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CHAPTER 6

The genetics of handedness, cerebral dominance and lateralization

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'The fact that left-handedness 'runs in families' has . . . attracted the attention of many observers, yet the people imagine the condition to depend entirely upon training or imitation. There is thus much of guesswork concerning the true nature of the condition'.

Ramaley (1913), p. 730.

Defining the phenotype

Handedness is deceptively simple and deceptively complex to define. At first sight there seems little problem, 90% of the population readily replying 'Right-handed' to a simple question such as 'Are

asymmetry causing a preference for the more skilful hand). A recent study of children with autism, who show population level asymmetries for hand preference but not for skill asymmetry, suggests that preference may be prior to skill asymmetry (McMa-

you right- or left-handed?'. However more sophisticated studies, dating back to Humphrey

noted that the reliability of preference is usually

responds to the everyday notion of handedness: dividuals in the same column. Properly the data

however degree of handedness is also important as should be reported according to the number of left-

it contains a substantial amount of the variance in a handed siblings present in sibships of size 1, 2, 3

TABLE 1b

Handedness in families as given in Table 1a, except data are broken down by approximate year of birth of propositi

Parental handedness		Offspring		
Father	Mother	Sons	Daughters	Total
(1880 – 1939)				
Right	Right	6.0%	5.1%	6.1%
Left	Left	35.1% (37)	33.3% (21)	40.9% (66)
(1940 – 1954)				
Right	Right	10.9% (16,028)	8.2% (13,721)	9.6% (33,153)
Right	Left	22.6%	21.8%	

mother. This question is discussed further below. There is also a suggestion in Table 1a of an interaction whereby the children of L × R matings have a higher prevalence of left-handedness in sons rather than daughters, but that the effect is almost absent in R × L matings. Table 1b, which subdivides the propositi according to their date of birth, suggests that the interaction is unstable, and probably there-

TABLE 3

Frequency of different handedness combinations in monozygotic and like-sexed dizygotic twins

Handedness	Monozygotic	Dizygotic
R-R	2184	1951
R-L	629	585
L-L	87	53

other twin was therefore used as evidence for mono-

can be distinguished from the transmission of en-

zygosity, meaning that the classification of handed-

vironment by means of adoption studies. Surpris-

dedness. A meta-analysis by Seddon and McManus (1990) of the prevalence of left-handedness in 100 populations involving 284,665 subjects found an overall prevalence of 7.78%, a value very close to that found by Coren and Porac (1977) who reported that 7.4% of 1180 works of art produced during the past five millenia portrayed unimanual hand usage with the left hand. The prevalence is however somewhat lower than the 10.8% observed in the 25 stu-

(NCES), in which parents reported the handedness of their children (see McManus and Crow, 1990). The effect is not readily explained by possible secular trends, which are typically suggested as topping out in recent decades (Levy, 1976), whereas the parent-offspring differences continue to be found in very recent data. Furthermore, as Ashton (1982) points out, if the effect is merely the result of secular trends—and if the effect has been present for a cen-

[redacted]

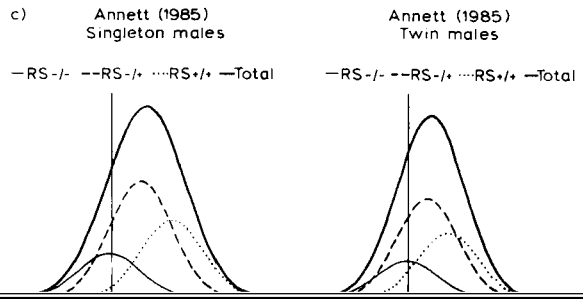
genes are essentially left-right agnosic, that is, they cannot code for asymmetries in any direct fashion, Morgan and Corballis argued that

