A Modern Reanalysis of McManus' Genetic Model of Handedness

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October 12, 2025

Abstract

We replicate and critically evaluate McManus' (1985) single-locus genetic model of handedness, which remains influential in laterality research. Using the original familial and twin datasets, we reproduce McManus' parameter estimates while correcting reporting errors and miscalculations. Our reproduction confirms that the model is reproducible but reveals sensitivity to dataset inconsistencies and outliers. We extend the framework by generalizing correction matrices, implementing simulations, and applying bootstrap methods to estimate confidence intervals. We further analyze a modern dataset from Flores and Adonara, Indonesia, providing a test of the model in a different cultural setting and comparing triplet versus multi-offspring representations. Our findings emphasize both the historical value and the current limitations of the Dextral–Chance framework, offering a modern foundation for testing genetic and cultural theories of handedness with contemporary datasets.

Introduction

Handedness, typically defined as the preferred hand used for everyday one-handed tasks (Porac, 2016), is a prominent human asymmetry that has fascinated researchers for over a century (Marcori & Okazaki, 2020; McManus, 2019). A related but distinct aspect is *hand performance*, which refers to measurable differences in efficiency between the two hands (Janßen, 2004). Although the two dimensions are frequently conflated under the umbrella of *handedness*, they are not interchangeable. Most large-scale familial and genetic studies, including those of McManus (1985), have operationalized handedness as hand preference, often measured by the writing hand. This choice of definition is not trivial: variation in whether researchers emphasize preference or performance has contributed to heterogeneity in reported rates of left-handedness across populations and generations (Peters, 1998).

Despite these challenges of definition and measurement, the predominance of right-handedness is an enduring feature of our species. Approximately 90 percent of individuals are right-handed, a figure remarkably consistent across time and space. Archaeological and anthropological evidence demonstrates right-hand bias in skeletal morphology, tool production, and artistic depictions extending back to Neanderthals (Coren & Porac, 1977; Uomini & Ruck, 2018). This persistence across millennia indicates a strong biological foundation, making handedness a key case study in efforts to unravel the interplay of genes, development, and culture in shaping human behavior (Marcori & Okazaki, 2020; McManus, 2019).

The first attempts to explain handedness invoked simple Mendelian inheritance. Early twentieth-century models posited a single recessive allele for left-handedness, predicting that offspring of two left-handed parents would be exclusively left-handed (Annett, 1964; Trankell, 1955; Chamberlain, 1928; Ramaley, 1913). Yet empirical findings contradicted these expectations. Familial data showed that two left-handed parents produced left-handed children only about 20 to 30 percent of the time, while offspring of two right-handed parents were occasionally left-handed. Twin studies posed an even greater challenge: concordance among monozygotic twins was far from 100 percent and only marginally higher than that of dizygotic twins (Pfeifer et al., 2022). These discrepancies revealed that single-gene dominance–recessive accounts could not adequately capture the inheritance of handedness.

To address these inconsistencies, Annett introduced the *right-shift theory* (Annett, 1972, 1975, 1978). Her model proposed that a genetic factor biases brain lateralization toward the right hemisphere, thereby increasing the probability of right-handedness but leaving room for developmental chance. Individuals without this factor, she suggested, had an equal probability of becoming right- or left-handed. By allowing probabilistic outcomes, Annett's model explained both the stability of handedness prevalence in the population and the imperfect concordance observed in twins. Later refinements incorporated heterozygote advantage and adjustments to account for twin-specific effects (Annett, 1994, 1995).

In parallel, McManus introduced a different but related genetic model, the Dextral-Chance (DC) model (McManus, 1985). Unlike Annett's emphasis on cerebral lateralization, McManus proposed that genes directly influence hand preference. In this model, individuals with a homozygous DD genotype are always right-handed, while homozygous CC genotype individuals are equally likely to be right- or left-handed. Heterozygotes (DC) have an intermediate probability of being left-handed, represented as $p(L|DC)$. Using maximum likelihood estimation on large familial and twin datasets, McManus estimated that the true

prevalence of left-handedness is about 7.75 percent, with roughly 25 percent of heterozygotes showing the trait. This model provided a simple genetic explanation that explained several puzzling empirical findings. Notably, McManus also developed correction procedures to address inconsistencies in classification across datasets, noting that prevalence estimates varied depending on whether handedness was assessed by writing, self-report, or behavioral observation. The DC model offered a parsimonious genetic account that has remained influential, serving as a benchmark for subsequent genetic and gene-culture models (Laland et al., 1995; Mariani et al., 2023; McManus et al., 2013).

Nearly four decades later, handedness remains conceptually unresolved. Researchers continue to debate its genetic, epigenetic, and cultural foundation, while McManus' model is still cited as a canonical starting point. Despite its prominence, however, no published study has attempted a strict reproduction of McManus' analysis to test whether the same data yield the same conclusions, nor have systematic evaluations probed the robustness of his findings against outliers or reporting inconsistencies.

Here, we address this gap. We perform the first full reproduction of McManus' (1985) genetic model of handedness, using the original datasets and implementing the analysis with modern computational tools. Our goals are threefold: first, to accurately reproduce McManus' reported parameter estimates and likelihood tests; second, to expand his framework by generalizing the correction matrices, adding simulations, and using bootstrap methods for confidence interval estimation; and third, to assess the stability of the model's conclusions through systematic testing of outlier effects and the log-likelihood surface. Fourth, we extend the model to a contemporary dataset drawn from a cultural context distinct from the one on which the model was originally based, thereby evaluating its applicability beyond the historical studies.

By integrating a reproduction with methodological enhancements, we highlight the strengths and weaknesses of the DC model and provide a clearer, more transparent foundation for future studies on genetic and cultural explanations of handedness.

Methods

Study design

We reproduced the analysis presented by McManus (1985), who proposed a genetic model of handedness and estimated its parameters using maximum likelihood estimation. His approach combined familial and twin datasets, likelihood-ratio tests to evaluate goodness-of-fit, and exclusion of outliers to refine parameter estimates.

In our reproduction, we followed the same overall structure and implemented all analyses in Python, using NumPy (Harris et al., 2020), Matplotlib (Hunter, 2007), SciPy (Virtanen et al., 2020), and Pandas (McKinney, 2010). Source code is available at https://github.com/yoavram-lab/McManus1985.

Genetic Model

McManus' model assumes a single locus with two alleles: D (dextral) and C (chance). The mapping of genotypes to phenotypes is shown in Table 1. Homozygous DD individuals are always right-handed, CC homozygotes are right- or left-handed with equal probability, and heterozygotes DC express left-handedness with probability $p(L|DC)$. From the true population

prevalence of left-handedness, $p(L_t)$, in combination with the heterozygote parameter $p(L|DC)$, the allele frequency of C is

$p(C) = 2p(L_t)$, if $p(L|DC) = 0.25$;

$$p(C) = \frac{p(L|DC) - \sqrt{p(L|DC)^2 + (0.5 - 2p(L|DC))p(L_t)}}{2p(L|DC) - 0.5}, \text{ otherwise.}$$

Data

McManus (1985) analyzed three types of datasets: (1) familial data from parents and their children, (2) extended family data including siblings and grandparents, and (3) twin data. The familial datasets reported the handedness of offspring based on the handedness of their parents, while the twin data showed concordance and discordance in handedness between monozygotic (MZ) and dizygotic (DZ) pairs.

