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COMMENTARY ON "THE RIGHT SHIFT THEORY" (MARIAN ANNETT)

Achilles' right heel: The vulnerabilities of the right shift theory

I. C. MCMANUS

University College London, U.K.

Annett has provided in this paper a very useful integration and review of the many stimulating papers she has written on laterality since 1964. In so doing however she makes somewhat clearer than before the key problem with the right shift theory, as it has been enunciated and developed over the years. In many ways it is a powerful and elegant mathematical theory, building a model of lateralisation upon mixture distributions comprised of separate normal distributions each determined by specific genotypes. Here though also lies the model's primary vulnerability – its Achilles heel. The problem can be clearly stated: *Although the right shift theory is inherently quantitative, its predictions are usually stated qualitatively*. Mathematics is a hard task master. It is unforgiving and strict, and the drawing of diagrams, the waving of arms, and the imprecisions of words are no substitute for formal quantitative analysis and precise calculation. It is here I believe that the right shift theory will eventually be found to be flawed.

Correspondence should be sent to I. C. McManus, Department of Psychology, University College London, Gower Street, London WC1E 6BT, England (e-mail: icm30@sm.ic.ac.uk).

Elsewhere I have already stated my problems with both the right shift theory of the genetics of handedness (which I believe fails ultimately because it does not fit the data as well as other models [Annett, 1985; McManus, 1985 a, b, & c]), and with the theory of a balanced polymorphism with heterozygote advantage (BP+HA) (McManus, Shergill, & Bryden, 1993). In the latter case I believe the overriding criticism of the theory arises from the twin facts that differences between handedness groups can be found in intellectually fairly homogeneous undergraduate populations in the top part of the IQ distribution – implying that the differences between genotypes must be large – and that there are only very small (albeit significant) differences in overall IQ between right and left-handers in population samples (Hardyck, Petrinovich, & Goldman, 1976; McManus & Mascie-Taylor, 1983; McManus et al., 1993) – implying that intellectual differences between genotypes must be orders of magnitude smaller than those implied both by the undergraduate data and indeed also by the data from schoolchildren. Mathematically this is a circle which cannot be squared, leaving the entire theory vulnerable as a result. There is little point in rehearsing these problems point by point again – interested readers are welcome to read the various papers and make up their own minds on the issues. Here I will restrict myself to one particular issue raised in the present paper, plus a number of other minor comments.

The frequency of the rs- gene

Annett makes it clear on p. 435, as is also clear from her 1978 monograph (Annett, 1978), that in the right shift model the frequency of the rs- gene is calculated from data on the proportion of the population with right-sided language, derived from four large series in which overall 60 out of 647 dysphasics (9.27%) had right-sided lesions. On the assumption that *only* rs-- individuals will show right-sided language, and that half of rs-- individuals will have right-sided language and half will have left-sided, then the frequency of rs-- individuals must be $.0927 \times 2 = .1854$ (see Table 1 for details of calculation). It is then necessarily the case that the frequency of the rs- gene is .43.

The problem with this derivation is that although early versions of the right shift theory (Annett, 1978) did indeed, like the model of Trankell (1955), assume that the gene was recessive in its expression (see McManus, 1985a, for a detailed account of the evolution of the models), subsequently, and seemingly because a recessive model simply cannot fit the data (see McManus, 1985c), the model became additive

(Annett & Kilshaw, 1983), with heterozygotes being expressed midway between the homozygotes (see Annett's Figures 3 and 4). That however now creates a problem for the model in its explanation of language dominance. Annett's Figure 3 suggests that left hemisphere advantage is "absent" in rs-- individuals (i.e., a normal distribution is centred at zero, and half are therefore less than zero and hence are *right* hemisphere language dominant), and it also suggests that rs+- individuals have only "moderate" left hemisphere advantage (by which it can only be assumed to mean the same as in the case of handedness, that there is a normal distribution which for the heterozygotes is centred at about 1 SD to the left [i.e., hemisphere, not hand], so that about 16% of individuals have right hemisphere language[1]). And similarly, a small proportion of the rs++ individuals will also be right-language dominant (roughly 5% since the distribution is about 2 SDs to the left). Given the frequency of the rs- gene as .43, the overall expected proportion of right hemisphere language in the population can then be calculated as 18.7% (see Table 1 for details). But that figure is clearly not compatible with the value of 9.27% so stoutly defended on p. 435. The problem arises from the gene frequency being derived under one model (recessive) and then being transferred uncritically to another model (additive) with which it is not compatible.

