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Handedness project: reviewing McManus 1985

Contents

[Abstract 2](#_Toc145605743)

[Introduction 3](#_Toc145605744)

[The Model 4](#_Toc145605745)

[Assumptions 4](#_Toc145605746)

[Requirements 4](#_Toc145605747)

[Parameters 4](#_Toc145605748)

[The data 6](#_Toc145605749)

[Familial data 6](#_Toc145605750)

[Twin data 9](#_Toc145605751)

[Correction to the prediction given the datasets 10](#_Toc145605752)

[Statistical analysis 11](#_Toc145605753)

[Results 11](#_Toc145605754)

[Discussion 14](#_Toc145605755)

[APPENDIX 1: CORRECTION MATRICES 17](#_Toc145605756)

[Correcting families with multiple children 18](#_Toc145605757)

[Correcting for twins 18](#_Toc145605758)

[APPENDIX 2: PROBABILITIES AND LIKELIHOOD FUNCTIONS 19](#_Toc145605759)

[Likelihood functions 21](#_Toc145605760)

[APPENDIX 3: RESEULTS OF THE MODEL C' 22](#_Toc145605761)

[Statistical analysis 22](#_Toc145605762)

[Prediction of the model 25](#_Toc145605763)

[Bibliography 26](#_Toc145605853)

**Table of tables**

[Table 1. Mating data from table 2 in McManus 1985 6](#_Toc146266594)

[Table 2. Mating data from table 3 in McManus 1985 8](#_Toc146266595)

[Table 3. Observations taken from table 5 in McManus 1985 9](#_Toc146266596)

[Table 4. Comparison of maximum likelihood fits of the present model, and the model of Mcmanus 12](#_Toc146266597)

[Table 5. results of fitting model C' over table 1 22](#_Toc146266598)

[Table 6. results of fitting the model over the data of table 3 23](#_Toc146266599)

[Table 7. results of fiting table 2 to model C' 24](#_Toc146266600)

[Table 8. The expected percentage for sibships of 1-5 families 25](#_Toc146266601)

[Table 9. The expected proportions of twin pairs by parental handedness and twin type 25](#_Toc146266602)

[Equation 1. The frequency of allele C in the population 19](#_Toc145611532)

[Equation 2. probabilities of progeny expressing left-handedness given parents handedness 19](#_Toc145611533)

[Equation 3. probability function of twins expressing phenotypes 20](#_Toc145611534)

[Equation 4. likelihood function for triplets 21](#_Toc145611535)

[Equation 5. likelihood function for families with multiple offspring 21](#_Toc145611536)

[Equation 6. likelihood function for twins 21](#_Toc145611537)

Abstract

This project presents a meticulous replication and critical evaluation of McManus' 1985 genetic model of handedness. McManus' model, which postulates a single gene with two alleles as the determinant of handedness, serves as a foundational framework for understanding the genetic foundations of this phenomenon. Through our replication efforts, we successfully obtained parameters closely mirroring McManus' original findings, while also rectifying reporting errors in the original statistical values, enhancing the model accessibility and applicability. Our revised model met McManus' established criteria for a genetic model of handedness, fostering continued exploration into the genetic foundations of handedness while reducing complexities and barriers in its utilization.

## Introduction

Handedness, most commonly defined as the preferred hand used in one-handed tasks [(Porac 2016)](https://sciwheel.com/work/citation?ids=15365161&pre=&suf=&sa=0&dbf=0), has intrigued researchers for decades [(McManus 2019)](https://sciwheel.com/work/citation?ids=14962387&pre=&suf=&sa=0&dbf=0). The majority of the human population exhibits right-handedness, a phenomenon evident not only in modern society but also in artistic representations spanning millennia [(Coren and Porac 1977)](https://sciwheel.com/work/citation?ids=10047819&pre=&suf=&sa=0&dbf=0). Moreover, archaeological discoveries provide evidence that this bias towards right-handedness has been a longstanding trait within human societies, with indications dating back to the era of Neanderthals.[(Conard 2011)](https://sciwheel.com/work/citation?ids=15365201&pre=&suf=&sa=0&dbf=0) This consistent occurrence of right-handedness across various historical periods and even in our ancient ancestors strongly hints at the genetic keystones of handedness, reinforcing the hypothesis that genetics play a significant role in determining an individual's preferred hand.

In the 1970s, Marian Annet introduced the "right shift theory" [(Annett 1972).](https://sciwheel.com/work/citation?ids=6366514&pre=&suf=&sa=0&dbf=0) as a novel genetic model for understanding handedness. Unlike earlier models suggesting a single gene with two alleles dictating handedness, with the recessive allele corresponding to left-handedness, Annet's model incorporated an element of chance into handedness determination. Her model proposed the existence of a genetic mechanism that shifts the distribution of handedness within the human population toward the right. Individuals inheriting the gene for right-shift are likely to present right-handedness, while for those without this gene, handedness is determined by chance, with an equal probability for both right- and left handedness. Building on Annet's framework, McManus proposed a similar genetic model[(McManus 1985)](https://sciwheel.com/work/citation?ids=15020506&pre=&suf=&sa=0&dbf=0), although with slight variations. McManus' model also used the element of chance in handedness determination but suggested that genes directly control hand preference rather than influencing brain lateralization, as Annet had hypothesized. To this day, researchers continue to engage in debates over the precise mechanisms governing handedness determination, and McManus' model remains one of the leading theories in this field.

In this project, we revisited McManus' genetic model of handedness using present-day computational tools to reaffirm the model's validity and to critically examine its underlying parameters. In the upcoming sections, we will describe the specifics of McManus' model, explaining its requirements and parameters. Then, we will examine the datasets used to construct the model, as well as the correction method applied to ensure the integrity of our analysis. Finally, we will describe the approach to estimating the model parameters through maximum likelihood estimation and test the goodness of fit of the model to the available data.

## The Model

In 1985, McManus introduced a genetic model of handedness, suggesting that a single gene with two alleles, D and C, controls handedness. When allele D is homozygous, it leads to a 100% occurrence of right-handed individuals, while allele C, when homozygous, results in a 50% chance of either handedness. The primary goal of this model is to calculate the expected proportion of left-handers among heterozygotes, denoted as p(L│DC), and determine the frequency of allele C within the population.

|  |  |  |
| --- | --- | --- |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

### Assumptions

The model operates under several assumptions. First, that there is no assortative mating, indicating that individuals do not exhibit a preference for selecting mates based on the presented phenotype of handedness. Second, the genes control the phenotypes of twins similarly to the way they control singletons. Third, each individual is either left-handed or right-handed, thus resulting in bimodal distribution, Fourth, the cause to difference in the observed sinistrality rates across generations and studies is due to fluctuations in the threshold or criteria for determining left-handedness. Fifth, the model assumes uniform allele frequencies throughout all studies.

### Requirements

McManus demanded his model to answer number of requirements:

1. Familial Pattern in Handedness: The model must account for the observed familial pattern in handedness. This pattern indicates that left-handers make up approximately 10% of the children of two right-handed parents, 20-25% of the children of one right-and one left-handed parent, and approximately 40% of the children of two left-handed parents.
2. Twins' discordance rate**:** The model must account for the literature that indicates a high proportion of monozygotic twin pairs that display discordant handedness, with one being left-handed and the other right-handed.
3. Different incidence of handedness: The model must incorporate the observed differences in the prevalence of left-handedness among different populations and generations.
4. Compatibility with other biological asymmetries: The model should align with the known inheritance patterns of other biological asymmetries, such as *situs inversus* (the inverted position of chest and abdominal organs), hand-clasping*,* and arm folding.
5. Biologically convincing: A genetic model can be applied to any dataset, provided that the dataset includes a diverse set of genetic variations (alleles) at different genetic loci and considers the varying penetrance of these alleles on the trait.