The triplet data, summarized in Table 2, relied on twelve independent studies and included over 25,000 children. Offspring were categorized based on their parents' handedness, resulting in three mating groups: R×R, R×L, and L×L. On average, 13.33% of the children were left-handed. When broken down by parental phenotype, clear patterns appeared: 11.29% of children with two right-handed parents were left-handed, compared to 23.67% from mixed-handed couples and 33% from two left-handed parents. Parental handedness rates came from the original studies, with some (Mascie-Taylor, Chaurasia & Goswami, Annett, 1978) directly cited by McManus based on observed frequencies. During our review of the data, we found discrepancies between McManus data and the sources, with some previously noted as typographical errors (Annett, 1996). Since our main goal was to assess the reproducibility of McManus' model, we used his reported data for parameter estimation. For analyses involving the observed incidence of left-handedness, corrected data were used when inconsistencies impacted the results.

The second dataset, shown in Table 3, comes from surveys that McManus carried out in 1977 at the University of Cambridge. These surveys included two groups: ICM1, which involved undergraduates, and ICM2, which surveyed graduate students. Participants provided information about their own handedness as well as that of their siblings, parents, and grandparents. Handedness was mainly determined by which hand they used for writing, except for individuals who had been forced to switch from left to right handedness; these were classified as left-handed. Based on these questionnaires, McManus developed several related datasets: one recording the handedness of students and their siblings based on parental handedness, and two others summarizing parental handedness depending on either maternal or paternal grandparents. These extended family datasets enabled the analysis of transmission patterns beyond nuclear families.

The third dataset summarized handedness in twins without referring to parental phenotype. Data from thirteen studies (Table 4) included 2,064 monozygotic (MZ) pairs and 1,757 dizygotic (DZ) pairs. Among MZ twins, 14.51 percent were left-handed, and the discordance rate was 22.82 percent, while among DZ twins, 13.15 percent were left-handed with a discordance rate of 22.88 percent. These rates, which are notably similar between MZ and DZ twins, challenge simple genetic models that typically predict much higher concordance among MZ twins.

Together, these three types of data, triplets, extended family surveys, and twins, formed the empirical basis for McManus' genetic model. In this study, we reanalyzed all of these datasets in their original form, replicating McManus' protocol while also addressing documented inconsistencies.

In addition to McManus' original datasets, we incorporated a modern dataset collected by Nurhayu et al. (2020)from the islands of Flores and Adonara, Indonesia (Tables 6, and 7). To align it with McManus' framework, we grouped individuals by generation: the first generation included individuals without children and their siblings; the second generation comprised their parents and their siblings; the third generation contained the grandparents of the first generation and their siblings; and so on, yielding five generations overall and four derived datasets. Because the older generations contained too few left-handed individuals to be informative, we restricted analyses to the first two generations. For the same reason, we further limited families to those with six or fewer offspring. These data were then represented in both triplet form (Table 6) and multi-offspring form (Table 7), allowing direct comparison of the two analytic approaches. Importantly, the reproduction of McManus' (1985) results was conducted solely on the original datasets; the Flores–Adonara dataset was analyzed separately to evaluate the model in a different cultural setting and to test the effect of data representation on parameter estimation.

Correction for criterion shifts

A key challenge in handedness research is the variability in the criteria used across studies. Some researchers determine handedness by writing hand, others through self-report questionnaires, and still others by direct behavioral observation, leading to inconsistencies in reported prevalence rates (Janßen, 2004; McGrew & Marchant, 1997; Peters, 1998; Porac, 2016). These discrepancies can cause significant variation in the measured incidence of left-handedness, even within the same population, an effect that McManus (1985) termed criterion shift.

To address this issue, McManus introduced an adjustment procedure that modifies model predictions before they are compared with the data. Let T denote the transmission matrix of true probabilities for offspring handedness given parental phenotypes, as determined by the DC model parameters. The observed data, however, reflect measured rather than true phenotypes. McManus proposed correcting the predictions by applying separate transformation matrices for parents and offspring. The adjusted prediction matrix, M, is given by

$$M = P \cdot T \cdot Q$$

where Q adjusts parental phenotypes, and P adjusts offspring phenotypes. The values in these matrices depend on the relationship between the observed incidence of left-handedness (L_m) and the true incidence implied by the model (L_t). When the measured rate exceeds the true rate of left-handedness, some true right-handers must have been misclassified as left-handed; conversely, when they fall below the true rate, some true left-handers must have been misclassified as right-handed. The proportions of these misclassifications are derived deterministically from the observed and expected incidences.

For twin data, where parental phenotypes are not reported, only the offspring adjustment matrix is applied. In this case, the transformation operates on the frequencies of pairwise concordance and discordance, yielding an adjusted matrix of expected outcomes for monozygotic and

dizygotic pairs. The explicit forms and derivations of matrices P and Q, along with their derivations, are provided in Appendix 1.

Model fitting

The two free parameters of the DC model are the true population rate of left-handedness, $p(L_t)$, and the probability of left-handedness among heterozygotes, $p(L|DC)$. Parameters were estimated by maximum likelihood estimation, following the procedure described by McManus (1985), and using the adjusted transmission matrix to account for criterion shifts. The explicit form of the likelihood function is provided in Appendix 2.

Estimation proceeded in two stages following the procedure described by McManus (1985). First, a grid search was performed across the parameter space, with $p(L_t)$ ranging from 0.02 to 0.2 and $p(L|DC)$ ranging from 0 to 0.5 in increments of 0.0025. The parameter pair that maximized the likelihood in this scan was then used as the starting point for local optimization with a quasi-Newton algorithm, which refined the estimates. Model fit was evaluated using a likelihood-ratio test against a saturated model that exactly reproduces the data, which McManus referred to as a "perfect fit". The test statistic is approximately chi-squared distributed, with degrees of freedom equal to the number of independent data points minus the number of estimated parameters. A p-value greater than 0.05 was interpreted as evidence that the model adequately fits the observed data.

Identifiability diagnostics

To quantify parameter precision and identifiability, we estimated the Hessian of the log-likelihood at the maximum-likelihood estimate (MLE). Instead of calculating the second derivatives of the entire model analytically, which involves complex transformations through the T, P, and Q matrices, we approximated curvature numerically by fitting a local quadratic to the likelihood surface. Specifically, we chose a 5×5 grid of parameter values around the MLE (i.e., a block of 25 points spanning two steps in each direction on the parameter grid) and fitted a quadratic function to the corresponding log-likelihood values. This local fit captures the surface's curvature near the optimum while reducing grid-level noise. From the quadratic fit, we extracted the second derivatives with respect to $p(L_t)$ and $p(L|DC)$ to compute the Fisher Information matrix (FIM). By inverting the FIM, we derived Hessian-based standard errors (SEs) and parameter correlations. We also report the eigenvalues and condition number of the FIM as indicators of identifiability: large condition numbers suggest a ridge-like likelihood surface and practical non-identifiability, meaning SEs should be interpreted cautiously (Raue et al., 2009).

