $s>0$ and $t>0$, then the polmorphism will be stable (Cavalli-Sforza & Bodmer, 1971). If the gene-frequencies are p and q (where $p+q=1$), then by the Hardy-Weinberg equilibrium the frequencies of the three genotypes are p^2, $2pq$ and q^2, and it can be shown that $p/q = t/s$; hence the proportions of the genotypes at the balance point are determined by the ratio of the relative costs of the two homozygous genotypes. It should be noted that this allows a polymorphism to be balanced for *any* values of p and q, as long as the values of s and t are legitimate. From this it can be seen that a balanced polymorphism will have allele frequencies of 0.5 only when the costs associated with the two homozygous genotypes are identical.

That conclusion from theoretical genetics conflicts with an argument put forward by Annett & Kilshaw (1982), and Annett (1985), and since reiterated by Annett & Manning (1989; 1990*a*) which says: '*rs*+/− is the most frequent genotype and...[its] proportion is about as high as possible in the population (maximum 50 per cent). This implies that *rs*+/− is the most favourable genotype, and that *rs*+/+ and *rs*−/− have relative advantages and disadvantages which are probably in equilibrium in the population as a whole.' (p. 550). The argument was repeated by Annett (1991*b*), who said that 'The evidence that the frequency of the *rs*+ gene has risen as high as required to give as many *rs*+/− genotypes as possible (maximum for a single locus is 50 per cent) but not much further shows that the *rs*+ gene must be "good for you" in a single dose but "bad for you" in a double dose' (p. 341). Although it is true that if the disadvantages of *rs*−/− and *rs*+/+ are equal (i.e. $s=t$) then it will be true that $p=q$ and hence *rs*+/− will be present in 50 per cent of the population, there is no sense in which the balanced polymorphism occurs or is necessary *because* of the particular numerical value taken by the frequency of the *rs*+/− genotype; the precise numerical value of the frequency of heterozygotes is simply irrelevant to the question of whether a balanced polymorphism is present, and the polymorphism could still have been balanced if either of the homozygotes was the most frequent in the population.

It should also be noted that the presence of a balanced polymorphism for the *rs* system as a whole does *not* mean, as Annett (1985) puts it, 'that there must be advantages associated with sinistrality' (p. 337). The *rs*− gene is stated to be less frequent in the population than the *rs*+ gene (Annett, 1985), and therefore at equilibrium the fitness of the *rs* −/− genotype must be less than that of the *rs*+/+ genotype. Since *rs* −/− individuals are more likely to be left-handed than are *rs* +/+ individuals, the net result is a *lower* degree of fitness associated with sinistrality.

(ii) *Heterozygote advantages have to do with reproductive fitness.* Balanced polymorphisms exist to keep two or more alleles in the gene pool when those homozygous for just one of the alleles are at a reproductive disadvantage. The important point here is that this has to do with reproduction, not competence. If there is a heterozygote advantage in the genetics of handedness, it is such that *rs*−/− and *rs*+/+ genotypes produce fewer offspring than *rs*+/− genotypes. There is nothing in the Annett model that relates genotypes to reproductive fitness [although that deficit is common in papers developing evolutionary arguments for cognitive functions (e.g. Anderson (1991*a*; 1991*b*)]. Properly speaking, her arguments imply that the impairments in reading (Annett & Manning, 1990*a*) and mathematical skill (Annett & Manning, 1990*b*) reported in some members of the population make them less likely to produce offspring. We know of no data to suggest that mild cognitive impairment is in any obvious or consistent way related to reproductive success.

(iii) *To show that a balanced polymorphism exists one needs to specify the costs incurred for both homozygotes.* Annett's series of papers has been principally concerned with the costs of being *rs*+/+; that is, she has produced evidence that strongly right-handed individuals are impaired relative to less strongly right-handed people. There seems to be little comparable attempt to show how *rs*−/− individuals are impaired, and without such evidence it is impossible to make detailed predictions concerning the relative frequencies of the genotypes. It is indeed true that Annett & Manning (Annett & Manning, 1990*a*) did show that their left-handed group, like their strongly right-handed group, were poorer at reading. However, as will be shown later, almost as many of the left-handed group are *rs*+/− as are *rs*−/−, and no attempt is made to differentiate these two genotypes; genotype and phenotype are therefore inextricably confounded. Since in this paper we will also show that a variant of Annett's model which suggests that only the *rs*+/+ genotype is intellectually impaired is incompatible with data on the intelligence of right- and left-handers, it is therefore essential for Annett's model to specify the impairment shown by the *rs*−/− individuals.

(iv) *The selection criteria in Annett's grouping of her subjects confound genotype with degree of hand skill.* In her studies Annett has attempted to isolate different genotypes by dividing the distribution of hand skill scores into four roughly equal groups, ranging fron strongly right-handed to a group comprised of all the left-handers and a similar number of very weak right-handers. In general Annett's concern has been to show that the extreme right-handed group, with the highest percentage of *rs*+/+ individuals, is inferior to the other right-handed groups. If there is a relation between degree of hand skill and ability (cf Bishop, 1990), then one might observe a similar relationship without it implying anything about the different genotypes or about heterozygote fitness.

(v) *The selection criteria for Annett's groups do not constitute clearly distinct groups in terms of genotype.* Annett's model of handedness indicates that the relationship between relative hand skill and genotype is that shown in Fig. 1a. If one were to subdivide this distribution into different groups to maximize the segregation of the three genotypes, one would cut it at the intersection of the *rs*+/+ and *rs*+/− curves, and again at the intersection of the *rs*+/− and *rs*−/− curves. To ensure that the behaviour under investigation is not simply a consequence of handedness *per se*, one might wish further to subdivide the *rs*−/− group into left-handers and right-handers. Rather than carrying out such an operation, Annett has divided the distribution of hand skill into four roughly equal groups, containing 20 per cent, 30 per cent, 30 per cent and 20 per cent of the population. Such a subdivision divides the population at non-optimal points, and leads to subgroups that contain complex mixtures of each of the three genotypes. Since each group contains all three genotypes, a small difference in observed ability between groups must correspond to a much larger true difference between genotypes, if the differences are indeed the consequence of genotype differences. Given the mixture of genotypes in Annett's different groups, the implied difference in ability between the genotypes is much larger than Annett seems to realize, and, in fact, may be much larger than is reasonably plausible.