### Parameters

The model estimates the values of two parameters describing the population:

1. : This parameter represents the true rate of left-handers in the population. As indicated by the third requirement of the model, the observed proportion of left handers varies across studies and generations. Therefore, it is necessary to determine the true incidence of left-handers in order to accurately account for this variability. It is assumed that the true incidence of left-handers in the population is constant across all the datasets used in fitting the model.
2. This parameter refers to the phenotype of heterozygotes. Identifying this phenotype is essential for characterizing the allele frequencies within the population and understanding the genetic system that governs handedness.

## The data

In fitting his model and to obtain estimates for the model parameters, McManus used two types of datasets: one describing familial data, including parental phenotypes and the phenotypes of the progeny resulting from such matings, and another presenting twin data. The twin dataset displayed observed numbers of twin pairs, both MZ and DZ, presenting the possible phenotypes of handedness (L×L, R×L, R×R).

### Familial data

The familial data is presented in two tables in McManus' article: the first table presents triplets (child and his parents), and the second table presents families with multiple children (siblings and their parents).The first table summarizes data about measured handedness from twelve distinct studies, that d escribing the incidence of left-handedness in the progeny resulting from different types of matings (L×L, R×L, R×R) used to fit the model. These studies contained families, demonstrating an average sinistrality of in progeny and sinistrality in parents. Specifically, the average sinistrality measured in children of both right-handed parents is , while it was in children of one right-handed and one left-handed parents, and for children of two left-handed parents. These statistics align with the first requirement of the model. The observed numbers of offspring with each phenotype (right- or left-handed) given the phenotypes of the parents, as described in McManus 1985 is presented in Table 1.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| study |  |  |  | |  | |  | | (df=1) |
| R | L | R | L | R | L |
| Ramaley (1913) | 0.1556 | 0.0809 | 841 | 115 | 113 | 54 | 1 | 7 | 18.897\*\*\* |
| *822.76* | *133.24* | *126.96* | *40.04* | *5.28* | *2.72* |
| Chamberlain (1928) | 0.0477 | 0.0333 | 6917 | 308 | 411 | 53 | 18 | 7 | 1.709 |
| *6912.7* | *312.3* | *412.74* | *51.26* | *20.56* | *4.44* |
| Rife (1940) | 0.0877 | 0.0450 | 1842 | 151 | 140 | 34 | 5 | 6 | 3.142 |
| *1837.84* | *155.16* | *141.42* | *32.58* | *7.74* | *3.26* |
| Merrell (1975) | 0.2363 | 0.1540 | 140 | 34 | 33 | 20 | 8 | 2 | 4.333\* |
| *135.44* | *38.56* | *38.73* | *24.27* | *6.83* | *3.17* |
| Annett (1973) | 0.1063 | 0.0407 | 6206 | 669 | 471 | 125 | 5 | 1 | 0.77 |
| *6203.64* | *671.36* | *474.23* | *121.77* | *4.13* | *1.87* |
| Ferronato et al. (1974) | 0.0976 | 0.0976 | 154 | 11 | 31 | 9 | 0 | 0 | 1.253 |
| *151.77* | *13.23* | *33.23* | *6.77* |
| Mascie-Taylor (unpub) | 0.0831 | 0.0930 | 232 | 17 | 41 | 7 | 3 | 1 | 0.109 |
| *232.71* | *16.29* | *40.31* | *7.69* | *2.98* | *1.02* |
| Chaurasia & Groswani(unpub) | 0.1407 | 0.0660 | 1060 | 144 | 122 | 46 | 3 | 4 | 3.745 |
| *1051.36* | *152.64* | *129.00* | *39.00* | *4.64* | *2.36* |
| Annett (1978) | 0.0850 | 0.0545 | 1656 | 130 | 170 | 40 | 4 | 0 | 2.855 |
| *1655.76* | *130.24* | *171.42* | *38.58* | *2.82* | *1.18* |
| Carter-Saltzmann (1980) | 0.1300 | 0.0750 | 303 | 37 | 45 | 15 | 0 | 0 | 0.36 |
| *301.29* | *38.71* | *46.71* | *13.29* |
| Coren & Porac (1980) | 0.1842 | 0.0800 | 315 | 68 | 57 | 16 | 0 | 0 | 1.093 |
| *318.46* | *64.54* | *53.54* | *19.46* |
| McGee & Cozad (1980) | 0.2415 | 0.1825 | 848 | 211 | 325 | 150 | 30 | 22 | 13.487\*\*\* |
| *318.46* | *64.54* | *53.54* | *19.46* | *318.46* | *64.54* |
| The numbers in italic are fitted values. | | | | | | | | | |

Table 1. The results of 12 studies of the frequency of right- and left-handed progeny from R×R, R×L and L×L matings (mating data from table 2 in McManus 1985)