Simulations

To further evaluate McManus' model, we created synthetic population data under controlled conditions. These simulations helped us evaluate how accurately the estimation process retrieved known parameter values and tested the method's robustness across different scenarios. Synthetic datasets were created using specified values of the two model parameters, $p(Lt)$ and $p(L|DC)$. For the familial data, the number of families was drawn from a uniform distribution $U(100, 2200)$, and the number of offspring per family was sampled according to the empirical distribution from Table 3, as $1 + Bin(4, 0.354)$. Parental mating types were sampled from a binomial distribution with a success probability equal to the true incidence of left-handedness,

$p(L_t)$. Given the mating type, the number of left-handed offspring was then drawn from a multinomial distribution based on the probabilities specified by the model.

To simulate differences in handedness classification across studies, we introduced criterion shifts. Specifically, two observed handedness rates were selected from those reported in McManus (1985): one for the parental generation and one for the offspring generation. These rates were scaled relative to the model's assumed true incidence of left-handedness (0.0775) to create dataset-specific correction matrices. Transition matrices P and Q were then constructed accordingly, and the simulated offspring counts were adjusted using these corrections.

Using this simulation framework, we generated synthetic data for all three types used by McManus: triplets, families with multiple children, and twins. This ensured that the evaluation of the estimation method accurately reflected the structure of the original datasets.

Results

Statistical analysis

Applying maximum likelihood estimation (MLE) to the complete dataset, McManus (1985) reported a maximum log-likelihood of –11,446.441 for parameter estimates of $p(L_t) = 0.0767$ and $p(L|DC) = 0.2647$ (Model A). He calculated that a "perfect fit" would yield a log-likelihood of –11,330.736, resulting in a likelihood-ratio test statistic of –11,330.736 ($\chi^2_{169}=231.41$, $p=1.02\times10^{-3}$). On this basis, he concluded that the model provided a poor fit to the full dataset and suggested that this result might reflect the sensitivity of MLE to outliers.

To identify potential outliers, McManus re-estimated model parameters using rounded values ($p(L_t) = 0.0775$, $p(L|DC) = 0.25$; Model C) and evaluated goodness-of-fit for each dataset separately. The twin data yielded an overall $\chi^2_{26}=37.028$, $p=0.074$, indicating an adequate fit, although the DZ twins of Zazzo (1960) and both MZ and DZ twins of Loehlin & Nichols (1976) showed significant deviation at $p < 0.05$. The families-with-multiple-offspring data also fit well overall ($\chi^2_{133}=129.469$, $p=0.57$), pointing to several outliers. Specifically, the datasets of Chaurasia & Goswami, Ramaley, Merrell, and McGee & Cozad all failed to fit the model (all $p < 0.01$). After excluding these four datasets, the triplet table was consistent with the model ($\chi^2_8=11.078$, $p=0.197$). McManus then repeated the MLE using the reduced dataset and reported a maximum log-likelihood of –9431.723 with estimates of $p(L_t)=0.0642$ and $p(L|DC) = 0.2328$ (Model B), yielding χ^2_{165}=172.514, p=0.32, which he considered an adequate fit.

In our reanalysis of the complete dataset (Tables 2–4), we obtained a maximum log-likelihood of –11,445.0212 with estimates of $p(L_t)=0.0774$ and $p(L|DC)=0.2681$. For a perfect fit, we estimated the log-likelihood to be –11,322.317, which corresponds to a test statistic of $\chi^2_{169}=245.408$, $p=1.12\times10^{-4}$. Thus, like McManus, we found that the full dataset does not fit the model.

For the reduced dataset, our maximum log-likelihood was –9430.911 with parameter estimates of $p(L_t) = 0.0649$ and $p(L|DC) = 0.236$. Although these estimates were nearly identical to those of McManus' Model B, the likelihood-ratio test yielded $\chi^2_{165}=197.653$, $p=0.0421$, which just falls below the conventional threshold for a good fit.

We then revisited the process of identifying outliers using McManus' method of evaluating goodness-of-fit with parameters fixed at $p(L_t)=0.0775$ and $p(L|DC) = 0.25$. For the triplet data,

we found $\chi^2_{12} = 55.037,\ p = 1.78 \times 10^{-7}$, again indicating poor fit. Dataset-level analysis confirmed the four outliers identified by McManus (Chaurasia & Goswami, Ramaley, McGee & Cozad, and Merrell). After excluding these, the triplet data fit the model ($\chi^2_8 = 11.02,\ p = 0.202$).

The families-with-multiple-offspring data showed an overall good fit ($\chi^2_{133} = 153.906,\ p = 0.104$), although the ICM2 maternal dataset did not ($\chi^2_{28} = 47.579,\ p = 0.012$). The twin datasets were also consistent overall ($\chi^2_{26} = 37.067,\ p = 0.074$), with MZ twins fitting well ($\chi^2_{13} = 12.552,\ p = 0.483$), but DZ twins showed a lack of fit ($\chi^2_{13} = 24.515,\ p = 0.0267$). This misfit was mainly due to the Loehlin & Nichols (1976) dataset, which was significant for both MZ ($\chi^2_1 = 4.402,\ p = 0.036$) and DZ twins ($\chi^2_1 = 5.917,\ p = 0.015$), as well as in the combined analysis ($\chi^2_1 = 10.319,\ p = 0.005$). Removing this dataset greatly improved the fit, resulting in $\chi^2_{24} = 26.748,\ p = 0.316$ for the full table, with both MZ ($\chi^2_{12} = 8.15,\ p = 0.773$) and DZ ($\chi^2_{12} = 18.598,\ p = 0.099$) twins fitting adequately.

Finally, when we repeated the MLE on the dataset excluding all identified outliers, we obtained a maximum log-likelihood of –8910.999 with parameter estimates of $p(L_t) = 0.0675$ and $p(L|DC) = 0.25$ (Model D). This likelihood was only 1.606 units higher than that from the full dataset (Model A), indicating that removing outliers did not significantly change the parameter estimates. Additionally, the difference between Model D and McManus' Model C was less than one log-likelihood unit, which suggests that the two models are nearly equivalent. A summary of the model comparisons is provided in Table 5 and shown in Figure 1.

While the likelihood ratio tests evaluate overall fit, they do not address how well the parameters are estimated. To quantify parameter precision and identifiability, we used Hessian-based diagnostics. Across models A, B, and D, the standard errors for $p(L_t)$ were large (0.33–0.37), whereas those for $p(L|DC)$ were much smaller (0.032–0.035). Parameter correlations were small (0.088–0.097), but the Fisher Information matrices were highly ill-conditioned, with condition numbers around 100. These results indicate that while estimates of the heterozygote parameter are stable, the model provides little information about the true incidence of left-handedness, consistent with the ridge-like likelihood surfaces observed in the contour plots (Figure 1).

Analysis of the quality of the reproduction

A central objective of this study was to assess whether McManus' (1985) analysis could be exactly reproduced from the information in the manuscript. While our reanalysis mostly matched his conclusions, we found several differences between his reported values and those from a strict reproduction.