In this paper we firstly review the empirical studies carried out by Annett. We then discuss the ways in which genotypes are identified within the Annett studies, we show that this is inefficient, and then describe a more powerful and sensitive method that we use in our own empirical study. In the discussion we address theoretical issues concerning the size of the heterozygote advantage in both whole populations and student populations, and consider the power of studies for detecting the effect. Finally we consider the implications of the theory for differences in intelligence between right- and left-handers.

Annett's empirical studies

Annett & Manning (1989) reported a study in which 348 children of mean age 8.7 years were assessed on several measures of intellectual ability, and differences in hand skill were assessed using the Annett (1970*b*) pegboard. Grouping of children into four approximately equal sized groups showed a significant linear trend on the Raven's Coloured Progressive Matrices test of non-verbal ability with the most dextral children having the lowest ability scores; although the graph shows a suggestion of an inverted-U relationship between skill and ability, the non-linear trend was not significant (calculated by the present authors as $F(2,338) = 0.66$). Analysis of scores of educational attainment in English in a subset of 146 children showed a similar pattern of results, with the most dextral children having lowest attainment scores, and there being no significant evidence of a non-linear trend. Annett and Manning consider the disadvantage of strong dextrals (presumptively of genotype *rs*+/+), in conjunction with a presumed but undemonstrated disadvantage of *rs*−/− genotypes, who 'seem likely to risk developmental problems of speech and associated language functions' (p. 215), as support for their hypothesis of heterozygote advantage. In the final paragraph of their paper they also cite an earlier finding (Annett & Kilshaw, 1984), that in a school control sample 'vocabulary IQ' showed a quadratic relationship with R–L differences (in fact significant only in females).

Annett & Manning (1990*a*) described the reading ability of children [in what is the same sample as that reported earlier (1989)] in relation to R–L differences in hand skill. They reported a significant quadratic relationship between reading quotient (derived from the Schonell Graded Word Reading test) and R–L difference, with a similar pattern of results when the analysis was restricted to the standardised residuals after the effect of intelligence was partialled out. The children had been divided into four approximately equal groups, comprising about the bottom 20 per cent of R-L scores (group 1), the next 30 per cent (group 2), the next 30 per cent (group 3) and the top 20 per cent (group 4). Group 2 showed the highest performance on reading, with groups 1 and 4 showing the lowest scores.

Annett & Manning (1990*b*) reported an additional study which described the arithmetic ability of a subset of 149 of the children described in the earlier study (Annett & Manning, 1989). Once again, a strong linear relationship was found whereby the children with the least degree of skill asymmetry showed the greatest mathematical ability; in addition children in the top quartile of mathematical ability showed an incidence of left-handed writing (13 per cent of 39) which was more than four times higher than that of the lowest quartile of arithmetic ability (3 per cent of 37). The balanced polymorphism hypothesis does not make a clear prediction as to whether the *rs*+/− or *rs*−/− genotype should be better at mathematical ability, although it is stated clearly that the *rs*+/+ should be at a disadvantage. It should be noted that in the study of arithmetic, unlike that of reading (Annett & Manning, 1990*a*), no attempt was made to consider a specific mathematical component after taking general intelligence into account.

The studies of Annett described above (Annett & Manning, 1989; 1990*a*, *b*) were all carried out on schoolchildren and represented, to a first approximation, unselected samples of the whole population. A more recent study (Annett, 1991*a*), has extended the approach and considered a group of 233 university and polytechnic students who were assessed for their ability to read a passage of unfamiliar, continuous prose when it was spatially inverted. Subjects were divided into four groups on the basis of their peg-moving ability. The subjects in Groups 2 and 3 scored more highly than those in Groups 1 and 4, a similar pattern of results to that found in studies of schoolchildren, which was interpreted in terms of heterozygote advantage.

Identifying the genotypes of individuals within the right shift theory

Annett's genetic model of handedness proposes that individuals differ primarily along a continuum which corresponds to differences in relative skill of the right and left hands, with preference being a secondary phenomenon; in this respect it differs substantially from the genetic model of McManus (1991) which proposes that individuals differ primarily in their hand preference and skill differences are only a secondary phenomenon. Annett proposes that there are three genotypes, *rs*+/+, *rs*+/− and *rs*−/−, with the heterozygote being mid-way in expression between the homozygotes. The *rs*−/− genotype expresses without any 'right shift', so that the distribution of right–left (R–L) skill differences is normally distributed with a mean of zero. The *rs*+/+ genotype expresses phenotypically as a similarly shaped distribution shifted about two standard deviations to the right, so that R–L is positive in most individuals.

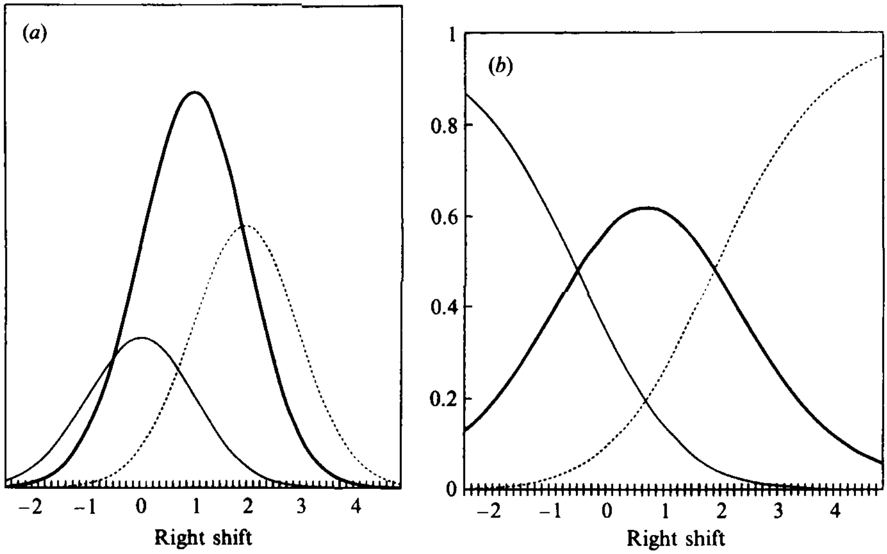

Figure 1. (*a*) Shows the distributions of R–L differences for each of the three genotypes in the version proposed by Annett in the version of her model described by Annett & Kilshaw (1983). —— *rs* − / − ; · · · · *rs* + / + ; —— *rs* + / − . (*b*) The probability of individuals of particular degrees of skill asymmetry being each of the three genotypes, —— rs − / − ; · · · · *rs* + / + ; —— *rs* + / − .