The second table presents the results from two surveys conducted by McManus among students at the University of Cambridge. These students were asked to provide information regarding their own handedness, their siblings' handedness, as well as their parents' and grandparents' handedness.  
The first survey (referred as ICM1) was conducted in May 1977 and was administered to undergraduate students. Handedness was classified based on the hand used for writing, except for those who wrote using their right hand due to being forced to switch from writing using their left hand. Such cases were classified as left-handers.  
The second survey (referred as ICM2) took place in June and was given to graduates on the eve of the graduation ceremony. The classification of handedness in this questionnaire was similar to the first survey. From these questionnaire, three datasets were obtained: one for students and their siblings, considering their parents' handedness, and two datasets for the parents' and their siblings' handedness given the grandparents' handedness, with distinction between paternal and maternal family. The data from both surveys are presented in table 2.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Family size |  | | | | | |  | | | | | |  | | | | | |  |
| 0 | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 |
| ICM1 | 0.1518 | 0.1005 | 1 | 58 | 9 |  |  |  |  | 14 | 5 |  |  |  |  | 0 | 0 |  |  |  |  | 40.16  df = 44 |
| *57.92* | *9.08* |  |  |  |  | *14.88* | *4.12* |  |  |  |  |  |  |  |  |  |  |
| 2 | 211 | 57 | 3 |  |  |  | 35 | 16 | 5 |  |  |  | 0 | 0 | 1 |  |  |  |
| *204.02* | *60.52* | *6.47* |  |  |  | *34.73* | *18.27* | *3.00* |  |  |  | *0.50* | *0.40* | *0.10* |  |  |  |
| 3 | 123 | 63 | 6 | 0 |  |  | 22 | 24 | 6 | 1 |  |  | 2 | 1 | 1 | 0 |  |  |
| *126.69* | *53.56* | *10.75* | *1.00* |  |  | *26.29* | *19.75* | *6.18* | *0.78* |  |  | *1.45* | *1.66* | *0.76* | *0.13* |  |  |
| 4 | 70 | 39 | 6 | 1 | 0 |  | 8 | 8 | 7 | 1 | 0 |  | 0 | 0 | 1 | 0 | 0 |  |
| *67.47* | *36.29* | *10.29* | *1.80* | *0.15* |  | *9.61* | *9.18* | *4.12* | *0.99* | *0.11* |  | *0.27* | *0.38* | *0.25* | *0.08* | *0.01* |  |
| 5 | 9 | 12 | 6 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| *14.94* | *9.62* | *3.44* | *0.85* | *0.14* | *0.01* | *0.65* | *0.74* | *0.43* | *0.15* | *0.03* | *0.00* | *0.20* | *0.34* | *0.28* | *0.14* | *0.04* | *0* |
| ICM2 (propositi) | 0.134 | 0.101 | 1 | 134 | 15 |  |  |  |  | 17 | 9 |  |  |  |  | 1 | 0 |  |  |  |  | 37.67  df = 27 |
| *131.52* | *17.48* |  |  |  |  | *20.81* | *5.19* |  |  |  |  | *0.72* | *0.28* |  |  |  |  |
| 2 | 91 | 22 | 2 |  |  |  | 19 | 3 | 3 |  |  |  | 0 | 0 | 0 |  |  |  |
| *90.26* | *22.50* | *2.24* |  |  |  | *16.18* | *7.64* | *1.17* |  |  |  |  |  |  |
| 3 | 22 | 7 | 0 | 2 |  |  | 6 | 11 | 3 | 0 |  |  | 0 | 0 | 0 | 0 |  |  |
| *21.77* | *7.67* | *1.43* | *0.13* |  |  | *10.58* | *7.10* | *2.07* | *0.25* |  |  |  |  |
| 4 | 10 | 5 | 0 | 0 | 0 |  | 3 | 1 | 0 | 0 | 0 |  | 1 | 0 | 0 | 0 | 0 |  |
| *9.48* | *4.21* | *1.10* | *0.19* | *0.02* |  | *1.74* | *1.48* | *0.62* | *0.14* | *0.01* |  | *0.29* | *0.39* | *0.24* | *0.08* | *0.01* |  |
| 5 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *2.29* | *1.21* | *0.40* | *0.09* | *0.01* | *0* |
| ICM2 maternal | 0.0893 | 0.0609 | 1 | 74 | 4 |  |  |  |  | 6 | 2 |  |  |  |  | 0 | 0 |  |  |  |  | 47.58\*  df = 28 |
| *72.09* | *5.91* |  |  |  |  | *6.51* | *1.49* |  |  |  |  |  |  |  |  |
| 2 | 107 | 18 | 3 |  |  |  | 11 | 3 | 0 |  |  |  | 2 | 0 | 0 |  |  |  |
| *110.20* | *16.21* | *1.60* |  |  |  | *9.33* | *4.10* | *0.56* |  |  |  | *0.99* | *0.82* | *0.19* |  |  |  |
| 3 | 81 | 16 | 4 | 0 |  |  | 16 | 1 | 0 | 2 |  |  | 0 | 0 | 0 | 0 |  |  |
| *81.56* | *16.18* | *3.00* | *0.26* |  |  | *10.46* | *6.63* | *1.72* | *0.19* |  |  |  |  |
| 4 | 31 | 10 | 1 | 0 | 0 |  | 0 | 0 | 0 | 2 | 0 |  | 0 | 0 | 0 | 0 | 0 |  |
| *32.01* | *7.64* | *2.00* | *0.33* | *0.03* |  | *0.91* | *0.75* | *0.28* | *0.06* | *0.01* |  |  |
| 5 | 19 | 7 | 1 | 1 | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *20.24* | *5.46* | *1.80* | *0.42* | *0.06* | *0.00* | *1.91* | *1.89* | *0.89* | *0.26* | *0.05* | *0.00* |
| ICM2 paternal | 0.091 | 0.047 | 1 | 86 | 4 |  |  |  |  | 8 | 1 |  |  |  |  | 0 | 0 |  |  |  |  |
| *82.77* | *7.23* |  |  |  |  | *7.29* | *1.71* |  |  |  |  |  |  |  |  |
| 2 | 100 | 27 | 0 |  |  |  | 7 | 5 | 0 |  |  |  | 0 | 1 | 0 |  |  |  | 28.5  df = 34 |
| *108.31* | *16.97* | *1.71* |  |  |  | *7.95* | *3.55* | *0.50* |  |  |  | *0.50* | *0.41* | *0.09* |  |  |  |
| 3 | 65 | 11 | 2 | 0 |  |  | 4 | 3 | 2 | 0 |  |  | 0 | 1 | 0 | 0 |  |  |
| *62.14* | *13.15* | *2.49* | *0.22* |  |  | *4.91* | *3.16* | *0.84* | *0.09* |  |  | *0.35* | *0.43* | *0.19* | *0.03* |  |  |
| 4 | 39 | 11 | 2 | 0 | 0 |  | 2 | 1 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |  |
| *38.95* | *9.92* | *2.65* | *0.45* | *0.04* |  | *1.35* | *1.12* | *0.42* | *0.09* | *0.01* |  |
| 5 | 13 | 9 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *16.29* | *4.70* | *1.58* | *0.38* | *0.06* | *0.00* | *0.38* | *0.38* | *0.18* | *0.05* | *0.01* | *0* |
| The numbers in italic are fitted values. | | | | | | | | | | | | | | | | | | | | | | |

Table 2. The numbers of families with particular numbers of left-handed children by family size and parental handedness for 4 separate data sets(mating data from table 3 in McManus 1985)

### Twin data

The data about twin phenotypes in McManus' paper presented in a single table, distinguishing between MZ and DZ twins and showing the observed number of twins matching each phenotype, without considering parental phenotypes. This data was collected from thirteen different twin studies, containing a total of 1908 couples of MZ twins with a sinistrality rate of and a discordance rate of . Additionally, the data include couples of DZ twins with a sinistrality rate of and a discordance rate of . This data is consistent with the second requirement of the model. observed data from these studies is presented in Table 3.

Table 3. The observed numbers of R-R, R-L and L-L pairs of MZ and DZ twins from 13 differant studies (observations taken from table 5 in McManus 1985)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| study | MZ twins | | | | | DZ twins | | | | |
|  |  |  |  | df=1 |  |  |  |  | df=1 |
| Wilson & Jones (1932) | 0.1071 | 56 | 13 | 1 | 0.769 | 0.1138 | 97 | 24 | 2 | 0.166 |
| *56.88* | *11.24* | *1.88* | *97.52* | *22.95* | *2.52* |
| Stocks (1933) | 0.0952 | 35 | 6 | 1 | 0.003 | 0.1064 | 76 | 16 | 2 | 0.037 |
| *35.04* | *5.92* | *1.04* | *75.79* | *16.43* | *1.79* |
| Newman et al. (1937) | 0.19 | 34 | 13 | 3 | 0.223 | 0.1100 | 39 | 11 | 0 | 2.399 |
| *33.44* | *14.13* | *2.44* | *39.99* | *9.03* | *0.99* |
| Bouterwek (1938) | 0.1885 | 80 | 38 | 4 | 1.122 | 0.1714 | 23 | 12 | 0 | 3.203 |
| *81.88* | *34.24* | *5.88* | *24.26* | *9.48* | *1.26* |
| Rife (1940) | 0.1188 | 176 | 41 | 6 | 0.061 | 0.1541 | 104 | 39 | 3 | 0.804 |
| *176.48* | *40.04* | *6.48* | *105.47* | *36.06* | *4.47* |
| Thyss (1946) | 0.1845 | 72 | 24 | 7 | 1.634 | 0.1628 | 60 | 24 | 2 | 0.43 |
| *69.82* | *28.35* | *4.82* | *60.86* | *22.28* | *2.86* |
| Rife (1950) | 0.1283 | 261 | 76 | 6 | 3.749 | 0.1161 | 164 | 45 | 2 | 2.281 |
| *265.66* | *66.68* | *10.66* | *166.43* | *40.14* | *4.43* |
| Dechaume (1957) | 0.2424 | 19 | 12 | 2 | 0.079 | 0.1970 | 21 | 11 | 1 | 0.281 |
| *19.30* | *11.39* | *2.30* | *21.49* | *10.03* | *1.49* |
| Zazzo (1960) | 0.1332 | 199 | 51 | 9 | 0.087 | 0.1090 | 264 | 69 | 2 | 5.72\*\* |
| *198.34* | *52.32* | *8.34* | *268.54* | *59.93* | *6.54* |
| Carter-Saltzmann et al. (1976) | 0.1711 | 132 | 46 | 9 | 0.235 | 0.1932 | 115 | 54 | 7 | 0.098 |
| *130.95* | *48.10* | *7.95* | *115.67* | *52.66* | *7.67* |
| Loehlin & Nichols (1976) | 0.1411 | 380 | 123 | 11 | 4.402\* | 0.1111 | 261 | 70 | 2 | 5.917\*\* |
| *386.52* | *109.96* | *17.52* | *265.64* | *60.72* | *6.64* |
| Springer & Searleman (1978) | 0.1667 | 53 | 19 | 3 | 0.004 | 0.1596 | 35 | 9 | 3 | 1.997 |
| *53.09* | *18.83* | *3.09* | *33.52* | *11.97* | *1.52* |
| NCDS (unpublished) | 0.1512 | 32 | 9 | 2 | 0.184 | 0.1477 | 66 | 18 | 4 | 1.182 |
| *31.58* | *9.84* | *1.58* | *64.54* | *20.93* | *2.54* |
| The numbers in italic are fitted values. | | | | | | | | | | |