Regarding the estimated parameters, our results closely match those reported by McManus. Minor differences seem to result from factors such as typographical errors in the reported left-handedness rates (as noted earlier by Annett, 1996), variations in rounding precision during intermediate calculations, and differences in the computational tools used for optimization. Since our estimates of the key parameters are, for all practical purposes, identical to those of McManus, we consider this aspect of the reproduction successful.

More significant differences appeared in the results of the likelihood-ratio tests, which McManus used to evaluate model fit. To resolve these discrepancies, we compared the test statistics for each dataset individually. For 27 of the 29 datasets, our results closely matched

his reported values, and the small differences could be explained by the issues mentioned earlier. However, for the remaining two datasets, Merrell and ICM2 maternal, we identified clear inconsistencies. Using McManus' own reported fitted values, we determined that the correct test statistic for the Merrell dataset should have been $\chi^2_1=4.347$, and for the ICM2 maternal dataset, $\chi^2_{28}=47.262$. Both corrected values matched our calculations, showing that McManus had likely miscalculated these two cases.

If these errors arose from mistakes in calculating the "perfect fit" values, then the corrected log-likelihoods McManus should have reported are –11,324.394 for Model A and –9,334.158 for Model B. With these corrections, the discrepancies between his reported results and our reproduction are fully resolved. On this basis, we can also infer the test statistics that McManus would have obtained had the calculations been correct: for Model A, the statistic would have been 1.314 units smaller than our result, and for Model B, 2.523 units smaller, corresponding to a borderline model fit with $p = 0.0544$.

In summary, our reanalysis confirms that McManus' genetic model can be reliably reproduced. The differences in his published results are not due to flaws in the model but rather due to minor calculation errors in two datasets and inconsistencies in how "perfect fit" values were reported. Once these issues are corrected, our findings closely align with McManus', reinforcing his analysis.

Evaluation of the estimation method

McManus did not evaluate the performance of his estimation method. To assess its reliability, we conducted multiple simulations where synthetic datasets were created using known parameter values. These simulations aimed to achieve two main goals: first, to see if the maximum likelihood estimation could accurately recover the true parameters; and second, to evaluate how sensitive the estimation method is to sampling variability and dataset size.

Estimation accuracy

We began by assessing the accuracy of the parameters reported by McManus, namely $p(L_t) = 0.0775$ and $p(L|DC)= 0.25$. To do this, we simulated 5,000 synthetic datasets with a criterion shift and estimated the model parameters for each dataset. A *differential evolution* algorithm with a population of 50 was used to identify the maximum likelihood estimator. The distribution of the 5,000 estimated parameter sets shows that both parameters are accurately estimated when the data are generated from the model (Figures 2a and 2b).

To evaluate generalizability, we simulated an additional 5,000 datasets with a criterion shift, this time sampling $p(L|DC)$ uniformly from 0 to 0.5. The parameters were then re-estimated for each dataset. The mean squared error between the true and estimated values was 0.0008 for $p(L_t)$ and 0.0089 for $p(L|DC)$, confirming that the method reliably estimates the true parameters across a wide range of conditions (Figures 2c and 2d).

Confidence interval and coverage

We next examined the accuracy of the confidence intervals produced by the estimation procedure. A confidence interval (CI) is a range of values for a parameter, calculated from the data, that reflects the uncertainty around the estimated value. A confidence interval with level $c\%$ is constructed so that, if the same study were repeated many times, the interval would

contain the true parameter in about *c%* of those repetitions. The proportion of cases in which the true parameter is contained within the CI is called *coverage* (Schall, 2012).
Using 5,000 synthetic datasets with a criterion shift and parameters sampled uniformly as described above, we applied a non-parametric bootstrap with 200 resamples for each dataset. From each resample, we obtained parameter estimates, which were then used to construct confidence intervals at multiple confidence levels. We then measured how often the true parameter fell within these intervals across all datasets. The results (Figures 2e and 2f) show that the coverage for both $p(L|DC)$ and $p(L_t)$ was slightly higher than expected but still close to the target levels.
Taken together, these results demonstrate that the estimation method is both accurate and robust. The MLE reliably recovers the true parameters across diverse conditions, and the bootstrap procedure produces well-calibrated confidence intervals, giving confidence in both the precision and reliability of the model parameter estimates.

Evaluating the Dextral-Chance Model in an Indonesian Population

To complement our reproduction of McManus' original analyses, we examined a dataset collected on Flores and Adonara, Indonesia (Nurhayu et al., 2020). This provided an opportunity to evaluate the Dextral–Chance (DC) model in a non-Western population and to assess whether different representations of family structure influence parameter estimation. Specifically, we compared two representations: the triplet representation (treating each parent–child trio as a data point) and the multi-offspring representation (retaining all children within a family).

Across both representations, likelihood profiles and bootstrap distributions indicated stable estimates for $p(L|DC)$, while Hessian-based diagnostics proved unreliable. The observed Fisher Information matrices were nearly singular, with condition numbers on the order of 10^{10} and one eigenvalue approaching zero. This produced implausibly large standard errors on the parameter estimates and near-perfect parameter collinearity, suggesting practical non-identifiability. We therefore emphasize bootstrap and profile-likelihood results and treat Hessian-based SEs as uninformative. This pattern matches the elongated ridge-like likelihood surfaces observed in the likelihood surface plots.

For the triplet analysis, the maximum log-likelihood was -1456.194 (Figure 3a), compared to -1455.259 for a perfect fit, showing that the model fits the data well ($\chi^2_2 = 1.869$, $p = 0.393$). The parameter estimates were $p(L|DC)=0.324$ with a 95% confidence interval of *0.281–0.444*, and $p(L_t)=0.0659$ with a 95% confidence interval of *0.0468–0.1035* (Figures 3b and 3c). Notably, the heterozygote estimate is significantly higher than McManus' canonical value of 0.25, indicating that the DC parameter deviates from the original model.

In the analysis of the multi-offspring dataset representation, the maximum log-likelihood was -992.568 (Figure 3d), compared to -930.494 for a perfect fit. Here, the estimates were $p(L|DC)=0.312$ with a 95% confidence interval of *0.144–0.448* and $p(L_t)=0.0551$ with a 95% confidence interval of *0.0409–0.0819* (Figures 3e and 3f). The heterozygote estimate is close to that from the triplet analysis ($p(L|DC)$=0.324), and both are somewhat above McManus' canonical value of $p(L|DC)$=0.25. The key difference is in the confidence intervals: in the

multi-offspring analysis, the canonical value falls within the CI, while in the triplet analysis, it falls outside. Both methods suggest a slightly lower true incidence of left-handedness ($p(L_t)$) than McManus' 0.0775, indicating population-level variation.

Together, these results indicate broad agreement between the triplet and multi-offspring approaches. The triplet analysis excludes McManus' canonical heterozygote probability, while the multi-offspring analysis includes it, but the discrepancy likely reflects statistical precision rather than a substantive biological difference. The key conclusion is that both parameterizations point to a somewhat increased $p(L|DC)$ and a slightly reduced $p(L_t)$ relative to McManus' estimates, with elongated likelihood ridges underscoring the model's partial non-identifiability.