In order to evaluate the relative fitnesses of genotypes so that one can assess the presence of heterozygote advantage it is necessary to be able to genotype individuals, either directly or indirectly. That is possible in the Annett model of handedness, since genotypes are proposed to differ in the extent of skill symmetry and therefore determination of skill asymmetry gives an approximate guide to genotype: in particular right-handers who show large R–L differences are probably *rs* + / +, those who show small differences are probably *rs* − / − and those who are intermediate are probably *rs* + / −. In statistical terms a heterozygote advantage therefore manifests as a quadratic relationship between ability and R–L skill differences, with ability being greatest at an intermediate value of R–L. It must be noted that the presence of a quadratic trend is only substantive evidence of heterozygote advantage if the maximum of the fitted function is within the range of actual R–L differences which is observed (i.e. the heterozygote must be fitter than *each* of the homozygotes).

Annett's method of demonstrating the existence of a heterozygote advantage requires an extrapolation from observed differences in skill asymmetry to postulated differences in genotype distribution, based on the right-shift genetic model. Figure 1a shows a conventional figure of the Annett model, in the version of Annett & Kilshaw (1983) [this version has been used to avoid undue complications arising from the sex differences introduced in Annett (1985)]. The three genotypes result in different distributions of skill asymmetry. For any particular degree of asymmetry one may calculate the probability that an individual has each of the three genotypes, and these probabilities are shown in Fig. 1b. A valid assessment of the hypothesis of heterozygote advantage then requires comparison of groups which differ in their probabilities of having the three genotypes. In their papers Annett & Manning (1989; 1990*a*, *b*) and Annett (1991*a*) divide their population into four groups. It should be noted that using conventional criteria of handedness, in which between 5 and 15 per cent of the population are typically left-handed, one may expect that a substantial proportion of Annett's Group 1 will be left-handed. Knowing the population percentiles of the individuals in each group one may readily calculate the proportion of each genotype in the four groups. Table 1 shows this for the subjects studied by Annett & Manning, and Table 2 shows the expected mean scores for each group on the basis of various assumptions to be described in the discussion.

It can be seen that the proportion of heterozygotes is greatest in Annett's Group 2, and least in Group 4, thereby justifying Annett's choice of an *a priori* comparison between these groups. Although a quadratic effect will be present (see Table 2 and discussion), Group 1 scoring less than Group 2, this will be difficult to interpret since many of Group 1 will consist of left-handers, who might differ from the right-handers of Groups 2, 3 and 4 for other reasons. The method of data analysis of Annett cannot therefore fully demonstrate heterozygote advantage (in the sense of comparing *rs*+/− with *rs*−/−) except by comparing right-handers with left-handers; and in so doing, by comparing Group 1 with Group 2 it will confound degree and direction of handedness with genotype. Finally it should be noted that although comparison of Groups 2, 3 and 4 shows a quadratic effect of intellectual ability upon group, in the sense of a non-linear statistical trend, that alone is not sufficient to demonstrate a heterozygote advantage, which requires not merely non-linearity, but a true non-monotonicity, and hence a maximum at the middle of the three right-handed groups compared; only thus can one demonstrate a genuine superiority of the heterozygote when compared with *each* of the heterozygotes.

In this paper we use a modification of Annett's method which allows a more powerful comparison between the groups, enabling a quadratic effect to be tested within right-handers only, and making more efficient use of the subjects tested. In a two-stage design a large group of subjects is firstly given a group test of skill asymmetry and a preference inventory. In the second stage, individuals who show left-handed preference are excluded from further study, and amongst the remaining right-handers are selected subgroups with high degrees of asymmetry, low degrees of asymmetry and average asymmetry, and these are tested in detail on a range of psychometric tests, and again on the tests of skill asymmetry. For clarity we will anticipate some of the methods and results section in order to describe the study design. Of 429 subjects, 31 (7.3 per cent) were left-handed by preference (group L); in the Annett model these can be expected to be the 7.3 per cent least right-shifted subjects in the population. Of the remaining 398 subjects, three groups of 24 subjects were selected, 24 with the lowest degree of skill asymmetry, 24 with mid-range asymmetry, and 24 with the most extensive asymmetry (Groups R1, R2 and R3 respectively). The percentile ranks of these individuals in degree of right shift can therefore be expected to correspond to 7.3–12.8 per cent, 43.6–49.2 per cent and 94.4–100 per cent, relative to the entire population. The expected proportion of the three genotypes in each group is given in Table 1. In Group R1 the *rs*−/− and *rs*+/− genotypes are almost equally represented and therefore it has a lower expected mean score (see Table 2) than does Group R2 in which the majority of subjects are heterozygotes. This method of selecting subjects therefore allows the demonstration of a true heterozygote advantage within right-handers alone.

Table 1. The expected proportions of subjects in each of (a) the Annett & Manning groups and (b) the groups in the present study, who are expected to be of genotype *rs*−/−, *rs*+/− and *rs*+/+.

