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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'.

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 (McManus, Murray, Donaldson, 1992). Finally, the 111

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

noted that the reliability of preference is usually higher than for measures of skill.

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

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

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

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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 monozygosity, which can be distinguished from the transmission of en-

vironment by means of adoption studies. Surpris-

zygosity, meaning that the classification of handed-

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 con-

we do not know the order in which they will be [redacted] controversial topic, in part because its definition is not

here, and hence cannot explain such effects. An in [redacted] clear, and in part because there have been few direct

1. The following table shows the results of a survey of 100 people who were asked to rate their level of agreement with the statement "I am a good person".

Agree



Disagree

1. The following table shows the results of a survey of 100 people who were asked to rate their level of agreement with the statement "I am a good person".

genes are essentially left-right agnostic, that is, they can code for enantiomorphic (mirror-image) objects except by comparison

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

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

‘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”:

comparison with an asymmetric reference — a cellular ‘signpost’ as it has been called (McManus and Mascie-Taylor, 1979). An extension of the principle

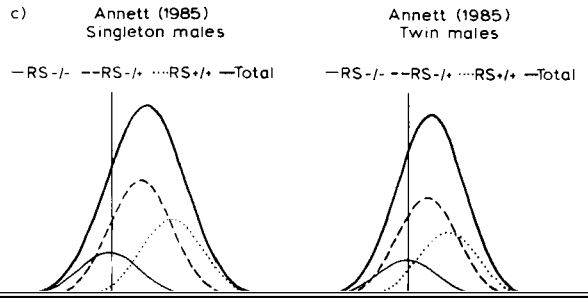
is that since genes cannot code asymmetry within

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

producing mirror-image phenotypes.

Genotype

% Left

% Right

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 $R \times L$ than in $L \times R$ matings, compared with the figure of $1.393 \times$ 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 handedness and language dominance within indivi-

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 heterozygotes and 16% for the Annett model. Formal

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. The model of handedness argues that the preferred

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

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

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 (1980). Annett (1967) studied rhesus monkeys, and

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

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 selected

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
chromosome was identified in the

from the mother Crow's hypothesis of a pseudo

(2) The ontogeny of handedness and cerebral

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 etc. pseudo-autosomal location, and have suggested

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

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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

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