## Correction to the prediction given the datasets

Evident from the tables is the variation in sinistrality rates across different studies and generations. McManus suggested that the disparities in study outcomes might have been due to different criteria used to measure handedness. Therefore, when making predictions based on model parameters and the frequency of left-handedness in the population, there is a need to adjust the predictions for the criterion shift in each dataset. McManus outlined the approach for applying these corrections within datasets featuring triplets, using the matrices P, Q, and T.

Matrices P and Q serve as transition matrices, operating on the progenies and the parents, respectively. P is a matrix whose entries characterize the probabilities that progeny measured as right- or left-handed is truly a right- or left-handed. On the other hand, Q is a matrix encapsulating the probabilities that specific phenotypes observed in mating ( being true phenotypes (.   
Matrix T compiles the predicted probabilities associated with offspring displaying specific phenotypes based on the parental phenotypes. This matrix is crafted in accordance with the Mendelian system and the model assumptions regarding the phenotype-genotype system.

By utilizing these three matrices, we derive the corrected matrix M, where its elements represent the predicted probabilities of offspring manifesting as right- or left-handed being born to matings classified as .

In alignment with McManus' matrix construction methodology for triplet data, we have extended a parallel correction approach to datasets involving families with multiple children and those involving twins. The comprehensive mathematical derivations underlying the matrix construction are explained upon in the appendix section (appendix 1).

Fitting the model

To acquire the optimal parameters estimates of and , and to evaluate the model's alignment with observed data, we utilized a maximum a maximum likelihood estimation method. The fitting process involved multiple steps: initially, we selected a pair of parameter values. These values were then applied along with the measured rate of left-handedness in each dataset to compute the corrected predicted distribution for the dataset. Subsequently, the log-likelihood score was calculated using the data in the datasets with the corrected predictions for handedness in each dataset. The method was executed in two phases.

In the first phase, various combinations of within the range of with increments of , and within the range with increments of , were examined to find the pair with maximal likelihood. This analysis provided an approximation to the functions' maximum point.

In the second phase, the point obtained in the previous phase served as the initial input for quasi-Newton method (L-BFGS-B), enabling the determination of the coordinates at which the likelihood function reaches its peak.

To evaluate how well the obtained parameters and model fitting align with each dataset, as well as with the data as a whole, we used Wilks' likelihood ratio test. The test statistic was calculated by measuring the difference between the level of support indicated by the model and the theoretical level of support expected from a 'perfect fit' of the model to the data, scaled by a factor of 2. This statistic is treated as the statistic.

## Statistical analysis

Upon applying the maximum likelihood estimation across all the datasets McManus found maximum support with a log-likelihood score of for the estimates and (referred to as Model A). For these data he calculated that 'perfect fit' will result in support of . The statistical test, indicated a lack of adequate fit to the data. Therefore, McManus concluded that the model was not suitable.

He suggested that this outcome might be attributed to the susceptibility of maximum likelihood methods to be influenced by outlier data points. McManus proceeded to fit the model to each dataset individually, using parameter values of and , which aligns with McManus' model C. Through this analysis, he identified four datasets of triplets that stood out as outliers: the datasets of Chaurasia & Goswami, Ramaley, Merrell, and McGee & Cozad. After excluding these datasets, McManus found maximum support of , for the estimators , and . The statistic calculated by him indicated an adequate fit to the model, and this reduced model referred as model B.

Using a similar approach to identify outlier datasets, we found in agreement with McManus that the datasets of Chaurasia & Goswami, Ramaley, and McGee & Cozad were outliers. Additionally, we identified the dataset of Loehlin & Nichols, which feature twins, as an outlier. Consequently, we designated the model obtained after excluding these datasets as Model D.

## Results

In our analysis of the complete dataset from tables 1, 2, and 3, which is analogous to Model A as proposed by McManus, we obtained a maximum likelihood score of -11443.219. This result aligns with parameter values of and . In a hypothetical scenario where a 'perfect fit' to the entire dataset would be achieved, the score would be . these outcomes resulted in of and degrees of freedom, corresponding to p-value of . Therefore, as suggested by McManus, the model fails to adequately explain the data presented in the tables.

For the data analogous to the data used in McManus' model B, we found maximum likelihood of for the estimates of and . Despite the small difference in the maximum likelihood and between the estimates compared to the results reported by McManus, we calculated a corresponding to a p-value of . Which led to the conclusion that the model obtained is still not adequate.

Therefore, using the parameters declared by McManus ( and ) we attempted to identify outlier datasets. Upon examining each table, we found that for table 1,  
, resulting in highly significant p-value. It appeared to us that the lack of fit is attributed to three datasets out of the four identified by McManus: Ramaley, Merrell, McGee & Cozad, each with significance level of less than . After removing these datasets, we obtained , correspondung to p-value of .

In Table 2, which presents the family data collected by McManus, a dataset with significant p-value (ICM2 maternal) was present. However, the overall value received for the data was implying adequate fit to the table.

For the twins datasets in table 3, the overall value received was indicating that the model fits well. However, upon further examination of the table, we noticed that while the monozygotic twins datasets fit well with the model ( 8), the results for the dizygotic datasets resulted in , corresponding to p-value of . This outcome seems to stem from the dataset of Loehlin & Nichols. This dataset exhibited significant values of for both MZ and DZ twins ( respectively) and an overall score of (). After removing this dataset, a score of 26.748 was obtained for the entire table, and the values obtained for both MZ and DZ twins separately indicated adequate fit.

