A MODEL FOR THE GENETICS OF HANDEDNESS

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Manuscript received August 30, 1971
Revised copy received April 3, 1972

ABSTRACT

Experimental data and theoretical work on the inheritance of handedness and cerebral dominance are reviewed. A two-gene, four-allele model, one locus pertaining to left or right hemispheric dominance and the other to contralateral or ipsilateral hand control relative to the dominant hemisphere, is constructed. It is in excellent agreement with all quantitative information regarding this problem. Refinements designed to explain relevant qualitative facts are proposed and discussed.

I. INTRODUCTION

THE hypothesized relationship between handedness and cerebral dominance for speech has gone through several stages. Clinical reports of right hemiplegia and aphasia in dextrals and left hemiplegia and aphasia in sinistrals led to the idea that the language-dominant hemisphere was always contralateral to the preferred hand. This view, first proposed in the 19th century (see GOODGLASS and QUADFASAL 1954 for a historical review), has had such a strong influence that GIRARD in 1952 defined a left hander as one who speaks with the right hemisphere. Contradicting this mirror symmetry idea, are dozens of cases of crossed aphasia both in right handers with right-hemisphere lesions and in left handers with left-hemisphere lesions (CONRAD 1949; BINGLEY 1958; PENFIELD and ROBERTS 1959; RUSSELL and ESPIR 1961), as well as asymptomatic patients with lesions in the hemisphere contralateral to the preferred hand. Based on such observations, some researchers (WEPMAN 1951; MILNER 1952; ROBERTS 1963) have suggested that, except in pathological cases involving early childhood injury to the speech areas of the left cerebrum, all people have language-dominant left hemispheres. The difficulty with this position is that it cannot account for the right-hemisphere aphasias resulting from sudden brain injury (ZANGWILL 1967).

Any effort to explain the relationship between handedness and cerebral dominance should take into account the following facts:

(1) The vast proportion of dextrals have language-dominant left hemispheres, but some small fraction have language-dominant right hemispheres.

(2) Approximately 53% of sinistrals have language-dominant left hemispheres

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while 47% have language-dominant right hemispheres (GOODGLASS and QUADFASAL 1954). These percentages were calculated on the basis of 123 sinistrals having unilateral lesions in the language area. GOODGLASS and QUADFASAL suggest that possibly these proportions are biased because some of the cases were published as illustrations of the classical theory, thus artificially raising the percentage of sinistrals with right-hemisphere dominance, while other cases were published as examples of crossed aphasia which would spuriously increase the proportion with left-hemisphere dominance. These authors believe that impartially tabulated data would give 65% of left handers with left-hemisphere speech. It should be pointed out, however, that among neurological patients the percentage of phenotypic sinistrals is higher than in the population at large. This is presumably due to the fact that, since most people control hand movement from a contralateral left hemisphere, equal proportions of right and left hemisphere lesions in the hand-control region will produce a much larger number of right hand to left hand shifts than vice versa, so that the percentage of phenotypic sinistrals among the brain damaged is larger than the percentage of sinistral genotypes. If, after such a shift in handedness, language remains centered in the left hemisphere, more left handers with left hemisphere language will be seen among a brain-injured population than is representative of the normal genotypic sinistrals. Since, with the data available, it is impossible to calculate exactly what the unbiased proportions would be, we shall take 53%–47% as offering a reasonable estimate.

(3) According to LURIA's tabulations (see ZANGWILL 1960) 48 of 137 (35%) right handers either had no aphasia at all or recovered fully from it following lesions to the speech area of the left hemisphere, whereas 15 of 23 (65%) sinistrals or ambidexters suffered no aphasia or recovered completely under these conditions.

Since the above data establish that a correlation exists between hemispheric dominance and handedness, the most reasonable inference is that both are under genetic control and that the genetic mechanisms controlling the two are in some way related.