Group	Percentiles	*rs*−/−	*rs*+/−	*rs*+/+
Annett-1	0–20	.496	.454	.049
Annett-2	21–50	.208	.607	.185
Annett-3	51–80	.071	.525	.403
Annett-4	81–100	.015	.297	.686
L	0–7.3	.645	.336	.019
R1	7.3–12.8	.467	.484	.049
R2	43.6–49.2	.138	.606	.256
R3	94.4–100	.004	.176	.820

Table 2. Expected mean IQ scores of unselected subjects based on a 3.4-point range, a 10-point range, a 21-point range and a 45-point range (SDs 14.95, 14.3, 12 and 10 respectively). The lower half of the table shows power calculations for the sample sizes used in Annett & Manning's (1989) study of Raven's (1977) matrices and English attainment scores, and for the present study. The percentage in the power calculations shows the probability of obtaining a result significant at the 5 per cent level using a one-tailed test, and the figure in parentheses shows the sample size necessary to give an 80 per cent chance of a significant result on a similar criterion.

		Point difference			
Group	Percentiles	3.4	10	21	45
Annett-1	0–20	99.65	98.90	97.85	95.41
Annett-2	20–50	100.28	100.83	101.75	103.75
Annett-3	50–80	100.18	100.54	101.15	102.45
Annett-4	80–100	99.64	98.95	97.80	95.29
L	0–7.3	99.22	97.72	95.18	89.73
R1	7.3–12.8	99.75	99.27	98.47	96.73
R2	43.6–49.2	100.34	100.99	102.09	104.47
R3	94.4–100	99.34	98.06	95.92	91.26
Power calculations					
Annett-2 vs. Annett-4, $N = 175$		< 10%	20%	52%	98%
(Raven's matrices)		(15454)	(1715)	(363)	(82)
Annett-2 vs. Annett-4, $N = 68$		< 10%	11%	22%	65%
(English attainment test)		(15454)	(2470)	(508)	(185)
R2 vs. R3, $N = 30$		< 10%	15%	30%	73%
		(6867)	(616)	(152)	(36)
R1 vs. R2, $N = 30$		< 10%	< 10%	15%	40%
		(15454)	(1715)	(427)	(97)

Method

Stage 1

A large number of undergraduate medical students at two London medical schools were tested during the course of one of their lectures. Hand preference was assessed by means of a 28-item handedness inventory with five response categories for each item, which has been described elsewhere (McManus, 1979), and contains items from a number of other shorter inventories (Annett, 1970*a*; Crovitz & Zener, 1962; Oldfield, 1971) and has similar psychometric properties to them. Skilled performance of the left and the right hand was assessed by means of the method of Tapley & Bryden (1985), in which subjects used a pen or pencil to make as many dots as possible within a set of circles 3 mm in diameter during a 20 s period. Subjects were given one practice session, and then were tested on their dominant hand (defined as the hand with which they normally write), followed by the non-dominant hand (twice), and then by the dominant hand. The timing of trials was controlled by one of the experimenters. A laterality index for the Tapley & Bryden task was calculated as $100 \times (R-L)/(R+L)$.

Stage 2

Subjects who were followed into Stage 2 were tested in groups of two to eight subjects, and were given two tests of intellectual ability: the AH6 (Heim, Watts & Simmonds, 1983), a timed test specially designed for assessing ability in undergraduate university students, which is extensively used in the United Kingdom, and which has three separate scales entitled Verbal (V), Numerical (N), and Diagrammatic (D); and the Mill Hill Vocabulary scale (Raven, 1977), administered in the form of the multiple choice parts of both Forms 1 and 2, and given without any time limit.

Skilled hand performance was assessed in two ways. Firstly the Tapley & Bryden circle marking task, as described in Stage 1, was re-administered. Secondly each subject was tested individually on the Annett pegboard task (Annett, 1970*b*), being tested four times overall in the order Right, Left, Left, Right. The total time taken for each hand was measured, and an asymmetry score calculated as $100 \times (L-R)/(L+R)$. Although the pegboard is conventionally scored as $L-R$ rather than $100 \times (L-R)/(L+R)$, studies on these and other data (McManus, Murray, Doyle & Baron-Cohen, 1992) show that the correlation between the two measures is extremely high, and the asymmetry score has the advantage over the L–R measure of being dimensionless.

Procedure

Stage 1

431 undergraduate medical students were tested, 230 male, 198 female and 3 whose sex was not stated. Two subjects had disabilities which precluded them carrying out the skill asymmetry task, and they were excluded from further analysis.

Hand preference. A conventional laterality index ($LI = 100 \times (R-L)/(R+L)$) was calculated for the 28 items in the McManus hand preference inventory. The distribution was clearly bimodal, as in previous uses of the measure (McManus, 1979). Three hundred and ninety-eight subjects with a score of greater than zero were regarded as right-handed, and the remaining 31 (7.3 per cent) were considered as left-handed and excluded from the second stage of the study.

Hand skill. A laterality index was calculated based on the number of dots marked with the right hand (R) and with the left (L), combining across the occasions of testing for each hand. Figure 2 shows the distribution of scores in relation to hand preference on the McManus test, coded as right or left. As in the original report by

Tapley & Bryden (1985), the distribution is clearly bimodal, and shows a strong correlation with direction of hand preference. Subjects for Stage 2 were selected if they had laterality indices on the skill task (rounded to the nearest integer) of less than or equal to 14 (Group R1), equal to 24 (Group R2) or greater than or equal to 37 (Group R3). Seventy-two subjects were thereby selected and asked to attend for the second stage of testing.

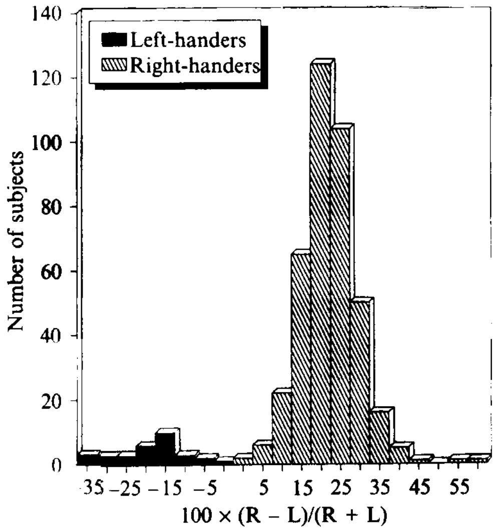

Figure 2. The distribution of scores of subjects on the Tapley & Bryden (1985) tapping test. Subjects were classified as right- or left-handed according to their scores on the hand preference inventory (McManus, 1979).