The maximum likelihood found for model D is for and . This likelihood value is 0.853 units higher than the likelihood calculated for the parameters derived from the entire dataset, indicating that the exclusion of the outlier datasets did not significantly shift the estimates. Furthermore, when compared, the parameters of model D and the parameters from McManus' model C showed difference of only 1.222 support units. This finding suggests that both models demonstrate comparable data-fitting abilities, implying their near equivalence. A comparison of the models' goodness of fit is presented in Table 4, and Figure 1.

Table 4. Comparison of maximum likelihood fits of the present model, and the model of Mcmanus

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Data | | df | Maximum support |  |  |  | Support Difference from McManus |
| Fitted total data | Perfect fit (McManus calculations) |  |  | - | - | - | - |
| McManus' model A |  |  |  |  |  | - |
| Perfect fit (our calculations) |  |  | - | - | - | - |
| Our model A |  |  |  |  |  | -3.222 |
| Fitted reduced data (McManus) | Perfect fit (McManus calculations) |  |  | - | - | - | - |
| McManus' model B |  |  |  |  |  | - |
| Perfect fit (our calculations) |  |  | - | - | - | - |
| Our model B |  |  |  |  |  | -0.765 |
| Fitted reduced data (ours) | Perfect fit (our calculations) |  |  | - | - | - | - |
| Our model D |  |  |  | 0.067 |  | - |

A close-up of a person's face

Description automatically generated

Five points (A, B, C, D, C') represent the model parameters of each of the five models. Contours represent the difference in support units from the maximum likelihood found.  
left – likelihood calculated for the complete datasets (i.e., model A)  
middle - likelihood calculated for the reduced datasets (i.e., model B)   
right – likelihood calculated for the reduced datasets (i.e., model D)

Figure 1.A contour map of the goodness-of-fit of the models

## Discussion

Up to this point, we've described the steps to reconstruct McManus' 1985 genetic model of handedness. In this section, we will address several questions to measure our success in replicating the model and illuminate new insights regarding the model and its parameters revealed through our work.

Our success in this attempt was determined by two crucial factors: the ability to obtain similar model parameters through maximum likelihood estimation and the resemblance of our statistical test results with the fit between the model and the observed data.

With respect to the acquired parameters, it's worth highlighting that the parameters obtained through our research, along with the log-likelihood support calculated for these values, show no significant differences compared to those determined by McManus in 1985. It is probable that any discrepancies that appear can be attributed to the enhanced precision inherent in the present computational methods we used, which enhanced the accuracy of our calculations.

Concerning the statistical tests, when comparing the statistics computed for each dataset independently, we identified only two datasets displaying significant differences between our calculations and those reported by McManus. First, in the case of the observations of triplets from Merrell 1975, our calculations yielded , while McManus reported . Upon examination of the fitted values provided by McManus, it became evident that an error had occurred in the report, and according to our calculations the result that should have been reported is , which is very similar to our calculation.  
Secondly, in the ICM2 maternal family dataset (Table 2), McManus declared a result of , whereas our computation yielded. Subsequent analysis of McManus' fitted values for this dataset revealed a result in close proximity to our own, . Given the corrections we identified, particularly with respect to the statistics reported by McManus, it is reasonable to infer that the overall fitness of the model should align closely with what we have uncovered in our replication efforts. Therefore, we can confidently conclude that we have successfully replicated the model.

In light of the modifications we made to McManus' statistical analysis results, two significant questions have arisen. Firstly, we need to evaluate whether all the datasets removed in model B should have been excluded. Secondly, we must consider whether the parameters chosen are appropriate to describe the model.

Regarding the first question, which concerns the removal of datasets in model B, it is essential to reevaluate whether all the datasets that were removed should have been excluded. While we acknowledge that removing outlier datasets is a valid method to reassess the model's fitness, we strongly disagree with the decision to remove the dataset of Merrell. As demonstrated earlier, this dataset was mistakenly classified as an outlier, and our examination of the data revealed that it aligns with the model. Thus, its removal is inappropriate and unjustified, as there is no compelling reason to exclude it.

Furthermore, we believe that the datasets chosen for removal in our model D provide a more appropriate correction. Model D not only addresses the issue of outliers and overall fit of the model but also accounts for the problematic fit of the dizygotic twins datasets to the model. This approach ensures more balanced and accurate representation of the data, without excluding datasets that appear to align with the model.

Facing the second question, and building on the conclusion from the previous question, we can now examine whether the estimators to the parameters selected for the model by McManus (Model C) are appropriate to describe the model. Upon comparing the support calculated for the parameters of model C both when using the complete dataset and the reduced dataset, we found that while the estimation of is very much appropriate, while for the estimation of we found the values of more ideal (referred as model ).

While both estimations of show a rather similar fit to the datasets when analyzing each dataset alone, and have only a difference of support units between the likelihood, we argue that the new estimation is more faithful to the results of models A and D. This is because the new value of lies between the estimations found in both models. Additionally, while the p-value for the overall fit of the estimates suggested by McManus remains below 0.05 when calculated for the complete dataset and the two reduced datasets, the new estimation of yields p-value of for the data used to obtain model D, reinforcing the validity of the new estimation.

Since we proposed different estimations to the models' parameters from the ones proposed by McManus, it is essential to demonstrate that we still meet the five requirements for a genetic model of handedness outlined by McManus. Considering the first, the second, and the third requirements, as indicated by the results of the statistical analysis presented in Appendix 3, the model fits well with the literature.   
Regarding the fourth requirement, we consider it rather irrelevant. Since 1985, our understanding of the mechanisms that control these phenomena has evolved, rendering the insistence on complying with this requirement somewhat missing the original intent it was meant to achieve.  
The fifth requirement is satisfied by the datasets and McManus' description of the general model. Hence, the adjustment of the parameters has resulted in a practical model, tables 8 and 9 in Appendix 3 display the anticipated distribution of handedness within families for this model.

Finally, we need to address the weaknesses of the model and consider its future implications, continuing the research to enhance its performance and applicability. In addition to the issues raised by McManus in the original paper, we have identified a few more deficiencies. First, as illustrated in figure 1, there is a range of values for the true incidence of left handedness which yields similar fitness between the model and the data, whether we analyze each dataset separately, each table individually, or the fitness of the entire dataset. This phenomenon may be attributed to the assumption of uniform distribution of the alleles between all the studies used. Since as presented in equation 1, there is a connection between the allele frequencies, the true incidence of left-handers and the anticipated proportion of left-handers among heterozygotes.

Second, the model relies on data collected almost half a century ago. Since then, social and demographic changes may have influenced the prevalence of left-handedness. Therefore, it might be worth in the future to revalidate the model using present day data in order to maintain its relevance.

Third, in the time since the publication of the original model in 1985, there have been other models presented that succeeded in fitting more of the datasets that have been used than this model. It may be worth comparing our model with these alternative models using additional datasets that represent diverse populations and generations. Such a comparative analysis can provide valuable insights into the mechanisms determining handedness and help us refine our understanding of handedness.

In conclusion, our replication of McManus' 1985 genetic model of handedness has been successful, with parameters closely matching the original model and corrections made to reported statistical values. However, we must acknowledge its weaknesses and the need for future research to enhance its performance and relevance. The model continues to be a valuable tool for understanding handedness, but ongoing updates and refinements are necessary to keep it aligned with modern knowledge and demographic changes.

## APPENDIX 1: CORRECTION MATRICES

In this appendix, we outline the correction matrices used to adjust the predictions of the model to the datasets. Between the datasets involving triplets, families with multiple children, and twins the correction method stays similar, although slight changes are made with the matrices.  
  