ANNETT (1964) tried to formulate a genetic model which explained both cerebral dominance and hand usage. She suggested that handedness was inherited as a single-gene, two-allele Mendelian trait, the homozygous dominant being right handed and left brained, the homozygous recessive being left handed and right brained, and the heterozygote having the capacity to appear as either the dominant or the recessive phenotype. ANNETT postulates certain frequencies of the dominant and recessive alleles and a particular degree of penetrance for the heterozygote. She does not state her reasons for her choice of parameters, but, since she claims that in her model with the selected parameters "expected proportions of left-handed offspring of the three possible matings are close to those observed in three studies of familial handedness", presumably, she picked them to minimize the deviations of her predicted fractions of left and right handers resulting from the three possible matings (right × right, right × left, and left × left) from the observed fractions. She does not, however, present either her

theoretical breeding ratios, or χ^2 tests of them against the empirical proportions. For reasons to be discussed later, one of the three studies of familial handedness (CHAMBERLAIN 1928) is unusable for deriving these proportions. Using ANNETT's parameters, we calculated the χ^2 values for RAMALEY's (1913) and RIFE's (1940) studies. Although the deviations between ANNETT's predicted values and RAMALEY's empirical ones are much too large to be attributed to chance, there was tolerable agreement with RIFE's data ($\chi^2 = 2.49$, $df = 1$, $P \cong 0.115$). In any case, since the RAMALEY paper did not give the criteria used for determining handedness and, in addition, employed a sample size only ½ that of RIFE's, the latter investigation is much more likely to be valid and reliable.

However, except in cases of cerebral injury, when she suggests that heterozygotes can switch dominance, in her model there appears to obtain a perfect correlation between handedness and cerebral dominance for both homo- and heterozygotes. Such a perfect correlation conflicts with experimental fact. Furthermore, in her model, no sinistrals should suffer permanent aphasia from left hemisphere lesions, while, actually, 35% are permanently aphasic. In sum, although the model gives a fair prediction for the breeding ratios, it totally fails to account for known experimental findings with respect to the relationship between hand usage and cerebral organization.

TRANKELL (1955) has also proposed a model for the inheritance of handedness. He, too, suggests a single-gene two-allele model, but, in this case, it is only a certain percentage of the recessive homozygotes who are phenotypic sinistrals. Although, with this model, TRANKELL can accurately predict the observed breeding ratios, it yields no information about cerebral organization and treats all sinistrals as a single genotype. Since it is known that there are at least two sinistral phenotypes—those with left-hemisphere language and those with right-hemisphere language—it seems unlikely that TRANKELL's model describes all the essentials of the problem.

In this paper we propose a model for the inheritance of handedness and cerebral dominance which is in excellent agreement with the filial proportions from the three types of matings and the aphasia recovery rate for left and right handers. It employs the observed percentages of left and right hemisphere dominance in left handers and predicts that a very small fraction of right handers should have a dominant right hemisphere.

II. THE MODEL

We postulate the existence of two genes, one determining which hemisphere is language dominant, the alleles being L and l, and the other, with alleles C and c, deciding whether hand control is contralateral or ipsilateral to this hemisphere. L and C are dominant while l and c are recessive. Complete penetrance is assumed. We suppose that those forms of selection which would produce an association between linked alleles are absent.[1] Because Australopithecus was predominantly dextral (DART 1949), we know that approximately 2 million

[1] We thank Professor W. F. BODMER for helpful correspondence regarding this point.

years have elapsed since the alleles relevant to hand control entered the human gene pool. Then, if equilibrium, defined stringently by requiring the gametic determinant to have been reduced by a factor of at least a thousand, has still *not* been reached after about 100,000 generations of presumed random mating, the fraction of crossovers (constant, by assumption, during this period) is easily shown to be *less* than 6.9×10^{-5} (Li 1955). Such close linkage seems highly unlikely. Hence, the distribution of genotypes is necessarily that for independent assortment (Li 1955). Thus, the model implies the existence of the following genotypes:

Sinistral genotypes	Dextral genotypes
CC;ll	CC;LL
Cc;ll	CC;lL
cc;LL	Cc;LL
cc;lL	Cc;lL
	cc;ll

The above genotype-phenotype relations are postulated to obtain under normal, non-pathological conditions. However, in order to make predictions regarding recovery from aphasia, we suppose also that when an injury occurs in the speech area of the left hemisphere, the homozygote, LL, behaves differently from the heterozygote, lL. Whereas the heterozygote has the capacity to develop language in the right hemisphere, the homozygote does not, so that only genotypes homozygous for L fail to recover from aphasia resulting from a left-hemisphere lesion.