Clearly something has to change: 9% and 18% are simply not the same. The most obvious resolution of the problem is to argue that the additive model now requires a better estimate of the gene frequency, so that indeed it still predicts 9.27% right hemisphere language. That would seem to be a reasonable idea, to derive all the model's parameter estimates simultaneously from the data, rather than having one parameter being set *a priori* on the basis of a theoretical assumption, of a recessive gene, which is clearly flawed and already abandoned. However when one calculates the results (see Table 1) it then becomes apparent that the frequency of the rs- gene has to fall from .43 to .165. Such a model can adequately fit the proportion of right-sided language, giving a value of 9.3%. Another problem though now begins to rear its head. The frequencies of the three genotypes are p(rs--) = 2.7%, p(rs+-) = 27.6%, and p(rs++) = 69.7%, and suddenly it is very clear that the most frequent genotype is not rs+-, the heterozygote, as Annett

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1. I am assuming here that the threshold, x, is necessarily set at zero since 50% of rs-- individuals are right language dominant.

TABLE 1. Calculations for the proportion of individuals with right-sided language in relation to the frequency of the rs- allele.

Annett (1978) recessive model: gene frequency = .43

Genotype	Proportion of genotype with right-sided language	Frequency in gene-pool	Proportion in population with right-sided language
rs--	.50	$.43^2 = .1845$	$.5 \times .1845 = .0923$
rs+-	0	$2 \times .43 \times (1-.43) = .4902$	$0 \times .4902 = 0$
rs++	0	$(1-.43)^2 = .3242$	$0 \times .3242 = 0$

Proportion in population with right-sided language: .0923 + 0 + 0 = **9.23 %**

Additive model: gene frequency p(rs-) = .43

Size of shift	Proportion of genotype with shift < 0 (i.e., right-sided language)	Frequency in gene-pool	Proportion in population with right-sided language
0 SDs	.50	$.43^2 = .1845$	$.5 \times .1845 = .0923$
1 SD	.16	$2 \times .43 \times (1-.43) = .4902$	$.16 \times .4902 = .0784$
2 SDs	.05	$(1-.43)^2 = .3242$	$.05 \times .3242 = .0162$

Proportion in population with right-sided language: .0923 + .0784 + .0162 = **18.7%**

Additive model: gene frequency p(rs-) = .165

Size of shift	Proportion of genotype with shift < 0 (i.e., right-sided language)	Frequency in gene-pool	Proportion in population with right-sided language
0 SDs	.50	$.165^2 = .0272$	$.5 \times .0272 = .0136$
1 SD	.16	$2 \times .165 \times (1-.165) = .2755$	$.16 \times .2755 = .0441$
2 SDs	.05	$(1-.165)^2 = .6972$	$.05 \times .6972 = .0348$

Proportion in population with right-sided language: .0136 + .0441 + .0348 = **9.3%**

has consistently argued, but the rs++ homozygote. This should not at first sight produce any problems at all. After all, gene frequencies can take any value between 0 and 1 and polymorphisms can be balanced at any gene-frequency between 0 and 1 by appropriate selection coefficients for the three genotypes. It *is* however a problem for Annett, since she has argued forcefully and repeatedly that, "the genotype frequencies are fundamental to the argument for a BP+HA", and "the question at the heart of the BP+HA hypothesis is why the proportion of heterozygotes is so high, when it certainly does not need to be" (p. 465). Something has to give here. Either:

a) the frequency of the rs- gene is adequate at .43, in which case the additive version of the right shift genetic theory predicts a far too high figure for the proportion of individuals with right language dominance (nearly 19%), or

b) the gene-frequency is actually much lower, at about .165, the proportion of the population with right-sided language is correctly specified (about 9%), but now there is no evidence that the rs+- heterozygote is the commonest of the three genotypes, and, to use Annett's phrase, "the question at the heart" of the BP+HA hypothesis is wrong. Once again, "The BP+HA hypothesis appears to be impaled on one or other horn of a dilemma" (p. 468).