Correcting triplets datasets

For datasets presenting triplets we used the correction matrices as devised by McManus:

P is the transition matrix for the progeny, and it is created using two parameters: t (the true incidence of left-handedness in the population) and p (the observed frequency of left-handedness in the progeny, calculated from the dataset). In creating this matrix, its assumed by McManus that either some left-handers been misclassified as right handers (resulting in ), or that some right-handers been misclassified as left handers (resulting in , but not both. Therefore, the probabilities can be defined as follows:

Q is the transition matrix for the parents, created using two parameters: t (the true incidence of left-handedness in the population) and q (the observed frequency of left-handedness in the parents, calculated from the dataset). Also, the same assumptions about misclassifying handedness as in the creation of P been used. Therefore, Q can be defined as:

Matrix T compiles the anticipated probabilities of offspring displaying specific phenotypes based on the parental phenotypes, following the Mendelian system and the model assumptions regarding the phenotype-genotype system. Detailed calculations are provided in Appendix 2.

Matrix M represents the expected frequencies of children manifesting specific phenotypes, based on the observed parental phenotypes. It is calculated as

### Correcting families with multiple children

For datasets featuring families with multiple children, the matrices P and T are adapted to account for scenarios with N children within a family.

For matrix P, originally presented the chances of progeny's handedness being measured as given their true handedness is , a similar approach applied for multiple offspring. In this scenario, P should represent the chances of the handedness of N progenies being measured given their true handedness is . misclassifications occur either as some of the left-handers being misclassified as right-handers or some right-handers being misclassified as left-handers, but not both, the probabilities can be formulated as follows:

The probabilities for each progeny calculated as in P:

In matrix T, the column corresponds to the probabilities of having progenies expressing left-handedness, resulting from the mating of parents with true phenotypes and and producingoffspring. These probabilities are computed using the model parameters, and the comprehensive calculations are provided in Appendix 2.

Similar to the approach used for triplets, we can employ the transition matrices to transform matrix T into matrix M. In matrix M, the column illustrates the anticipated frequencies of having progenies measured as left-handers, based on the observed parental phenotypes.

### Correcting for twins

For datasets involving twins, we use a single transition matrix P, as parental phenotypes are not available.

P is calculated similarly to the case of families with 2 children .  
Matrix T is computed differently for monozygotic twins and dizygotic twins, with detailed calculations presented in Appendix 2.  
Matrix M, presenting the expected probabilities for encountering twins of phenotype can be received by multiplying T by P.

## APPENDIX 2: PROBABILITIES AND LIKELIHOOD FUNCTIONS

The model proposed by McManus assumes that the genes responsible for determining handedness follow the Mendelian laws of heredity. Under this assumption, along with McManus's suggested probabilities for handedness in homozygote, we were able to create probability functions for the familial data, MZ twins, and DZ twins.

Allele C frequency:  
To determine the frequency of allele C in the population, we utilized the model parameters . This This determination is based on the expression of the frequency of left-handedness:

Given the genetic system involves only alleles C and D, we deduce , resulting in:

Adding the constraints we receive:

ifand else.

Equation 1. The frequency of allele C in the population

Probabilities of handedness in progeny:

Using Mendel's laws of heredity, we can determine the chances of the resulting offspring from the mating of two genotypes (G1×G2) having each of the genotypes DD, DC, and CC. By using these probabilities, we can find the probabilities of the offspring the present each phenotype:

Subsequently, through the application of the binomial distribution, we can derive the probabilities of progenies within a family of N exhibiting left- handedness:

Thus, given the phenotypes of two parents, the probability of them having n out of N offspring who manifest left-handedness is calculated by:

Equation 2. probabilities of progeny expressing left-handedness given parents handedness

Probabilities of handedness in twins:

In twin data analysis, parental phenotypes are unknown. Dizygotic twins, unlike monozygotic twins, can have different genotypes similar to two non-twin siblings. Given the parents genotypes the probabilities of having twin couple is:

For monozygotic twins, since both twins share the same genotype, Given the parents genotypes the probabilities of having twin couple is:

Therefore, the probability of having twins with phenotypes given the parental phenotypes is:

Thus, the probability of having twin couple with phenotypes is:

Equation 3. probability function of twins expressing phenotypes

### Likelihood functions

To find the best estimates for and , a maximum likelihood estimation approach was used over the datasets in Tables 1,2,3. The probabilities used in the likelihood function obtained from applying correction matrices on the datasets, resulting in different likelihood function for each dataset. Multiplying all the likelihood functions together, the likelihood function of the model was obtained. These functions were also later used for the statistical test.

In Table 1, which presents triplets datasets, using Equation 2 yields the following function for each presented dataset:

Equation 4. likelihood function for triplets

Where represents the observed number of progenies expressing phenotype (right if , left if ) resulting from mating .

In Table 2, which presents families with multiple offspring, using Equation 2 for each dataset yields the following function:

Equation 5. likelihood function for families with multiple offspring

Where represents the observed number of families of size with left-handed progenies resulting from mating .

For table 5, likelihood functions were applied separately for DZ and MZ twins, using the matching probabilities from Equation 3:

Equation 6. likelihood function for twins

Where is the observed number of twins couples where one presents phenotype and the other presents phenotype .

## APPENDIX 3: RESEULTS OF THE MODEL C'

As previously discussed, McManus' Model C has exhibited inadequate fit to the overall dataset. Consequently, we propose revising the estimated incidence of left-handers to 7.25%. In this section, we present the results of our statistical analysis of the model and provide anticipated proportions of left-handers in the population.

### Statistical analysis

We conducted statistical analysis of the model across three different variations of the datasets. Our aim was to determine how well Model C' aligns with models derived through maximum likelihood estimation.

When evaluating the fit of Model C' to the entire dataset, we obtained a support log-likelihood of . This result only support units different from the result calculated for model A, with a matching and p-value of *.*Assessing the model fit to McManus reduced dataset, we found a support log-likelihood of , differing by support units from the result obtained for model B. The corresponding , yielding a p-value of .  
For our reduced dataset. Model C' produced a support log-likelihood of , with a difference of support units from the result calculated for model D. matching and p-value of and Therefore, fitting the data.

Upon examining the fitness of model to each table, we observed results similar to the results of McManus' model C in terms of fitness. For table 1, presenting triplets we calculated a matching p-value of . With failure to fit the same datasets as model C. Details of the fitting results are presented in Table .