An objection to the model might be raised on the grounds that there is no evidence showing that hand control ever derives from the ipsilateral hemisphere. It is possible, for example, to suppose that, even in those left handers who have speech in the left hemisphere, motor control of the hand comes from the right hemisphere and their ability to write depends on trans-callosal information. First, autopsies have revealed that some people have only a direct pyramidal tract, the pyramidal decussation being totally absent (Peele 1961). Of necessity, such people have to rely on ipsilateral pathways. Second, studies with commissurotomy patients demonstrate that either hemisphere gains the ability to control either hand as soon as three months after surgery, indicating that even in people who had used only contralateral pathways, the ipsilateral ones retain functional capacity. (Gazzaniga and Sperry 1967; Gazzaniga, Bogen and Sperry 1967).

In addition, observations by the senior author indicate that a majority (60%) of normal left handers, in fact, control their left hands from a language-dominant left hemisphere (Levy 1971; Levy and Mandel 1972). Although it has generally been supposed that sinistrals who write with the hand inverted do so as a peripheral adaptation to left-to-right writing with the left hand, inferential evidence suggests that inversion reflects ipsilateral control. In tachistoscopic lateral field tests for recognition of verbal material, as well as a dot location task, sinistrals who write with the hand inverted (60%) show the same results as dextrals, while those who write normally (40%) show the reverse. This supports the idea of a language-dominant left hemisphere for the former group and a language-

dominant right hemisphere for the latter. That hand inversion is a peripheral adaptation is also contradicted by the fact that the junior author, who, to some extent, is ambilateral, but who has always written with his right hand, writes with his hand inverted, suggesting that he is one of the small portion of people having the genotype ccll. It is interesting that he shows the same large disparity between verbal and performance I.Q.'s as left handers (LEVY 1969; 1970).

In the following section, quantitative results for the breeding ratios and the aphasia recovery rate in sinistrals and dextrals are deduced. Only RIFE's (1940) data are used for testing the goodness of fit of our theoretical breeding ratios. Since, as mentioned above, RAMALEY (1913) did not provide his criteria for defining handedness, we are unsure of the meaning of his findings. Although TRANKELL (1955) uses certain values from CHAMBERLAIN's (1928) paper as representing the breeding proportions, in fact, careful analysis of CHAMBERLAIN's paper reveals that it contains a minimum of 13 inconsistencies such that it is not possible to decide on rational grounds which data represent the actual empirical values. As examples, CHAMBERLAIN in Table 1 on p. 558 gives 307 as the number of sinistrals from R × R matings, but on p. 559 states that the number is 166. In Table 1 he also asserts that 307 represents 3.9% of all R × R progeny. If so, the total number of R × R progeny would be 7872, whereas he claims on pp. 557 and 558 that total progeny from all matings (R × R, R × L, L × L) is only 7714. In addition to numerous other inconsistencies of this nature, he is extremely misleading in saying that the filial generation had twice as many left-handed males as females. Actually, the whole filial population had twice as many males as females since CHAMBERLAIN chose the population by selecting male students and then obtaining data on them and their siblings. Therefore, not only is it impossible to decide whether to believe figures on one page or another, in a table or in the body of the text, but also, the sample is biased in favor of males.

For the above reasons, we felt constrained to use only RIFE's data to test the validity of our model. Elsewhere (NAGYLAKI and LEVY 1972), we explain why we do not attempt to fit his data on the distribution of handedness within sibships.