Discussion

This study aimed to reproduce and modernize McManus' (1985) genetic model of handedness. Using the same datasets and modern computational techniques, we successfully reproduced the key findings: the model proposes a single locus with two alleles, and the parameter estimates we obtained closely matched those originally reported. This strong agreement, despite differences in methodology and computational tools, highlights the robustness of McManus' model.

At the same time, our analysis found several discrepancies between McManus' published results and those from strict reproduction. These differences are due to typographical errors in the handedness rates (as noted by Annett, 1996), variations in rounding and calculation precision, and in two cases (Merrell and ICM2 maternal), rounding practices, and miscalculated test statistics in a few cases. After correcting these issues, our results aligned with the original ones. This highlights both the robustness of the model and the importance of transparent, code-based reporting to avoid ambiguity in future work.

Simulations confirmed that the estimation framework is well-calibrated: maximum-likelihood reliably recovers true parameters, and bootstrap intervals achieve expected coverage. In practice, this means that parameter estimates are statistically sound even when studies differ in handedness definitions, strengthening confidence in the model as an analytic tool for family and twin data.

We also expanded the framework to include recent data from Flores and Adonara, Indonesia (Nurhayu et al., 2020), testing the model on non-Western populations where it was originally developed and comparing two methods of representing family data. Both the triplet and multi-offspring approaches produced consistent estimates of $p(L\ |DC)$ (0.31–0.32). The estimate of $p(L_t)$ was slightly lower than 0.0775. The triplet analysis excluded $p(L|DC)$=0.25 from its interval estimates, while the multi-offspring analysis included it. This difference arises from how family structure is modeled: triplets treat all offspring equally, whereas multi-offspring representation give more weight to larger families. Although both methods face some non-identifiability, the multi-offspring approach offers slightly more stable estimates by utilizing family size more comprehensively. These results show that methodological choices impact the level of uncertainty but do not change the main conclusion: the heterozygote parameter remains relatively stable, whereas the true prevalence is still poorly determined.

Several limitations of the model are evident. Statistical limitations: log-likelihood surfaces show elongated ridges, and Fisher Information matrices are nearly singular, resulting in *p(Lt)* being weakly identified and uninformative standard errors from Hessian approximations. Data limitations: model adequacy depends on excluding datasets that have poor model fit, and most empirical support comes from historical studies that used inconsistent or narrow criteria to classify handedness. Model limitations: the original DC model is highly simplified, assuming a single gene with no environmental or cultural influences. While useful as an initial formalization, later research has shown contributions from polygenic, epigenetic, and developmental factors (Paracchini, 2021; Schmitz et al., 2017). McManus himself has since developed multilocus versions informed by genome-wide association studies (McManus et al., 2013).

In conclusion, our reproduction confirms both the strengths and the weaknesses of the 1985 DC model. The framework is reproducible, its estimation procedure is statistically sound, and it remains historically influential. Yet its apparent success depends on the selective treatment of datasets, its parameters are only weakly constrained, and its genetic assumptions are now outdated. By fixing reporting errors, refining estimation methods, expanding the correction process, and applying the model to new data, we offer a transparent and modern platform for evaluating genetic and cultural theories of handedness.

Acknowledgements

This work was partly supported by the John Templeton Foundation (YR 61809), Minerva Stiftung Center for Lab Evolution (YR) and a fellowship from the Edmond J. Safra Center for Bioinformatics at Tel Aviv University (TO).

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Figures

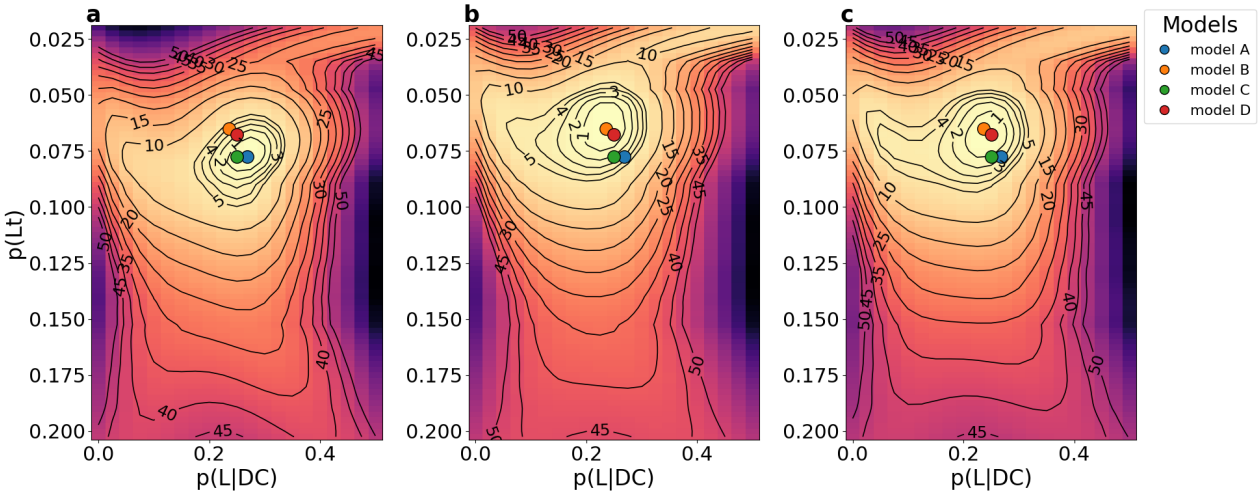

Figure 1. Maximum-likelihood estimates slightly decrease when datasets are omitted. The contour map shows the log-likelihood of four models, with four markers (A, B, C, D) representing the model parameters for each model. Contours indicate the difference in log-likelihood from the maximum value. The y-axis is inverted, consistent with McManus (1985). **(a)** Log-likelihood computed using all datasets. **(b)** Log-likelihood computed without McManus' omitted datasets. **(c)** Log-likelihood computed without our omitted datasets. Omitting datasets (markers B and C; log-likelihood surface in panel b) reduced $p(L_t)$ by 13% and $p(L|DC)$ by 12%.