Stage 2

45 of the 72 selected subjects (63 per cent) were tested; there were about the same numbers in each of groups R1, R2 and R3 ($N = 15$, 16 and 14 respectively). One subject was not tested on the Mill Hill Vocabulary scale, and two subjects could not be tested on the Annett pegboard task.

Skill asymmetry. On the second testing using the Tapley & Bryden task, the three groups showed large differences, as they also did on the Annett pegboard task (Table 3), confirming the validity of the separation of subjects in Stage 1 into groups differing in L – R. The Pearson correlation between the Tapley & Bryden scores assessed at Stages 1 and 2 was 0.765 ($N = 45$, $p < .001$), and the Annett pegboard task correlated 0.513 ($N = 43$, $p < .001$) with the Tapley & Bryden task during Stage 1 and 0.428 ($N = 43$, $p < .01$) during Stage 2. As in the studies of Annett & Manning (1989; 1990*a*, *b*) and Annett (1991*a*) the differences between individuals with large and small degrees of skill asymmetry are entirely the result of differences in the performance of the left hand, rather than of the right hand (Table 3).

Intellectual ability. Table 3 shows the scores of groups R1, R2 and R3 on the total score and the three subscores of the AH6, and the Mill Hill Vocabulary score. None of the

Table 3. Mean scores (with standard deviations in parentheses) of subjects in Stage 2 in groups defined in Stage 1 as R1 (weakly dextral), R2, and R3 (strongly dextral).

	R1	R2	R3	Linear trend	Quadratic trend
Tapley & Bryden tapping task: laterality index	14.1 (4.11)	20.6 (2.94)	26.0 (6.71)	$F(1,42) = 45.59, p < .001$	$F(1,42) = 0.16$, n.s.
Annett pegboard task: laterality index	1.50 (3.41)	2.67 (4.58)	7.71 (4.58)	$F(1,40) = 15.07, p < .001$	$F(1,40) = 2.05$, n.s.
Tapley & Bryden task: Right hand	50.87	49.94	51.43	$F(1,43) = .007$, n.s.	$F(1,43) = .245$, n.s.
Tapley & Bryden task: Left hand	39.37	32.78	29.89	$F(1,43) = 25.99, p < .001$	$F(1,43) = 1.36$, n.s.
Annett pegboard task: Right hand (s)	10.36	10.40	9.73	$F(1,43) = 3.20$, n.s.	$F(1,43) = 1.42$, n.s.
Annett pegboard task: Left hand (s)	10.59	11.03	11.37	$F(1,43) = 4.43, p < .05$	$F(1,43) = .02$, n.s.
AH6: Total score	31.26 (9.31)	32.81 (7.09)	34.35 (8.91)	$F(1,42) = 0.97$, n.s.	$F(1,42) = 0.00$, n.s.
AH6: Verbal score	9.80 (3.19)	9.62 (3.18)	10.78 (3.40)	$F(1,42) = 0.64$, n.s.	$F(1,42) = 0.43$, n.s.
AH6: Numerical score	10.53 (4.99)	11.19 (3.10)	11.57 (5.36)	$F(1,42) = 0.38$, n.s.	$F(1,42) = 0.01$, n.s.
AH6: Diagrammatic score	10.93 (3.73)	12.00 (3.32)	12.00 (2.80)	$F(1,42) = 0.76$, n.s.	$F(1,42) = 0.26$, n.s.
Mill Hill Vocabulary test	38.46 (6.65)	39.66 (6.33)	38.50 (4.64)	$F(1,41) = 0.01$, n.s.	$F(1,41) = 0.38$, n.s.

linear trends nor the quadratic trends are significant, nor show any trends towards significance.

Asymmetry on the Annett pegboard. The classification of subjects in the previous paragraphs has used the Tapley & Bryden tapping task. Although this correlates highly with scores on the Annett pegboard it does have a different distribution, and therefore failure to find correlations with intellectual ability may be due to the Annett pegboard measuring some component of handedness which is absent from the Tapley & Bryden task. A multiple regression was therefore used to assess the relation between linear and quadratic components of the pegboard score and the intellectual ability tasks. The AH6 total score, the AH6 numeric subscore and the AH6 diagonal score all showed significant linear trends upon pegboard score ($p = .045$, .035 and .048 respectively), in each case the beta coefficient being positive (.509, .323, .303), indicating that increased intellectual ability was associated with *increased* differences between the hands [i.e. an effect in the opposite direction to that reported by Annett (1991*a*)]. None of the other linear trends were significant, and no quadratic trends were significant (p values = .218, .263, .349, .477 and .148).

Discussion

This study has found no empirical evidence to support Annett's contention that handedness is maintained as a balanced polymorphism by the intellectual advantage shown by heterozygotes relative to homozygotes (Annett, 1991*c*). On theoretical grounds it has been shown that Annett's method of dividing subjects into groups is not sufficiently sensitive to distinguish clearly between *rs*−/− and *rs*+/− genotypes, since her Groups 2 and 3 are dominated by the *rs*+/− individuals, and her Group 1 is necessarily contaminated by left-handers, for whom different constraints may apply, and thus genotype differences will be confounded with differences in direction and degree of handedness. It must be emphasized that since the balanced polymorphism theory for the right shift theory strictly concerns *genotypes* then differences should still be found in individuals all of whom are phenotypically right-handed but who differ in genotype alone. The method we have described allows one, in principle, to distinguish the ability of *rs*−/− from *rs*+/− genotypes; however we have been unable to find any evidence for significant effects.

Our study has assessed several separate areas of intellectual ability, in particular verbal, numerical, spatial and vocabulary, all of which are broadly similar to the tasks used in the various studies of Annett & Manning. The only exception is the exclusion of any test of reading ability *per se*, as opposed to measures of verbal ability and vocabulary, with which it is probably broadly correlated. Reading ability is difficult to assess in a group of adults who are as highly expert and practised as are undergraduate students, and we were unable for practical reasons to carry out Annett's inverted reading test.