III. ANALYSIS

We let α, β, and γ denote the frequency of left handers with right hemisphere language, left handers with left hemisphere language, and right handers, respectively. Thus,

$$\alpha + \beta + \gamma = 1 . \tag{1}$$

The frequencies C, c, L, l of the alleles C, c, L, l, respectively satisfy

$$C + c = 1 \tag{2}$$

and

$$L + l = 1 \tag{3}$$

Our phenotypic equations are

$$2Ccl^2 + C^2l^2 = \alpha, \tag{4}$$

$$2c^2lL + c^2L^2 = \beta, \tag{5}$$

$$2C^2lL + C^2L^2 + 4CclL + 2CcL^2 + c^2l^2 = \gamma. \tag{6}$$

Since adding Eqs. (4), (5), and (6) yields the binomial identity

$$(C+c)^2\,(L+l)^2=1, \tag{7}$$

therefore, given Eqs. (1) to (5), Eq. (6) is an identity. The solution of Eqs. (2) to (5) is

$$l=\sqrt{x}, \tag{8}$$

$$c=\sqrt{1-\alpha/x}, \tag{9}$$

$$C=1-c, \tag{10}$$

$$L=1-l, \tag{11}$$

where $$x=\tfrac{1}{2}\,(\delta-\sqrt{\delta^2-4\alpha}), \tag{12}$$

with $$\delta=1+\alpha-\beta. \tag{13}$$

Now, from Eqs. (8) and (9)

$$c^2l^2=x-\alpha. \tag{14}$$

Since, empirically[2], $c^2l^2 \ll \gamma < 1$ and $\alpha, \beta \ll 1$, therefore we wish to have $x \ll 1$. Hence, the possible root in Eq. (12) with a positive sign in front of the radical was discarded.

We denote by $P_{L,RR}$, $N_{L,RR}$, and N_{RR} the probability of the birth of a sinistral in a dextral × dextral mating, the number of sinistrals from dextral × dextral matings, and the number of dextral × dextral matings, respectively. The other breeding ratios and frequencies are defined similarly. We define, further, Q_R (Q_L), K'_R (K'_L), M_R (M_L), and R_R (R_L) to be the fraction homozygous for L among dextrals (sinistrals), the number of dextrals (sinistrals) in the aphasia observations, the number of dextrals (sinistrals) not recovering from aphasia, and the number of dextrals (sinistrals) recovering from aphasia, respectively. A prime will always indicate the experimental value of a variable.

$$P_{L,RR}=\frac{1}{\gamma^2}\,[g_7(4g_5+6g_7+4g_8+4g_9)+g_5(g_5+2g_9)+g_8(g_8+2g_9)], \tag{15}$$

$$\begin{aligned}P_{L,RL}=\frac{1}{\gamma(1-\gamma)}\,[&g_5(2g_1+g_2+g_3)+g_7(4g_1+2g_2\\&+4g_3+2g_4)+g_8(g_1+2g_3+g_4)\\&+g_9(g_1+g_2+g_3+g_4)]\,,\end{aligned} \tag{16}$$

$$\begin{aligned}P_{L,LL}=\frac{1}{(1-\gamma)^2}\,[&g_1(3g_1+4g_2+4g_3+2g_4)\\&+g_2(g_2+2g_3)+g_3(3g_3+4g_4)+g_4{}^2]\,,\end{aligned} \tag{17}$$

where the g's are the genotypic frequencies, without the numerical coefficients, subscripted precisely in the order in which they appear in Eqs. (4) to (6). E.g., $g_1=Ccl^2$. Fortunately, given the length of Eqs. (15) to (17), one can apply a simple consistency check to them. This was satisfied numerically in all our computations. Since a sinistral must come from one of the three possible matings,

[2] The genotype, ccll, representing a right hander with right hemisphere language dominance, constitutes 1.8% of the population according to Zangwill's tabulation (1967) of five studies from the literature on aphasia with right hemisphere injury in dextrals. However, Subirana (1964) suggests that many such right handers have been misclassified and are really ambilaterals. If so the actual percentage may be much less.

therefore, correctly weighted by the probabilities of the matings, the sum of the breeding ratios must reproduce the proportion of sinistrals among the offspring. Hence,

$$\gamma^2 P_{L,RR} + 2\gamma(1-\gamma)P_{L,RL} + (1-\gamma)^2 P_{L,LL} = 1-\gamma\,. \tag{18}$$