To my eye the problem is easily resolved. The gene-frequency is undoubtedly too high for the additive model of language dominance as described, and there is actually no reason to be found within conventional genetic theory for requiring the heterozygote to be the most frequent of the genotypes in a polymorphism. Both aspects of the model could therefore be changed without altering its principal impact. That however would still not solve the far more serious difficulty of the effect size for the heterozygote advantage being inconsistent across different types of data (McManus et al., 1993); but that problem, as we argued elsewhere, is probably insuperable.

An additional problem also rises. The distribution of the population into quartiles is now a far from optimal procedure for distinguishing between genotypes. When p(rs-), the gene frequency, is .43, then it is indeed the case that "groups 2 and 4 [are] expected to include the highest proportions of rs+- and rs++ genotypes, respectively" (p. 449) – see Table 2. However, revising the gene frequency to p(rs-) = .165 means that in all of the four groups the most common genotype is rs++, and that although rs+- is indeed somewhat more common in group 2 than in group 4, it is doubtful that any study of the size described would have the power to detect the small differences between

the groups, all groups being dominated by the rs++ genotype, which is now much more common. The likelihood of finding a quadratic effect, whereby rs+- is better than rs--, is now minimal, none of the four groups containing reasonable proportions of the rs-- genotype, these being concentrated in left-handers where about 62% are rs--, 36% are rs+-, and only 2% are rs++.

TABLE 2. Estimated proportions of right-handers (the most dextral 91.5% of the population) in each of the four dextrality quartiles on the Annett peg-board test, who are of each of the three genotypes, rs--, rs+-, and rs++, on the basis of the original Annett estimate of the rs- gene frequency of .43, or of the revised estimate of .165.

	Original Annett model with p(rs-) = .43			Revised Annett model with p(rs-) = .165		
	rs--	rs+-	rs++	rs--	rs+-	rs++
Group 1: Lowest quartile of right-handers	33%	57%	10%	4%	45%	51%
Group 2: Second quartile	15%	60%	25%	1%	28%	71%
Group 3: Third quartile	6%	51%	43%	0.3%	17%	83%
Group 4: Highest quartile of right-handers	2%	31%	67%	0.01%	8%	92%

Other points

Chance in the McManus theory. Annett claims that her view of the role of chance "contrasts strongly" (p. 439) with that proposed in my own genetic theory. I am not really sure that this is the case. I suspect we both believe that the biological base-line for chance is the phenomenon known as *fluctuating asymmetry* (Palmer & Strobeck, 1986; Parsons, 1990; Livshits & Kobyliansky, 1991; Yeo & Gangested, 1993): certainly I have tried to put that position forward in many of my papers (Batheja & McManus, 1985; McManus, 1985c, 1991, 1882; McManus & Bryden, 1992, 1993; McManus & Mascie-Taylor, 1979; Morgan & McManus, 1988). Annett's fine metaphor of how "a complex structure like a building, model ship or a garment may be designed

to be symmetrical but develop asymmetries in the course of construction..." is an elegant account of the very same process. Readers should not, of course, be misled by shorthand turns of phrase in my own writing such as "a gene for chance" or "a gene for right-handedness", any more than they would falsely think that someone who spoke of "the sun rising" did not believe in a heliocentric theory of the solar system.