> "genes do not, perhaps cannot, encode the direction of a structural asymmetry. Rather, genetic factors may serve to 'buffer' an organism against asymmetrical nongenetic influences, or conversely, to permit some nongenetic asymmetry to be expressed. Thus genetic variation may influence the degree but not the direction of asymmetry":

phic (mirror-image) objects except by comparison with some other enantiomorphic reference object. Since genes are inherently unidimensional, being linear strings of base-pairs, they cannot code mirror-symmetric information within their structure, so that enantiomorphs may only be distinguished in comparison with an asymmetric reference — a cellular 'signpost' as it has been called (McManus and Mascie-Taylor, 1979). An extension of the principle is that since genes cannot code asymmetry within

under genetic control, and fluctuates randomly which in its homozygous form *(iv/iv)* exactly half of

discordance is to be expected (in just the same way that if a pair of MZ twins each tossed a coin we would also expect discordance in the outcomes).



Annett's 1978 model

Annett (1978) published a genetic model of handedness which was radically different from the earlier model published in 1964. Its development is described in Annett (1985a). In her 1978 mono-

will be right-hemisphere dominant for language. Since 9.27% of a group of dysphasic patients showed right hemisphere language the frequency of the RS−/− genotype must therefore be 0.1854, and hence the frequency of the RS− gene must be

advantage which would explain the balanced polymorphism of handedness.

The Annett (1983) model underwent a further change in Annett (1985a) in which it is proposed (see Fig. 2c) that the right shift is different in males and

in pure directional asymmetry so that 100% are right-handed and none left-handed. These alleles, as

TABLE 4a

Summary of McManus' (1985a) genetic model of handedness

Genotype	% Left-	% Right

ducing mirror-image phenotypes.

McManus model was a better fit to the data unless one allowed the Annett model to use parameters which seem implausible.

Phenotypics and the differences between the Annett and McManus genetic models

The seeming irrelevance of phenotypics often makes straightforward in that it reflects the commonsense view of right and left-handedness as being two discrete categories, corresponding to the definiton of direction of handedness given earlier. Although right- and left-handers differ, there are no measurable differences in skill asymmetry between a right-hander with a DD genotype and a right-hander with a DC or with a CC genotype. Differences in degree

metric bimodal' model of skill differences (McManus, 1985b). The differences between such models can readily be tested by fitting them to the peg-moving data of Annett and Kilshaw (1983), or to handedness data from the National Child Development Study. McManus (1985b) has carried this out

in Table 1a); and left-handed offspring are expected to be 1.062 times more common in the offspring of R × L than in L × R matings, compared with the figure of 1.393 × for the actual data of Table 1a.

Sex differences in the McManus model might be incorporated (as suggested by McManus 1985a, p.

clear evidence that the Annett model provides a less good account of the data. In reply Annett (1985b) has suggested that the right-shift distribution is not

handedness in the heterozygotes, the only part of the model not specified *a priori*. Different phenotypic expression in male and female heterozygotes (as

(a) Annett (1985a): the right shift is 2.4 and 2.0 for RS + / + , 1.2 and 1.0 for RS + / − and 0 and 0 for RS − / − in females and males respectively, and the frequency of the RS − allele is 0.4306. (b) A modified McManus (1985a) model: the proportions of left-handedness in the DC genotype are 21.48% for females and 28.52% for males, and the frequency of the C allele is 0.155. (c) The modified McManus (1985a) model with a sex-linked modifier gene, as specified in Table 4b. Calculations are shown separately for an overall prevalence

more male left-handers will be genotypically DD but with the normal phenotype masked by the modifier gene), and hence their offspring are more likely to be left-handed. Table 5c shows that the maternal effect

dedness in twins (Springer and Searleman, 1978) is too small for formal genetic analysis.

Genetic models of cerebral dominance are therefore restricted to explaining the association of

McManus models, R × L matings producing 1.179 times more matings than L × R matings, a figure rather more compatible with the effect found in Table 1a, accounting for 46% of it, compared with 4% for the McManus model with differential he-

duals, and cannot be regarded strictly as genetic qua genetic tests of the models in the absence of meiosis or recombination.