For aphasia, from Eqs. (4) to (6), we have, at once,

$$Q_R = \frac{1}{\gamma}(g_6 + 2g_8)\,, \tag{19}$$

$$Q_L = \frac{g_4}{1-\gamma}\,. \tag{20}$$

The various predicted frequencies are calculated as shown below:

$$N_{L,RR} = N'_{RR}\,P_{L,RR}\,, \tag{21}$$
$$N_{L,RL} = N'_{RL}\,P_{L,RL}\,, \tag{22}$$
$$N_{L,LL} = N'_{LL}\,P_{L,LL}\,, \tag{23}$$
$$N_{R,RR} = N'_{RR} - N_{L,RR}\,, \tag{24}$$
$$N_{R,RL} = N'_{RL} - N_{L,RL}\,, \tag{25}$$
$$N_{R,LL} = N'_{LL} - N_{L,LL}\,, \tag{26}$$
$$M_R = K'_R Q_R\,, \tag{27}$$
$$M_L = K'_L Q_L\,, \tag{28}$$
$$R_R = K'_R - M_R\,, \tag{29}$$
$$R_L = K'_L - M_L\,. \tag{30}$$

Finally, we exhibit the χ^2 for the breeding ratios,

$$\begin{aligned}\chi_1^2 = {} & (N'_{L,RR} - N_{L,RR})^2/N_{L,RR} + (N'_{R,RR} - N_{R,RR})^2/N_{R,RR} \\ & + (N'_{L,RL} - N_{L,RL})^2/N_{L,RL} + (N'_{R,RL} - N_{R,RL})^2/N_{R,RL} \\ & + (N'_{L,LL} - N_{L,LL})^2/N_{L,LL} + (N'_{R,LL} - N_{R,LL})^2/N_{R,LL}\end{aligned} \tag{31}$$

and for aphasia,

$$\begin{aligned}\chi_2^2 = {} & (M'_R - M_R)^2/M_R + (M'_L - M_L)^2/M_L + (R'_R - R_R)^2/R_R \\ & + (R'_L - R_L)^2/R_L\,.\end{aligned} \tag{32}$$

Since χ_1^2 and χ_2^2 are two independent χ^2 variables, therefore their sum

$$\chi_T^2 = \chi_1^2 + \chi_2^2 \tag{33}$$

is also a χ^2 variable.

IV. NUMERICAL CALCULATIONS AND RESULTS

Numerical investigation shows that, in the empirically allowed range $0.80 \leq \gamma \leq 0.99\,, \frac{35}{65} \leq \frac{\alpha}{\beta} < 1$, the results are quite insensitive to α/β. So, we fix this ratio at its experimental value, as discussed in Sec. I,

$$\frac{\alpha}{\beta} = \frac{47}{53} \tag{34}$$

and have, therefore, from Eq. (1),

$$\alpha = 0.47\ (1 - \gamma)\ , \tag{35}$$

$$\beta = 0.53\ (1 - \gamma)\ , \tag{36}$$

Then it is easy to see from Sec. III that all predicted quantities are functions of the single parameter γ. We minimize χ_T^2 and (in order to satisfy readers sceptical about the aphasia hypothesis) χ_1^2 with respect to γ. In Tables 1 and 2, we give the two fits in this order. The minimization is performed trivially (total cost = \$1.45!) on a computer. The experimental results reported by RIFE (1940), GOODGLASS and QUADFASAL (1954) and ZANGWILL (1960) are shown.

Since it involves 6 variables, which satisfy the 3 constraints of Eqs. (24) to (26) and depends on 1 free parameter, γ, χ_1^2 has 2 degrees of freedom. Similarly, taking note of the 2 constraints of Eqs. (29) and (30), χ_T^2 has $(6 + 4) - (3 + 2) - 1 = 4$ degrees of freedom.

TABLE 1

Fit A, Breeding Ratios and Aphasia

	Sinistrals				Dextrals			
	Frequency		Percent		Frequency		Percent	
	E	O	E	O	E	O	E	O
R × R matings	145	151	7.29	7.58	1848	1842	92.71	92.42
R × L matings	37.8	34	21.7	19.5	136.2	140	78.3	80.5
L × L matings	7.02	6	63.8	54.5	3.98	5	36.2	45.5
Aphasia recovery	15.38	15	66.9	65.2	51.8	48	37.8	35.0
Aph. nonrecovery	7.62	8	33.1	34.8	85.2	89	62.2	65.0