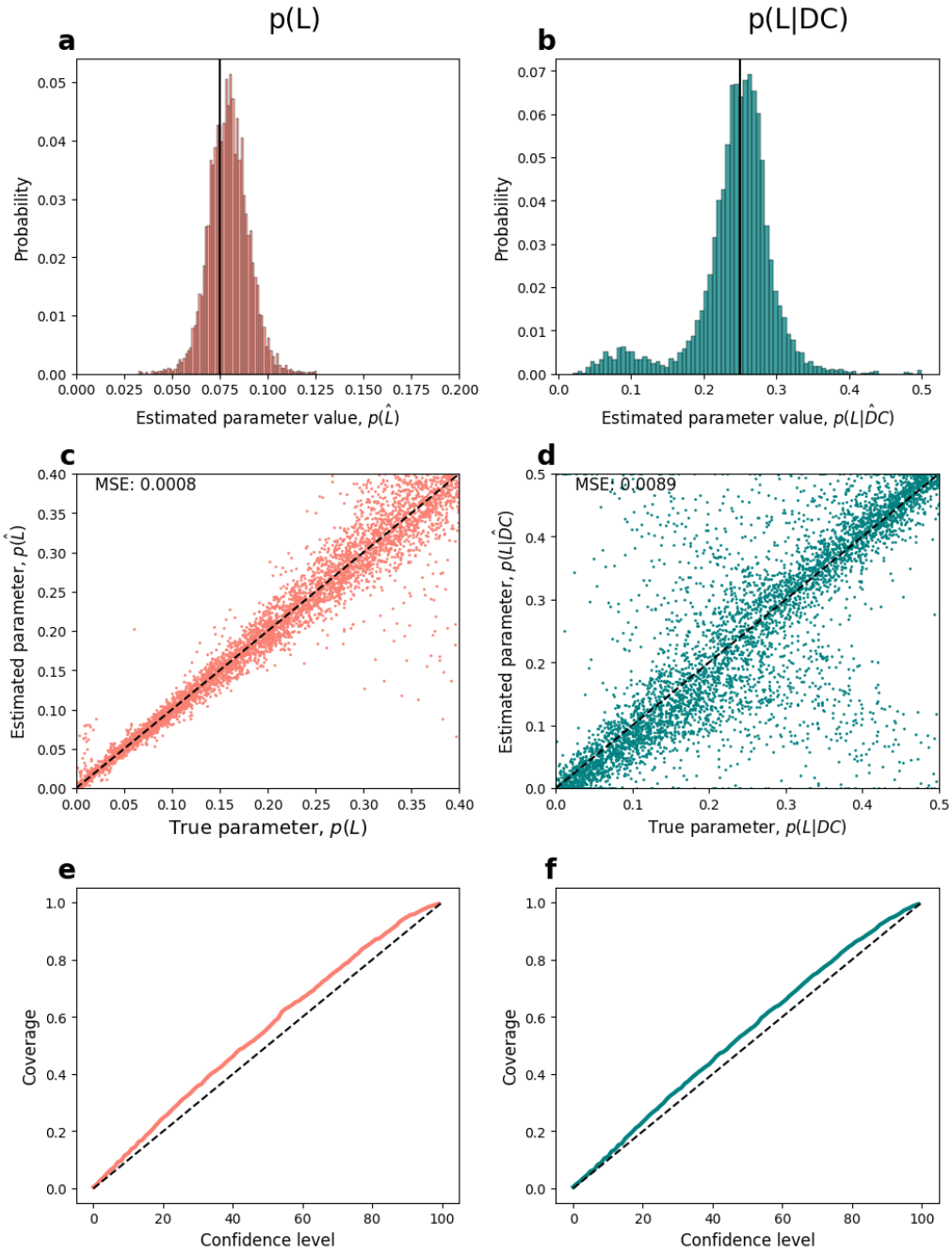

Figure 2. Performance of the estimation method on simulated data. (a, b) The distribution of $\hat{p}(L_t)$ and $\hat{p}(L|DC)$ estimated from synthetic data simulated using parameter values estimated by McManus (solid lines; $\hat{p}(L_t)$=*0.0775* in panel a and $\hat{p}(L|DC)$=*0.25* in panel b). **(c, d)** Scatter plots of parameter estimates (y-axis) vs. the true parameter (x-axis). **(e, f)** Coverage for various confidence levels: the rate at which the true parameter value falls within the confidence interval at a given confidence level.

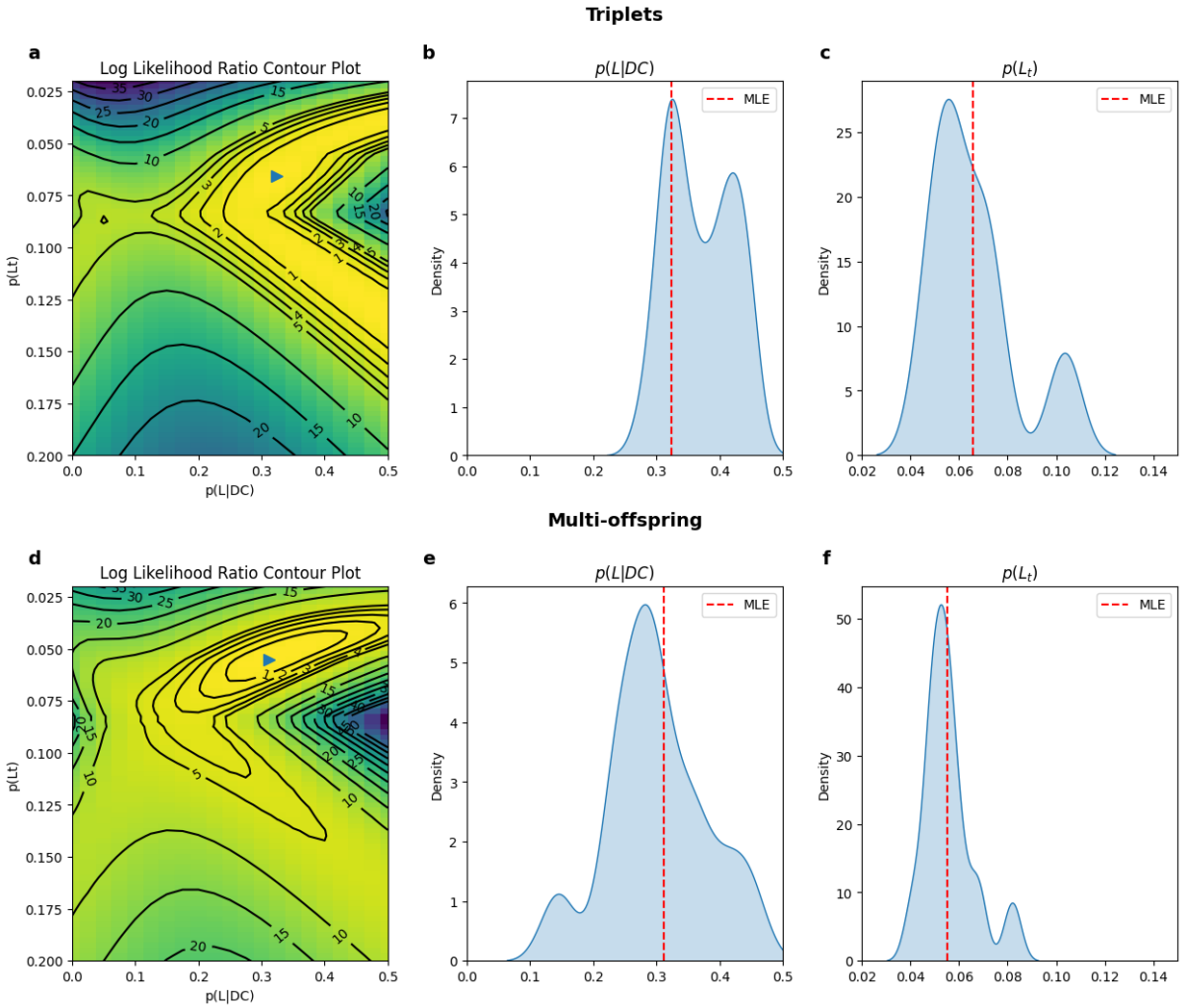

Figure 3. Comparison of triplet and multi-offspring analyses of the Flores–Adonara dataset. Log-likelihood surfaces show ridges, and the bootstrap distributions are wide, suggesting practical non-identifiability, possibly because the dataset is small (Tables 6 and 7). **(a, d)** Log-likelihood ratio contour plots under the triplet (a) and multi-offspring (d) representations. **(b, e)** Bootstrap distributions of the heterozygote parameter *p(L|DC)* for the triplet (b) and multi-offspring (e) representations, with red dashed lines indicating the maximum-likelihood estimates. **(c, f)** Bootstrap distributions of the true incidence parameter $p(L_t)$ for the triplet (c) and multi-offspring (f) representations.