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| study |  |  |  | |  | |  | | (df=1) |
| R | L | R | L | R | L |
| Ramaley (1913) | 0.1556 | 0.0809 | 841 | 115 | 113 | 54 | 1 | 7 | 20.528\*\* |
| *821.77* | *134.23* | *127.85* | *39.15* | *5.37* | *2.63* |
| Chamberlain (1928) | 0.0477 | 0.0333 | 6917 | 308 | 411 | 53 | 18 | 7 | 1.255 |
| *6915.35* | *309.65* | *410.36* | *53.64* | *20.29* | *4.71* |
| Rife (1940) | 0.0877 | 0.0450 | 1842 | 151 | 140 | 34 | 5 | 6 | 3.088 |
| *1837.97* | *155.03* | *141.31* | *32.69* | *7.72* | *3.28* |
| Merrell (1975) | 0.2363 | 0.1540 | 140 | 34 | 33 | 20 | 8 | 2 | 4.453\* |
| *135.28* | *38.72* | *38.84* | *14.16* | *6.88* | *3.12* |
| Annett (1973) | 0.1063 | 0.0407 | 6206 | 669 | 471 | 125 | 5 | 1 | 0.755 |
| *6204.02* | *670.98* | *473.86* | *122.14* | *4.13* | *1.87* |
| Ferronato et al. (1974) | 0.0976 | 0.0976 | 154 | 11 | 31 | 9 | 0 | 0 | 1.475 |
| *151.58* | *13.42* | *33.42* | *6.58* |
| Mascie-Taylor (unpub) | 0.0831 | 0.0930 | 232 | 17 | 41 | 7 | 3 | 1 | 0.046 |
| *232.43* | *16.57* | *40.54* | *7.46* | *3.02* | *0.98* |
| Chaurasia & Groswani(unpub) | 0.1407 | 0.0660 | 1060 | 144 | 122 | 46 | 3 | 4 | 3.668 |
| *1051.47* | *152.53* | *128.91* | *39.09* | *4.63* | *2.37* |
| Annett (1978) | 0.0850 | 0.0545 | 1656 | 130 | 170 | 40 | 4 | 0 | 2.858 |
| *1655.90* | *130.10* | *171.28* | *38.72* | *2.82* | *1.18* |
| Carter-Saltzmann (1980) | 0.1300 | 0.0750 | 303 | 37 | 45 | 15 | 0 | 0 | 0.434 |
| *301.13* | *38.87* | *46.87* | *13.13* |
| Coren & Porac (1980) | 0.1842 | 0.0800 | 315 | 68 | 57 | 16 | 0 | 0 | 0.871 |
| *318.08* | *64.92* | *53.92* | *19.08* |
| McGee & Cozad (1980) | 0.2415 | 0.1825 | 848 | 211 | 325 | 150 | 30 | 22 | 14.433\*\* |
| *817.73* | *241.27* | *349.01* | *125.99* | *36.26* | *15.74* |

Table 5. results of fitting model C' over table 1

The numbers in italic are fitted values for

For table 3, with a p-value of , model indicated better fit than model C. In the case of MZ twins, we calculated and all the datasets were found to fit within the model. For DZ twins, we received, with the same datasets showing poor fit as model C, although less significantly. These results show that model is better fit to the data of twins. Results Details are presented in table .

Table 6. results of fitting the model over the data of table 3

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| study | MZ twins | | | | | DZ twins | | | | |
|  |  |  |  | df=1 |  |  |  |  | df=1 |
| Wilson & Jones (1932) | 0.1071 | 56 | 13 | 1 | 0.664 | 0.1138 | 97 | 24 | 2 | 0.132 |
| *56.81* | *11.38* | *1.81* | *97.46* | *23.07* | *2.46* |
| Stocks (1933) | 0.0952 | 35 | 6 | 1 | 0 | 0.1064 | 76 | 16 | 2 | 0.055 |
| *35* | *6* | *1* | *75.74* | *16.52* | *1.74* |
| Newman et al. (1937) | 0.19 | 34 | 13 | 3 | 0.258 | 0.1100 | 39 | 11 | 0 | 2.328 |
| *33.40* | *14.21* | *2.40* | *39.96* | *9.08* | *0.96* |
| Bouterwek (1938) | 0.1885 | 80 | 38 | 4 | 1.014 | 0.1714 | 23 | 12 | 0 | 3.157 |
| *81.78* | *34.43* | *5.78* | *24.24* | *9.51* | *1.24* |
| Rife (1940) | 0.1188 | 176 | 41 | 6 | 0.019 | 0.1541 | 104 | 39 | 3 | 0.74 |
| *176.27* | *40.46* | *6.27* | *105.41* | *36.18* | *4.41* |
| Thyss (1946) | 0.1845 | 72 | 24 | 7 | 1.77 | 0.1628 | 60 | 24 | 2 | 0.396 |
| *69.74* | *28.52* | *4.74* | *60.82* | *22.36* | *2.82* |
| Rife (1950) | 0.1283 | 261 | 76 | 6 | 3.294 | 0.1161 | 164 | 45 | 2 | 2.121 |
| *265.34* | *67.32* | *10.34* | *166.33* | *40.34* | *4.33* |
| Dechaume (1957) | 0.2424 | 19 | 12 | 2 | 0.067 | 0.1970 | 21 | 11 | 1 | 0.267 |
| *19.28* | *11.44* | *2.28* | *21.47* | *10.06* | *1.47* |
| Zazzo (1960) | 0.1332 | 199 | 51 | 9 | 0.162 | 0.1090 | 264 | 69 | 2 | 5.393\* |
| *198.10* | *52.80* | *8.10* | *268.37* | *60.25* | *6.37* |
| Carter-Saltzmann et al. (1976) | 0.1711 | 132 | 46 | 9 | 0.313 | 0.1932 | 115 | 54 | 7 | 0.078 |
| *130.79* | *48.42* | *7.79* | *115.60* | *52.80* | *7.60* |
| Loehlin & Nichols (1976) | 0.1411 | 380 | 123 | 11 | 3.837 | 0.1111 | 261 | 70 | 2 | 5.591\* |
| *386.06* | *110.88* | *17.06* | *265.48* | *61.04* | *6.48* |
| Springer & Searleman (1978) | 0.1667 | 53 | 19 | 3 | 0 | 0.1596 | 35 | 9 | 3 | 2.06 |
| *53.02* | *18.96* | *3.02* | *33.50* | *12.01* | *1.50* |
| NCDS (unpublished) | 0.1512 | 32 | 9 | 2 | 0.22 | 0.1477 | 66 | 18 | 4 | 1.252 |
| *31.54* | *9.92* | *1.54* | *64.50* | *21.01* | *2.50* |
| The numbers in italic are fitted values. | | | | | | | | | | |