E = expected, O = observed

$\gamma = 0.893$ $\gamma_{OBS} = 0.912$ $\alpha = 0.0503$ $\beta = 0.0567$

$C = 0.755$ $c = 0.245$

$L = 0.769$ $l = 0.231$

$\chi_1^2 = 1.14$, P = 0.57 $\chi_2^2 = 0.473$, P = 0.79

$\chi_T^2 = 1.61$, P = 0.80

TABLE 2

Fit B, Breeding Ratios and Aphasia

	Sinistrals				Dextrals			
	Frequency		Percent		Frequency		Percent	
	E	O	E	O	E	O	E	O
R × R matings	148	151	7.41	7.58	1845	1842	92.59	92.42
R × L matings	38.1	34	21.9	19.5	135.9	140	78.1	80.5
L × L matings	7.03	6	63.9	54.5	3.97	5	36.1	45.5
Aphasia recovery	15.43	15	67.1	65.2	52.2	48	38.1	35.0
Aph. nonrecovery	7.57	8	32.9	34.8	84.8	89	61.9	65.0

E = expected, O = observed

$\gamma = 0.891$ $\gamma_{OBS} = 0.912$ $\alpha = 0.0513$ $\beta = 0.0577$

$C = 0.753$ $c = 0.247$

$L = 0.766$ $l = 0.234$

χ_1^2 1.07, P = 0.59 $\chi_2^2 = 0.582$, P = 0.75

$\chi_T^2 = 1.65$, P = 0.80

We note that the fits, A and B, to both the breeding ratios and the aphasia recovery are excellent. They are very close to each other and, in fact, by treating one as "observed" and the other as "predicted," it is easy to see, by means of a χ^2 test, that the difference between them is not statistically significant. We might also add that χ_2^2 is minimized quite near either fit, at $\gamma = 0.91$. It is, perhaps, worth reminding the reader that $\frac{\alpha}{\beta}$ was fixed at its empirical value. Hence, should the model not fit additional experimental data quite so accurately, minimizing χ^2 in both $\frac{\alpha}{\beta}$ and γ might produce significant improvement. At the present time this would be a needless exercise.

V. DISCUSSION

Without further assumptions, on the basis of our model, one can draw no conclusions with respect to certain well known aspects of brain organization. The most important of these is the difference in degree of lateral specialization between sinistrals and dextrals (GOODGLASS and QUADFASAL 1954; SUBIRANA 1964; ZANGWILL 1967). The latter have almost complete specialization of the hemispheres, while the former do not. In contrast to right handers, left handers tend toward ambilaterality. Aphasia in sinistrals is more frequently temporary and more likely to occur as the result of lesions in either hemisphere than in dextrals. It is possible to account for this difference in degree of lateralization within the framework of the model by supposing that full expression of the alleles occurs only when a dominant allele is present, in homozygous or heterozygous condition, at each of the two loci.

We can arrive at this hypothesis on the basis of two more detailed postulates, one pertaining to the effect of the L-l gene and the other to its interaction with the C-c locus. First, we assume that bilateral symmetry, being a property not only of the Chordates, but of other phyla as well, is under control of a set of genes which governs the general morphology of all animals who share in this symmetry. The various asymmetries of heart, stomach, liver, etc. are caused by mutations superimposed on the bilaterally symmetric form. For the human being, then, the L-l gene, imposing hemispheric asymmetry on a basically symmetric brain, would represent just such a mutation. The allele, L, being dominant, would cause sufficient production of an appropriate gene product to effect the development of full left-hemispheric dominance. Since the allele l is recessive, it would manufacture a product either too small in quantity or unsuitable in action for bringing about complete right-hemispheric dominance. The deviation of the L genotype from the bilaterally symmetric condition would, therefore, be larger than that of the l genotype.

The second postulate, that full expression of L only occurs in the presence of C, implies either that L and C interact directly at the level of transcription or translation, or that, subsequently, complete development of the brain organization necessary for language specialization in a single hemisphere requires that the primary pathways be contralateral. The developmental period probably be-

gins before birth, certainly by three months, when handedness is evident (GAUPP, quoted by SUBIRANA 1964), and continues asymptotically until puberty. Since sensory and motor fields are represented predominantly in the contralateral hemisphere of vertebrates, we tend to favor the latter type of interaction. Owing to lack of experimental evidence, we make no assertion regarding the effect on the degree of lateralization of the presence of only one dominant allele. It is, of course, possible that L or C alone can induce more lateralization than possessed by the phenotype with homozygous recessives at both loci.