Tables

Table 1. The expected probabilities of presenting right- and left-handedness by genotype.

$Genotype$	$p(L\|genotype)$	$p(R\|genotype)$
DD	0	1
DC	$p(L\|DC)$	$1 - p(L\|DC)$
CC	0.5	0.5

Table 2. Data from Table 2 in McManus (1985). Results of 12 studies on the incidence of right- and left-handed offspring from R×R, R×L, and L×L parents.

Study	p (L_m) progeny	p (L_m) parental	R×R		R×L		L×L		χ^2 (df=1)
			R	L	R	L	R	L	
Ramaley (1913)	0.1556	0.0803	841 *822.8*	115 *133.2*	113 *126.8*	54 *40.2*	1 *5.3*	7 *2.7*	18.733***
Chamberlain (1928)	0.0477	0.0356	6917 *6915.0*	308 *310.0*	411 *412.8*	53 *51.2*	18 *20.6*	7 *4.4*	1.666
Rife (1940)	0.0877	0.0524	1842 *1841.3*	151 *151.8*	140 *141.6*	34 *32.4*	5 *7.7*	6 *3.3*	3.041
Merrell (1957)	0.2363	0.1553	140 *135.4*	34 *38.6*	33 *38.8*	20 *14.3*	8 *6.8*	2 *3.2*	4.348*
Annett (1973)	0.1063	0.0405	6206 *6203.4*	669 *671.6*	471 *474.2*	125 *121.8*	5 *4.1*	1 *1.9*	0.772
Ferronato et al. (1974)	0.0976	0.0987	154 *151.8*	11 *13.2*	31 *33.3*	9 *6.7*	0	0	1.286
Mascie-Taylor (unpub)	0.0831	0.0930 #	232 *232.7*	17 *16.3*	41 *40.3*	7 *7.7*	3 *3.0*	1 *1.0*	0.109
Chaurasia & Goswami (unpub)	0.1407	0.1040 #	1060 *1054.5*	144 *149.5*	122 *133.8*	46 *34.2*	3 *5.0*	4 *2.0*	7.498**
Annett (1978)	0.0850	0.0547 #	1656 *1655.8*	130 *130.2*	170 *171.4*	40 *38.6*	4 *2.8*	0 *1.2*	2.855
Carter-Saltzmann (1980)	0.1300	0.0756	303 *301.3*	37 *38.7*	45 *46.7*	15 *13.3*	0	0	0.357
Coren & Porac (1980)	0.1842	0.0839	315 *318.5*	68 *64.5*	57 *53.9*	16 *19.1*	0	0	0.941
McGee & Cozad (1980)	0.2415	0.1818	848 *818.7*	211 *240.3*	325 *348.2*	150 *126.8*	30 *36.0*	22 *16.0*	13.431***

The observed parental rates p (L_m) were calculated directly from the original publications, except where marked with #, which indicates values cited from McManus (1985).

The observed progeny rates were calculated from the data as reported by McManus.

The numbers in *italics* are expected values under the DC model with $p(L_t)$=0.0775 and p(L|DC)=0.25 with criterion shift correction.

*p<0.05, **p<0.01, ***p<0.001

Table *3*. Mating data from Table 3 in McManus (1985). Number of families with specific incidences of left-handed offspring, categorized by family size and parental handedness.

	p (L_m) progeny	p (L_m) parental	Family size	$R \times R$						$R \times L$						$L \times L$						χ^2
				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 *57.92*	9 *9.08*					14 *14.88*	5 *4.12*					0	0					40.161 df = 44
			2	211 *204.02*	57 *60.52*	3 *6.47*				35 *34.73*	16 *18.27*	5 *3.00*				0 *0.50*	0 *0.40*	1 *0.10*				
			3	123 *126.69*	63 *53.56*	6 *10.75*	0 *1.00*			22 *26.29*	24 *19.75*	6 *6.18*	1 *0.78*			2 *1.45*	1 *1.66*	1 *0.76*	0 *0.13*			
			4	70 *67.47*	39 *36.29*	6 *10.29*	1 *1.80*	0 *0.15*		8 *9.61*	8 *9.18*	7 *4.12*	1 *0.99*	0 *0.11*		0 *0.27*	0 *0.38*	1 *0.25*	0 *0.08*	0 *0.01*		
			5	9 *14.94*	12 *9.62*	6 *3.44*	2 *0.85*	0 *0.14*	0 *0.01*	1 *0.65*	0 *0.74*	0 *0.43*	1 *0.15*	0 *0.03*	0 *0.00*	1 *0.20*	0 *0.34*	0 *0.28*	0 *0.14*	0 *0.04*	0 *0*	
ICM2 (propositi)	0.134	0.101	1	134 *131.52*	15 *17.48*					17 *20.81*	9 *5.19*					1 *0.72*	0 *0.28*					37.665 df = 27
			2	91 *90.26*	22 *22.50*	2 *2.24*				19 *16.18*	3 *7.64*	3 *1.17*				0	0	0				
			3	22 *21.77*	7 *7.67*	0 *1.43*	2 *0.13*			6 *10.58*	11 *7.10*	3 *2.07*	0 *0.25*			0	0	0	0			
			4	10 *9.48*	5 *4.21*	0 *1.10*	0 *0.19*	0 *0.02*		3 *1.74*	1 *1.48*	0 *0.62*	0 *0.14*	0 *0.01*		1 *0.29*	0 *0.39*	0 *0.24*	0 *0.08*	0 *0.01*		
			5	4 *2.29*	0 *1.21*	0 *0.40*	0 *0.09*	0 *0.01*	0 *0*	0	0	0	0	0	0	0	0	0	0	0	0	
ICM2 (maternal)	0.0893	0.0609	1	74 *72.09*	4 *5.91*					6 *6.51*	2 *1.49*					0	0					47.579* df = 28
			2	107 *110.20*	18 *16.21*	3 *1.60*				11 *9.33*	3 *4.10*	0 *0.56*				2 *0.99*	0 *0.82*	0 *0.19*				
			3	81 *81.56*	16 *16.18*	4 *3.00*	0 *0.26*			16 *10.46*	1 *6.63*	0 *1.72*	2 *0.19*			0	0	0	0			
			4	31 *32.01*	10 *7.64*	1 *2.00*	0 *0.33*	0 *0.03*		0 *0.91*	0 *0.75*	0 *0.28*	2 *0.06*	0 *0.01*		0	0	0	0	0		
			5	19 *20.24*	7 *5.46*	1 *1.80*	1 *0.42*	0 *0.06*	0 *0.00*	3 *1.91*	2 *1.89*	0 *0.89*	0 *0.26*	0 *0.05*	0 *0.00*	0	0	0	0	0	0	
ICM2 (paternal)	0.091	0.047	1	86 *82.77*	4 *7.23*					8 *7.29*	1 *1.71*					0	0					28.501 df = 34
			2	100 *108.31*	27 *16.97*	0 *1.71*				7 *7.95*	5 *3.55*	0 *0.50*				0 *0.50*	1 *0.41*	0 *0.09*				
			3	65 *62.14*	11 *13.15*	2 *2.49*	0 *0.22*			4 *4.91*	3 *3.16*	2 *0.84*	0 *0.09*			0 *0.35*	1 *0.43*	0 *0.19*	0 *0.03*			
			4	39 *38.95*	11 *9.92*	2 *2.65*	0 *0.45*	0 *0.04*		2 *1.35*	1 *1.12*	0 *0.42*	0 *0.09*	0 *0.01*		0	0	0	0	0		
			5	13 *16.29*	9 *4.70*	1 *1.58*	0 *0.38*	0 *0.06*	0 *0.00*	0 *0.38*	1 *0.38*	0 *0.18*	0 *0.05*	0 *0.01*	0 *0*	0	0	0	0	0	0	