Our study may be criticized on two possible grounds. Firstly, we did not classify subjects by the Annett pegboard but by the Tapley & Bryden tapping task. However it is clear from our data that, even with right handers, these tests show substantial correlation. The Tapley & Bryden task is highly reliable, and must be seen as a valid test of hand asymmetry. If it is the case that the Annett task alone predicts heterozygote advantage then it is difficult to see what crucial skill component it has which is not present in the Tapley & Bryden task and yet can still be construed as handedness within the normal meaning of the term. In the present study we also related handedness as assessed by the Annett pegboard to our measures of intellectual ability and while we found no quadratic effects, we did find a linear effect which was in the opposite direction to that reported by Annett & Manning (1989), higher ability being found in the most dextral rather than the least.

A second possible criticism involves the fact that we have used a highly selected group of individuals, undergraduate medical students, who necessarily have an intellectual ability above a certain level, for otherwise they would not have been admitted to a university; and studies suggest that their mean IQ is of the order of 125 (McManus, 1982). If right-shift genotypes do indeed differ in their intellectual ability then university students will have different proportions of *rs*−/−, +/− and +/+ genotypes from the general population. Should this be a valid criticism of our study, and indeed we will later show that it is, then it must also be a valid criticism of the study of Annett (Annett, 1991*a*), who studied university students and found a similar effect to that reported in her earlier population-based studies. In order to evaluate this criticism in more detail it will be necessary to consider the expected effect sizes that would be obtained in a population-based sample and a university-based sample.

Expected effect sizes in population-based samples. The effects of the difference in ability of heterozygotes and homozygotes can be assessed by choosing appropriate estimates of the true mean abilities of homozygotes and heterozygotes. Table 2 shows the estimated effect based on various estimates of the size of the advantage shown by the heterozygote, relative to the *rs*−/− homozygote. The second column considers a situation in which, quite arbitrarily, *rs*−/− and *rs*+/− individuals differ by 10 IQ points; such a '10-point advantage' is equivalent to 0.66 standard deviations on a standardized IQ test, and in evolutionary or genetic terms would almost certainly represent a substantial and important advantage for heterozygotes. The relative ability of the *rs*+/+ homozygote can be calculated from the fact that the fitness of the *rs*+/+ individuals relative to the heterozygotes must be in the same ratio to the fitness of the *rs*−/− individuals relative to the heterozygotes as the frequency of the *rs*− gene is to the *rs*+ gene (see above). Imposing a constraint that the mean population IQ should be 100 allows one to calculate that the mean scores for the three genotypes should be 94.31, 104.31 and 96.74. Given that the population standard deviation (SD) for IQ scores is conventionally set at 15, the within-group SD needs to be set at about 14.3.

By a similar computation, the relative advantage of the heterozygote can also be estimated from the data of Annett & Manning (1989; 1990*b*). Three separate calculations have been used. Firstly the data of Annett & Manning's (1989) Fig. 3 (combining across sexes) show that their Group 2 has a mean matrices percentile score of about 53, compared with a mean matrices percentile score of about 43 for Group 4; these scores are equivalent to mean IQ scores of 101.13 and 97.35. Using the data of Table 1 on the proportions of the various genotypes in the groups allows one to estimate that a 21-point advantage for *rs*+/− will predict a difference of 3.95 IQ points between Groups 2 and 4, resulting in mean IQs for the genotypes of *rs*−/− 88.06, *rs*+/− 109.06 and *rs*+/+ 93.15. In order for the population standard deviation (SD) to be 15, the within-group SD has to be about 12.

A separate estimate of the mean IQs of the genotypes can be obtained from Fig. 4 of Annett & Manning (1989), in which the mean scores of Groups 2 and 4 on English, combining the sexes, were about 106 and 94 respectively. This difference of 12 IQ points is approximately produced by a 45-point advantage for *rs*+/−, resulting in IQs for the three genotype of *rs*−/− 74.375, *rs*+/− 119.375 and *rs*+/+ 85.346 (the 45-point advantage in Table 2). It should be noted that it is not possible with these mean values for the population SD to be as low as the 15 that is required for a standardized IQ score, since even a zero within group SD results in a population SD of about 19.4. In order to allow demonstration calculations a within-group SD of 10 has arbitrarily been used.

A third estimate can be obtained from the data of Annett & Manning (1990*b*). The mean arithmetic ability of Group 2 (see their Fig. 3) is approximately 11 points higher than that of their Group 4. Assuming that this principally represents the difference in ability of heterozygotes and *rs*+/+ homozygotes, then the heterozygote needs to show a 60-point advantage. This value is so extreme that it will not be considered further here.

Comparing in Table 2 the Annett samples and the samples of the present study shows that expected effect sizes are generally greater for our samples than for Annett's, thereby justifying our method of selection. Formal power analysis in Table 2 suggests that the present method is at least as powerful as that of Annett & Manning (1989), for their study of English attainment scores ($N = 68$), and only marginally less powerful than the same study's analysis of Raven's Matrices ($N = 175$).

Expected effect sizes in a university-based sample. By assuming that British university students have a minimum IQ of 120 (McManus, 1982) and that their distribution of IQ is the truncated part of the normal distribution to the right of 120, one can calculate their expected proportions of genotypes, and the expected mean IQ for groups subdivided according to right-shift, using the groups described earlier in Tables 1 and 2. If homozygotes are, in fact, less intelligent than heterozygotes, then, as the IQ cutoff for university entry is raised, fewer and fewer homozygotes will meet the criterion. Thus, the proportion of homozygotes will be decreased in a high IQ sample. Table 4 shows that as the difference between heterozygotes and homozygotes

Table 4. Expected mean scores of university students (IQ > 120) based on a 3.4-point range, a 10-point range, a 21-point range and a 45-point range (SDs 14.95, 14.3, 12 and 10 respectively). The lower three lines of the table show the expected proportions of the three genotypes for each effect size.