It should be pointed out that, intrinsic to the mathematically confirmed aspects of the model, we have already postulated a certain type of interaction between the genes L-l and C-c. Whether the pathways controlling the dominant hand will be ipsilateral or contralateral to the dominant hemisphere is independently determined by the C-c gene, but the choice between the two ipsilateral or contralateral pathways depends on the L-l gene. In contrast, in our lateralization hypothesis, the occurrence of the allele C permits the maximal specialization of either hemisphere, but only the L allele is capable of accomplishing this total lateralization.

The difficulty with the foregoing suggestion is that, while it accounts entirely for the observed differences in lateral specialization between right and left handers, since it only leads to a single behavioral prediction other than those it was designed to explain, it is not easily testable. It implies that the dextral with genotype ccll will be at least as incompletely lateralized as sinistrals. In Sec. II, we noted our suspicion that the junior author has genotype ccll, and, as stated there, he shows the same verbal-perceptual I.Q. discrepancy as do sinistrals. This discrepancy has previously been interpreted (LEVY 1969; 1970) to indicate incomplete specialization. It might be mentioned that the predicted percentages of the genotype ccll from Fits A and B are 0.32% and 0.33%, respectively.

In addition to lateralization differences correlated with handedness, there are those associated with age. Should the dominant hemisphere be damaged, the younger a child, even if purely dextral, the greater is his capacity to utilize either hemisphere for speech. We do not feel that the explanation of this plasticity confronts us with any more problems than that of any other developing physiological system. During the entire maturational process, from fertilization to biological adulthood, the organism undergoes an increasing differentiation and a decreasing plasticity.

The presence of genes governing some trait, given the environmental history of the organism, specifies a certain range of reaction which narrows with age. The terminal range, as in the case of dextrals with lesions in their speech centers, may be so small that no flexible response to some environmental changes remains. Therefore, it seems to us that the capacity of children to develop language in either hemisphere is simply another example of the general physiological plasticity observed in all developing systems.

It was suggested previously that the L-l gene was a mutation for asymmetry specific to man. While other species, including mice, rats, monkeys, and chimpanzees, appear to have a preferred paw or hand, the evidence strongly supports

the idea that this lateral preference has no genetic basis and derives purely from accidental contingencies of initial environmental reinforcement subsequently magnified by a positive feedback loop. Eight generations of selection for paw preference in rats (PETERSON 1934) failed to change the 50–50 ratio of left and right paw preferences seen in the populations normally. COLLINS found that the fractions of left and right paw preference in several strains of inbred mice conformed with chance expectations (1968), and, since three generations of selection did not change these proportions (1969), concluded that no residual heterozygosity was responsible for pawedness differences. Although selective breeding experiments have not been carried out in monkeys and chimpanzees, the proportion having sinistral tendencies does not deviate significantly from 0.50 (FINCH 1941; ETTLINGER 1964), again indicating lack of genetic determination. Comparisons of the behavior of animals with experimental brain lesions to that of people suffering from similar brain damage led HÉCAEN and ASSAL (1968) to decide that these experiments emphasized an essential difference between animals and humans: the existence in the latter of cerebral dominance. HÉCAEN (1969) also reached the conclusion that "lateral preference in animals may not be considered as homologous with manual preference in man." We are currently preparing a critique of the recent theoretical paper by COLLINS (1970) in which he suggests that there is no support for the hypothesis that human handedness is under partial or complete genetic control (NAGYLAKI and LEVY 1972).

We believe that the most reasonable inference is that hemispheric differentiation was correlated with the development of language in the Hominid family. The adaptive advantage of functional lateralization in an animal with language was discussed in earlier work (LEVY 1969; 1970).

In spite of the assurance by CHAMBERLAIN (1928) that "there are too many variables in a problem of this kind for the human mind to cope with," we hope that our model is not completely devoid of validity.

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