Regarding the data of table 2, our calculations revealed , indicating a similar ability of Model C' to fit the data as Model C. For model the data of ICM2 maternal family showed inadequate fit, similarly to all the other models. See table for details on fitting table 2 to the model.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Family size |  | | | | | |  | | | | | |  | | | | | |  |
| 0 | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 | 0 | 1 | 2 | 3 | 4 | 5 |
| ICM1 | 0.1518 | 0.1005 | 1 | 58 | 9 |  |  |  |  | 14 | 5 |  |  |  |  | 0 | 0 |  |  |  |  | 40.31  df = 44 |
| *57.9* | *9.1* |  |  |  |  | *15.0* | *4.0* |  |  |  |  |  |  |  |  |  |  |
| 2 | 211 | 57 | 3 |  |  |  | 35 | 16 | 5 |  |  |  | 0 | 0 | 1 |  |  |  |
| *203.4* | *61.1* | *6.4* |  |  |  | *35.1* | *18.0* | *2.9* |  |  |  | *0.5* | *0.4* | *0.1* |  |  |  |
| 3 | 123 | 63 | 6 | 0 |  |  | 22 | 24 | 6 | 1 |  |  | 2 | 1 | 1 | 0 |  |  |
| *126.1* | *54.2* | *10.8* | *1.0* |  |  | *26.7* | *19.5* | *6.0* | *0.7* |  |  | *1.5* | *1.6* | *0.7* | *0.1* |  |  |
| 4 | 70 | 39 | 6 | 1 | 0 |  | 8 | 8 | 7 | 1 | 0 |  | 0 | 0 | 1 | 0 | 0 |  |
| *67.0* | *36.8* | *10.3* | *1.8* | *0.1* |  | *9.8* | *9.1* | *4.0* | *1.0* | *0.1* |  | *0.3* | *0.4* | *0.2* | *0.1* | *0.0* |  |
| 5 | 9 | 12 | 6 | 2 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| *14.8* | *9.8* | *3.5* | *0.8* | *0.1* | *0.0* | *0.7* | *0.7* | *0.4* | *0.1* | *0.0* | *0.0* | *0.2* | *0.3* | *0.3* | *0.1* | *0.0* | *0.0* |
| ICM2 (propositi) | 0.134 | 0.101 | 1 | 134 | 15 |  |  |  |  | 17 | 9 |  |  |  |  | 1 | 0 |  |  |  |  | 37.072  df = 27 |
| *131.4* | *17.6* |  |  |  |  | *20.9* | *5.1* |  |  |  |  | *0.7* | *0.3* |  |  |  |  |
| 2 | 91 | 22 | 2 |  |  |  | 19 | 3 | 3 |  |  |  | 0 | 0 | 0 |  |  |  |
| *90.0* | *22.8* | *2.2* |  |  |  | *16.4* | *7.5* | *1.1* |  |  |  |  |  |  |
| 3 | 22 | 7 | 0 | 2 |  |  | 6 | 11 | 3 | 0 |  |  | 0 | 0 | 0 | 0 |  |  |
| *21.7* | *7.8* | *1.4* | *0.1* |  |  | *10.7* | *7.0* | *2.0* | *0.2* |  |  |  |  |
| 4 | 10 | 5 | 0 | 0 | 0 |  | 3 | 1 | 0 | 0 | 0 |  | 1 | 0 | 0 | 0 | 0 |  |
| *9.4* | *4.3* | *1.1* | *0.2* | *0.0* |  | *1.8* | *1.5* | *0.6* | *0.1* | *0.0* |  | *0.3* | *0.4* | *0.2* | *0.1* | *0.0* |  |
| 5 | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *2.3* | *1.2* | *0.4* | *0.1* | *0.0* | *0.0* |
| ICM2 maternal | 0.0893 | 0.0609 | 1 | 74 | 4 |  |  |  |  | 6 | 2 |  |  |  |  | 0 | 0 |  |  |  |  | 47.687\*  df = 28 |
| *72.1* | *5.9* |  |  |  |  | *6.5* | *1.5* |  |  |  |  |  |  |  |  |
| 2 | 107 | 18 | 3 |  |  |  | 11 | 3 | 0 |  |  |  | 2 | 0 | 0 |  |  |  |
| *110.1* | *16.3* | *1.5* |  |  |  | *9.3* | *4.1* | *0.6* |  |  |  | *1.0* | *0.8* | *0.2* |  |  |  |
| 3 | 81 | 16 | 4 | 0 |  |  | 16 | 1 | 0 | 2 |  |  | 0 | 0 | 0 | 0 |  |  |
| *81.4* | *16.4* | *2.9* | *0.2* |  |  | *10.4* | *6.7* | *1.7* | *0.2* |  |  |  |  |
| 4 | 31 | 10 | 1 | 0 | 0 |  | 0 | 0 | 0 | 2 | 0 |  | 0 | 0 | 0 | 0 | 0 |  |
| *31.9* | *7.8* | *1.9* | *0.3* | *0.0* |  | *0.9* | *0.8* | *0.3* | *0.1* | *0.0* |  |  |
| 5 | 19 | 7 | 1 | 1 | 0 | 0 | 3 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20.1 | 5.7 | 1.7 | 0.4 | 0.1 | 0.0 | 1.9 | 1.9 | 0.9 | 0.3 | 0.0 | 0.0 |
| ICM2 paternal | 0.091 | 0.047 | 1 | 86 | 4 |  |  |  |  | 8 | 1 |  |  |  |  | 0 | 0 |  |  |  |  |
| *82.8* | *7.2* |  |  |  |  | *7.3* | *1.7* |  |  |  |  |  |  |  |  |
| 2 | 100 | 27 | 0 |  |  |  | 7 | 5 | 0 |  |  |  | 0 | 1 | 0 |  |  |  | 27.674  df = 34 |
| *108.3* | *17.1* | *1.6* |  |  |  | *7.9* | *3.6* | *0.5* |  |  |  | *0.5* | *0.4* | *0.1* |  |  |  |
| 3 | 65 | 11 | 2 | 0 |  |  | 4 | 3 | 2 | 0 |  |  | 0 | 1 | 0 | 0 |  |  |
| *62.0* | *13.3* | *2.4* | *0.2* |  |  | *4.9* | *3.2* | *0.8* | *0.1* |  |  | *0.4* | *0.4* | *0.2* | *0.0* |  |  |
| 4 | 39 | 11 | 2 | 0 | 0 |  | 2 | 1 | 0 | 0 | 0 |  | 0 | 0 | 0 | 0 | 0 |  |
| *38.8* | *10.2* | *2.6* | *0.4* | *0.0* |  | *1.3* | *1.1* | *0.4* | *0.1* | *0.0* |  |
| 5 | 13 | 9 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *16.2* | *4.8* | *1.5* | *0.4* | *0.1* | *0.0* | *0.4* | *0.4* | *0.2* | *0.1* | *0.0* | *0.0* |
| The numbers in italic are fitted values. | | | | | | | | | | | | | | | | | | | | | | |

Table 7. results of fiting table 2 to model C'

### Prediction of the model

Using the estimated values for and , we can calculate the expected rates of handedness in the population. For the parameter values of Model C', we determined that allele C frequency in the population is 14.5%. Refer to table 8 for the anticipated proportions of left-handers in children from families of size 1-5, according to parental handedness. Table 9 provides similar results for MZ and DZ twins.

Table 8. The expected percentage for sibships of 1-5 families with particular numbers ofleft-handed children by the handedness of the parents

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| family size | parents' phenotype | number of left handers | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 |
| 1 |  | 94.421 | 5.579 |  |  |  |  |
|  | 82.898 | 17.102 |  |  |  |  |
|  | 71.375 | 28.625 |  |  |  |  |
| 2 |  | 89.766 | 9.311 | 0.924 |  |  |  |
|  | 69.221 | 27.355 | 3.425 |  |  |  |
|  | 51.331 | 40.087 | 8.581 |  |  |  |
| 3 |  | 85.856 | 11.728 | 2.238 | 0.178 |  |  |
|  | 58.165 | 33.166 | 7.865 | 0.803 |  |  |
|  | 37.156 | 42.525 | 17.606 | 2.713 |  |  |
| 4 |  | 82.555 | 13.206 | 3.648 | 0.551 | 0.04 |  |
|  | 49.144 | 36.086 | 12.203 | 2.352 | 0.215 |  |
|  | 27.045 | 40.446 | 24.381 | 7.221 | 0.907 |  |
| 5 |  | 79.753 | 14.008 | 4.999 | 1.081 | 0.149 | 0.01 |
|  | 41.719 | 37.123 | 15.969 | 4.369 | 0.756 | 0.064 |
|  | 19.778 | 36.335 | 28.445 | 12.19 | 2.932 | 0.321 |

Table 9. The expected proportions of twin pairs of type R-R, R-L and L,-L by parental handedness and twin type

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| parents' phenotype | MZ | | | DZ | | |
|  |  |  |  |  |  |
|  | 90.392 | 8.057 | 1.55 | 89.77 | 9.311 | 0.924 |
|  | 70.87 | 24.056 | 5.074 | 69.22 | 27.36 | 3.425 |
|  | 54.003 | 34.744 | 11.253 | 51.33 | 40.09 | 8.581 |
|  | 87.575 | 10.349 | 2.075 | 86.8 | 11.9 | 1.3 |

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