		Point difference			
Group	Percentiles	3.4	10	21	45
Annett-1	0–20	126.84	126.78	126.40	127.74
Annett-2	20–50	126.93	126.92	126.41	127.74
Annett-3	50–80	126.92	126.84	126.35	127.74
Annett-4	80–100	126.85	126.57	126.15	127.73
L	0–7.3	126.77	126.62	126.37	127.74
R1	7.3–12.8	126.85	126.81	126.41	127.74
R2	43.6–49.2	126.94	126.92	126.40	127.74
R3	94.4–100	126.81	126.37	125.89	127.73
$rs-/-$		.1441	.0743	.0077	.0000
$rs+/-$		.5761	.7394	.9484	.9996
$rs+/+$		.2798	.1864	.0439	.0004

increases so the proportion of heterozygotes in a university population grows dramatically, so that even with an effect size of 10 points, nearly three-quarters of students would be expected to be heterozygotes, and for an effect size of 21 points nearly 95 per cent of students would be heterozygotes. The effect of this restriction in range of genotypes, coupled with the effect of truncating the IQ distribution at a lower bound of 120, is to mean that for almost any effect size the differences between handedness groups are so small as to be impossible to detect (see Table 4). Indeed as the heterozygote advantage increases so the differences between groups become *less*. The conclusion seems inescapable that if the balanced polymorphism hypothesis is true then it will be very difficult to test within university students, since no conceivable study is likely to have sufficient power to distinguish differences in mean IQ of small fractions of an IQ point.

Given such theoretical constraints it could be argued that the present attempt to replicate the effect reported by Annett was fundamentally misguided from the start. That may be true at a strong level, but is not necessarily true at a weak level, since, as noted earlier, Annett (1991*a*) has herself reported data on differences in reading ability in a student population, which she has interpreted as providing support for the hypothesis of a balanced polymorphism. Given that that study found significant differences between handedness groups then the present study was a legitimate attempt to find similar effects on other measures of intellectual ability in a group of students of similar intelligence level (and the differences might have been present empirically, irrespective of the truth or otherwise of the specific hypothesis of a balanced polymorphism). If our attempt to test the balanced polymorphism hypothesis *per se* using a student population was misguided then so also must have been that of Annett.

Intelligence in right- and left-handers. Since the proportion of left-handedness in a population is a function of the number of *rs* $-/-$, $+/-$ and $+/+$ genotypes, and because genotypes are hypothesised to vary in intellectual ability, then two consequences follow. Firstly, left-handers on average should have a different IQ to right-handers. Table 5 shows the estimated mean IQ of right- and left-handers for different degrees of heterozygote advantage. Many small-scale studies have investigated the relationship between handedness and intelligence (and/or talent), along with sex and familial sinistrality as moderating variables; in reviewing the topic O'Boyle & Benbow (1990) concluded that 'the variability of [the] findings speaks to the likelihood of a Type 1 error' (p. 364). They did not however consider in detail the only two major, large-scale, published studies of handedness and intelligence of which we are aware. As a base-line we will consider the very large National Child Development Study (NCDS), in which the handedness of over 12000 children was related to IQ. On average there was a small but significant intellectual advantage shown by right-handers, who were about 0.75 IQ points more intelligent than left-handers (McManus & Mascie-Taylor, 1983); the effect could not be explained away in terms of an excess of left-handers of very low IQ. The difference between left- and right-handers is of the same order of magnitude as that found in the only other large-scale study (Hardyck, Petrinovich & Goldman, 1976), in which, recalculating from the data presented in the paper, in 5700 children the right-handers showed a highly significant, but minute, advantage on the Lorge–Thorndike intelligence test of 0.35 IQ points.

Using the estimated effect size from the larger study (McManus & Mascie-Taylor, 1983), a difference in IQ of 0.75 points would be expected if heterozygotes showed

Table 5. The upper part of the table shows the expected mean IQ of right- and left-handers in the whole population, for effect sizes based on a 3.4-point range, a 10-point range, a 21-point range and a 45-point range (SDs 14.95, 14.3, 12 and 10 respectively). The lower part of the table shows the expected proportions of individuals in the whole population who would have IQ scores in particular ranges, for the same effect sizes.

		Point difference			
Group	Percentiles	3.4	10	21	45
Mean IQ	Left-handers	99.35	98.09	95.98	91.39
	Right-handers	100.07	100.21	100.45	100.96
% Left-handers	IQ < 80	10.83	12.74	16.68	19.15
	IQ 80–90	10.42	11.27	12.86	8.84
	IQ 90–100	10.12	10.26	9.98	4.67
	IQ 100–110	9.84	9.41	8.13	6.32
	IQ 110–120	9.58	8.74	7.51	7.50
	IQ 120+	9.27	8.17	7.48	7.58

an advantage of about 3.4 IQ points, a far smaller value of the heterozygote advantage than is capable of explaining the effects described by Annett & Manning. Table 5 shows, for the different extents of heterozygote advantage, the expected proportion of left-handers at each of a number of IQ levels. Despite the high power to detect a significant relationship conferred by the large sample size, data from the NCDS suggest that handedness in offspring is unrelated to social class. The implication is that the size of the advantage shown by heterozygotes is unlikely to be as large as 10 IQ points [since that would require individuals with an IQ of 80 to have a 50 per cent higher incidence of left-handedness than students with an IQ of 120, a figure incompatible with the data on social class in the NCDS (McManus, 1981)], and that therefore the best estimate of the extent of heterozygote advantage is of the order of 3.4 IQ points, or less.

Is the rs−/− genotype disadvantaged relative to rs+/−? As stated in the introduction, Annett's theorising about the heterozygote advantage does not explicitly state that the *rs*−/− genotype should be impaired relative to the heterozygote. Strictly the hypothesis of a balanced polymorphism requires that the three genotypes differ in their *fitness*, which must be construed in a strict sense in terms of differential survival of offspring. Any variation between individuals which results in such differences will contribute to the balancing of the polymorphism, even if the disadvantages of the two homozygotes manifest through different mechanisms. It might be that intellectual ability can be used as a surrogate for fitness (although it is not obvious that intellect and survival will be positively correlated, at least within species, and within the modern period higher intellect has generally been associated with a *decreased* number of offspring). If the disadvantage of the *rs*−/− genotype is on some other

Table 6. Expected mean IQ scores of subjects from the total population and from university students (IQ > 120) for a model in which the *rs*+/+ has a disadvantage of either 7.5 or 23 IQ points relative to both the *rs*+/− and *rs*−/− genotypes.