The power of studies. Twice, on pp. 442 and 462, Annett refers to the differential power of studies. On p. 442, she argues that studies are more powerful according to which variables are taken as dependent and which are independent. In particular she suggests it is more powerful "to classify for ability and test for handedness" than *vice versa* (p. 442). I am afraid I do not understand this point. From a statistical point of view one can regard oneself as assessing two approximately normal distributions with a bivariate normal distribution with some correlation, r. If one is to select a subset of that population, say the top $x\%$ and the bottom $x\%$ of the population on one measure, and then look for differences in mean score between the two groups on the other score, then it can make no difference which is chosen as the dependent and which is the independent. The correlation is the same in both cases, and since the sample size will also be the same ($2x\%$ of the total sample size) the results will have identical power. Of course the regression coefficients may be very different (just as the regression of y on x and x on y often differ dramatically), but their standard errors will also vary concomitantly, leaving the significance levels and hence the power the same. An analogous argument applies to contingency tables (Bryden, McManus, & Bulman-Fleming, 1994). The argument for a difference in power can only be correct if there is a small sub-group lurking in the tail of one distribution (i.e., it is a mixture distribution) and then Annett's argument may be correct, but I am not convinced that this is its origin. Instead on p. 442 the proposition seems to be derived from the causal pathways between the measures. Again I fail to see how in any conventional causal model (Kenny, 1979; Davis, 1985, Loehlin, 1992), the path from A to B can be different in strength from the path from B to A; the calculation is necessarily symmetric in each case, resulting in a single correlation which can be tested against data.

The family as a unit for selection. On p. 469 it is said to be impossible that "the genotypes of the rs locus should segregate by social class" since "the high frequency of rs+- genotypes in the population implies that all genotypes must be present in almost all families". It is

indeed true that rs-- × rs-- and rs++ × rs++ matings are indeed the only ones which necessarily breed true, and therefore do not have any rs+- offspring, and that these will, using Annett's genotype frequencies, represent only about 14% of families. That does not however mean that selection and social migration cannot together result in a social class gradient. Indeed if it were a strong argument then social class gradients would be impossible for any polymorphic gene above a certain critical gene-frequency. To my knowledge no geneticist has suggested such a proposition, and the strong social class gradients for phenomena such as intelligence, which are in part almost certainly due to polymorphism at many genetic loci, militate against the argument. The stronger claim is then made that "Different members of human families might enjoy the different skills associated with the three genotypes... [and that] this combination of skills [may] contribute to the reproductive success of the family unit" (p. 471). This is a remarkable suggestion to make at a time when group selectionist arguments have, for very good reasons, gone deeply out of fashion (Ridley, 1994). Certainly it seems unlikely that the mechanisms could play a particularly large role in the existence of family units *per se* since the rs+ gene is supposed to be unique to humans, whereas family units of some form are common throughout higher animals.

A Popperian question. The BP+HA hypothesis has slowly evolved. It has however rarely been clearly enunciated in advance of data being presented. Instead the usual pattern has been for new data to be given and a *post hoc* analysis given of how the results can be explained in terms of the model. Perhaps the most remarkable case of this is Annett's Figure 8, in which spatial ability is shown in relationship to the eight hand preference classes. The distribution is correctly described by Annett as W-shaped. The problem however arises to what extent this unlikely result could be explained *a priori* by the BP+HA hypothesis. It seems clear from Annett's Figure 3 that there should be a linear trend of problems with visuo-spatial ability against increasing dexterity. That does not however explain why spatial ability should suddenly leap up between groups 4 and 6 (there is no group 5 in this sample). In other words, the trend with dexterity seems only to be present *within* handedness groups (i.e., right-handers and left-handers), and goes in the opposite direction *between handedness groups* (and is shown most clearly in the jump between groups 6 and 4). The notch at group 2 is also a problem. It may be the case that "class 2 was more dextral than class 1 for hand skill" (p. 450), but surely that creates more problems than it

solves, since it suggests the data should have been plotted against hand skill in the first place. But the key problem is that if *this* data set can be explained by the BP+HA hypothesis then what data *cannot* be so explained. Perhaps Annett could follow a strictly Popperian line and make it clear precisely what novel data, should they be found, would mean that the BP+HA hypothesis would necessarily have to be rejected. Without such reassurance, there is a nagging worry that any data can somehow be explained.

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