McManus' model for the association of handedness and cerebral dominance is straightforward.

writing and tapping better with their left hand but are better with their right hand at carrying out other tasks, such as throwing, a dissociation which is rare in right-handers. If the different skills are controlled by separate cortical centres, both typically in the left hemisphere, then it can be predicted that 71% of

the single genotype to the two lateralised phenotypes.

Familial sinistrality as a predictor of atypical cerebral dominance

belief that FS divides the left-handed population into those who are 'naturally' left-handed and those who are 'pathologically' left-handed (see Harris and Carlson, 1988; p. 311).

From the above it should be clear that we do not believe that information about familial sinistrality is likely to be important in defining new subgroups. Our conclusions are drawn from what we see as the best genetic models presently available, and future models may change this picture. We do not intend

cally independent (McManus and Mascie-Taylor, 1979). Unlike handedness, there is evidence for strong geographical variation, with a strong cline across Europe and Asia, suggesting the possibility of genetic control coupled with random genetic drift (as occurs over the same range for the blood groups; Cavalli-Sforza and Bodmer, 1971; pp. 564 – 571). Genetic factors are directly implicated since left-hand clasping runs in families, albeit weakly. Genetic modelling suggests that for most populations the data are fitted adequately by two alleles

cross one particular leg over the other. Blau (1946) suggests that 66% of the population puts the right leg over the left. There are few studies of leg-crossing, although the unpublished data of Michael Reiss (Dresden) suggest both that it is independent

possible that it is another independent asymmetry akin to hand-clasping and arm-folding.

Eye-dominance

Eye-dominance takes several forms, labelled acuity dominance, motor dominance, and sighting dominance by Porac and Coren (1976). Only sighting

Handedness in animals

Handedness (or more properly, pawedness, clawedness or footedness) has been studied in a number of species, and reviewed by Annett (1967) and Walker

although individual animals show right- or left-handedness, there is no evidence for a population bias, 50% of individuals being right-handed and 50% being left-handed (as would be expected if handedness were due to fluctuating asymmetry). It is controversial whether monkeys might show a systematic population bias in handedness (see

has principally considered the genetics of the *direction* of handedness (except in so far as the Annett models consider degree of hand preference). Given the phenotypic model proposed earlier, of a bimodal distribution allowing variation in direction and degree of handedness, then *degree* of handedness might also be inherited. Few studies have examined the question, and there is some conflict with the animal studies.

ing a potpourri of weak right-handers, weak left-handers and strong left-handers.

The inheritance of degree of handedness is apparently different in animals and in humans. Collins (1985) has assessed the inheritance of degree of paw preference in mice by a selective breeding program. Animals with strong pawedness, defined as either 0 – 2 or 48 – 50 right paw entries (RPE) out of 50, or weak pawedness (10 – 40 RPEs out of 50) were selec-

Degree of handedness has been studied suprising-

tively bred for twelve generations. There was consis-

maintain the stability of the two alleles. It is a basic result in population genetics that if two alleles are

maintained by mutation since its prevalence in the gene pool is very high. Given the apparently cons

Finding the gene for left-handedness

atypical lateralisation) may be resolved if the

autosomal location for the handedness gene can be tested by studying handedness within families, classified by sex of parents and offspring. McManus and Crow (1990) have calculated the expected effect size given McManus' genetic model of handedness

alisation

Handedness and cerebral dominance are fixed fairly early in life, probably early in neural development. How the genes manifest and where may be assessed using in situ hybridisation to examine gene expres-

homologous genes, quite probably those for hand-clasping, arm folding and eye dominance, may be identified, and their evolutionary inter-relationships and nonhuman precursors identified.

Conclusions

The family, twin and genetic evidence cited in this review suggests that the direction of human handedness is under genetic control. Degree of hand preference may also show components which are heritable. The only successful genetic models of handedness take account of the biological constraints due to the process of fluctuating asymmetry. The model [illegible]

supported by a Killam Research Fellowship from Canada Council. The authors thank Susan Gaspé and Paul Brown at the University of Waterloo for their assistance in compiling the tables and the bibliography.

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