		Total population		IQ > 120	
Group	Percentiles	7.5	23	7.5	23
Annett-1	0–20	102.06	106.32	127.01	125.89
Annett-2	20–50	101.04	103.20	126.95	125.09
Annett-3	50–80	99.40	98.17	126.82	125.08
Annett-4	80–100	97.27	91.62	126.55	125.07
L	0–7.3	102.29	107.01	127.03	125.09
R1	7.3–12.8	102.06	106.32	127.01	125.09
R2	43.6–49.2	100.51	101.56	126.91	125.09
R3	94.4–100	96.28	88.59	126.37	125.06

dimension than that of intellect, then the theory predicts that *rs*−/− and *rs*+/− will have similar IQs, and that only the *rs*+/+ genotype will be intellectually impaired. If that is the case then the calculations described earlier would be invalid.

Table 6 summarizes calculations for the case in which only the *rs*+/+ genotype is impaired, showing results for a 7.5 and a 23 point deficit of *rs*+/+ relative to other genotypes. These values have been chosen since they produce an effect size equivalent to that of the studies analysed previously (Annett & Manning, 1989, 1990*a*). It can be seen that in a total population sample the model still predicts that Annett's Group 2 should be of greater IQ than Group 4, and that our Group R1 should be of higher ability than our Group 3, although now Group R2 does not have the highest ability. As in previous analyses, when one considers the subgroup with an IQ of greater than 120, then the effect sizes expected are very small, again making them almost impossible to detect in a highly selected university population. The revised version of the model, in which it is only *rs*+/+ which is disadvantaged intellectually, also has another important consequence; with a disadvantage of 7.5 points the model predicts that in the total population left-handers will have a ***higher*** intelligence ($M = 102.24$) than right-handers ($M = 99.75$), and with a disadvantage of 23 points left-handers should have a mean of 106.87 compared with 99.237 for right-handers. To our knowledge there are no substantial data to suggest that on average left-handers are intellectually superior to right-handers, and certainly not by such large amounts as 7.6 IQ points (an effect size of half a standard deviation). This latter point seems to render such a modified hypothesis unlikely. The conclusion must therefore be that if Annett's balanced polymorphism model is to have any viability it must assume that the disadvantages of both homozygotes are measured on the same metric, of intellectual ability. It would then be contingent upon the theory to demonstrate that such a metric is an adequate surrogate for the true metric on which all balanced polymorphisms must ultimately be assessed, fitness in terms of increased survival of offspring.

Conclusions

The analyses of the present study leave Annett's hypothesis of a balanced polymorphism for handedness resulting from an intellectual advantage for right-shift heterozygotes, in a difficult, if not impossible, position. Annett & Manning (1989; 1990*a*, *b*) have reported studies which demonstrate statistically significant differences between weak and strong right-handers. That method though, in which subjects are subdivided according to the extent of their right-hand advantage, cannot actually demonstrate true heterozygote advantage since it is unable to demonstrate that the $rs+/-$ genotype is superior to the $rs-/-$ genotype. The problem can however be circumvented by the method described at the beginning of this paper, albeit at the expense of requiring a larger initial sample size from which to draw subsamples. Calculation from the right-shift theory suggests that for the results which have been obtained by Annett & Manning then heterozygotes must have an advantage of about either 21 or 45 IQ points. However, such large differences would result in a strong IQ and social class gradient of handedness, and large scale studies such as the NCDS suggest that such differences are unrealistic, and at best compatible with a heterozygote advantage of the order of 3.4 IQ points. Such a small degree of heterozygote advantage would not however be detectable except by studies two orders of magnitude larger than those in which Annett & Manning have found differences which are claimed to be the result of heterozygote advantage. Within groups of university students the problems are more severe, and whatever the size of the heterozygote advantage it is unlikely that any study of realistic size could ever detect significant differences, despite Annett (1991*a*) claiming to find differences in precisely such a group; certainly if the present study has been unable to find any evidence that could be seen as consistent with those effects. Annett's hypothesis therefore requires a heterozygote advantage which is so small that her studies could not have detected it, or so large that social class and IQ gradients should have been readily apparent in other studies.

The conclusion can only be that those associations that Annett has reported between skill asymmetry and intellectual ability are not the result of heterozygote advantage but are instead the consequence of some other variable. If the empirical results demonstrated by Annett are replicated (and we have been unable to find any such effect in a university-based population) then they will require some form of explanation which does not invoke a balanced polymorphism. A possible hypothesis is that subjects differ in their response to being asked to carry out a skilled task with their non-dominant hand (Beaumont & Kenealy, 1990). Some subjects try very hard, and achieve results almost as good as those achieved with their dominant hand, and thereby show small degrees of skill asymmetry. Others, in contrast, who perhaps have lesser degrees of motivation, do not try hard with their non-dominant hand and therefore show large differences in apparent skill between the hands. The latter group, who are less motivated, may also be less motivated on the intelligence or other cognitive tests, and therefore show lower scores, so that intellectual ability would be less in those with the greatest degree of skill asymmetry. Such a hypothesis is attractive, not least because it can explain the fact that the majority of variance in skill asymmetry is contributed by the non-dominant hand; it cannot however explain the result reported here whereby individuals with the greatest degree of asymmetry showed the highest ability, but only when asymmetry was assessed using the Annett pegboard.

In summary, it is difficult to accept the studies of Annett as providing acceptable evidence for the hypothesis that the intellectual advantage of heterozygotes explains the balanced polymorphism for handedness. Indubitably Annett has asked an interesting question when she attempted to ask what the advantage was that maintained handedness in the population as a genetic polymorphism. The incidence of handedness seems stable and the incidence is too high to be maintained by mutation, and therefore the conclusion seems inescapable that some form of heterozygote advantage must exist. However there is no need for that advantage to manifest in terms of intellectual or other cerebral activities. The only requirement is that heterozygotes produce more offspring, i.e. they are fitter, than are homozygotes. The gene for handedness could of course produce that effect by many methods, none of which need involve lateralisation or, indeed, cerebral functioning.

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