The observed rates p(L_m) were calculated from the data as reported by McManus.

The numbers in *italics* are expected values under the DC model with $p(L_t)$=0.0775 and $p(L|DC)$=0.25 with criterion shift correction.

$* p < 0.05$

Table 4. Observed counts of RR, RL, and LL pairs of MZ and DZ twins from 13 different studies, as shown in Table 5 of McManus (1985).

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

The observed rates p(L_m) were calculated from the data as reported by McManus.

The numbers in italics are expected values under the DC model with $p(L_t)$=0.0775 and $p(L|DC)$=0.25 with criterion shift correction.

$* p < 0.05, ** p < 0.01$

Table 5. Comparison of the maximum log-likelihood of the present model and the model of McManus

Data		Degrees of freedom	Maximum log-likelihood	χ^2	$p(L_t)$	$p(L\|DC)$	Log-likelihood difference from the parameters of McManus 1985
Fitted total data	Perfect fit (McManus 1985)	171	−11330.736	-	-	-	-
	Model A (McManus 1985)	2	−11446.441	231.41	0.0767	0.2674	-
	Perfect fit (this study)	171	−11322.317	-	-	-	-
	Model A (this study)	2	−11445.021	245.408	0.0774	0.2681	-1.42
Fitted reduced data (McManus)	Perfect fit (McManus 1985)	167	−9345.466	-	-	-	-
	Model B (McManus 1985)	2	−9431.723	172.514	0.0642	0.2328	-
	Perfect fit (this study)	167	−9332.085	-	-	-	-
	Model B (this study)	2	−9430.911	197.653	0.0649	0.2359	-0.812
Fitted reduced data (ours)	Perfect fit (this study)	165	−8816.132	-	-	-	-
	Model D (this study)	2	−8910.94	189.732	0.0675	0.25	-

Table 6. Representation of the Flores–Adonara dataset (Nurhayu et al., 2020) as triplet data

	p (L_m) progeny	p (L_m) parental	R×R		R×L		L×L	
			R	L	R	L	R	L
Flores–Adonara 1	0.0823	0.0851	2707	184	438	94	19	6
Flores–Adonara 2	0.0875	0.0558	1439	106	178	48	10	2

Table 7. Representation of the Flores–Adonara dataset (Nurhayu et al., 2020) as multi-offspring data.

	p (L_m) progeny	p (L_m) parental	Family size	R×R							R×L							L×L						
				0	1	2	3	4	5	6	0	1	2	3	4	5	6	0	1	2	3	4	5	6
Flores–Adonara 1	0.0823	0.0851	1	119	19						21	7						0	2					
			2	170	27	2					26	12	1					3	0	0				
			3	164	29	3	0				15	15	1	1				0	1	0	0			
			4	149	33	3	1	0			9	10	4	0	2			1	0	0	0	0		
			5	94	29	5	1	0	0		15	10	3	0	0	0		0	1	1	0	0	0	
			6	51	9	3	0	0	0	0	8	4	2	1	0	0	0	0	0	0	0	0	0	0
Flores–Adonara 2	0.0875	0.0558	1	152	10						2	2						0	0					
			2	20	7	0					3	0	0					0	0	0				
			3	51	7	5	0				3	6	1	1				0	0	0	0			
			4	47	16	6	0	0			2	10	2	0	0			0	0	0	0	0		
			5	68	18	4	0	0	0		6	7	4	0	0	0		0	0	0	0	0	0	
			6	51	18	0	0	0	0	0	3	3	0	1	0	0	0	0	2	0	0	0	0	0

Appendix 1: Correction matrices

The correction procedure introduced by McManus (1985) was designed to adjust theoretical predictions to account for misclassification of handedness in empirical datasets. In his original work, the method was applied only to triplet data, where the handedness of two parents and one child was recorded. Here, we generalize the approach to families with multiple children and to twin datasets.

The correction operates by applying transition matrices that map between true and observed handedness states. Let *P* denote the offspring transition matrix, *Q* the parental transition matrix, and *T* the transmission matrix that links parental phenotypes to offspring outcomes. The corrected prediction is given by

$$M = P \cdot T \cdot Q$$

Correcting triplet datasets

In the triplet case, McManus assumed that misclassification occurred in only one direction: either some left-handers were recorded as right-handed, or some right-handers were recorded as left-handed, but not both at the same time. The offspring transition matrix P therefore specifies the probability that an observed phenotype reflects the true underlying phenotype, given the discrepancy between reported (p) and true (t) incidence rates.

$$P = \begin{cases} \begin{pmatrix} 1 & 0 \\ 1-\frac{p}{t} & \frac{p}{t} \end{pmatrix}, p \le t \\ \begin{pmatrix} 1-\frac{p-t}{1-t} & \frac{p-t}{1-t} \\ 0 & 1 \end{pmatrix}, p > t \end{cases}$$

Similarly, the parental transition matrix *Q* is constructed from the difference between observed (q) and true parental (t) incidences.

$$Q = \begin{cases} \begin{pmatrix} \left(\frac{1-t}{1-q}\right)^2 & 2\frac{1-t}{1-q}\cdot\frac{t-q}{1-q} & \left(\frac{t-q}{1-q}\right)^2 \\ 0 & \frac{1-t}{1-q} & \frac{t-q}{1-q} \\ 0 & 0 & 1 \end{pmatrix}, q \le t \\ \begin{pmatrix} 1 & 0 & 0 \\ 1-\frac{t}{q} & \frac{t}{q} & 0 \\ \left(1-\frac{t}{q}\right)^2 & 2\frac{tq-t^2}{q^2} & \left(\frac{t}{q}\right)^2 \end{pmatrix}, q > t \end{cases}$$

The transmission matrix *T* encodes the expected probabilities of offspring phenotypes under Mendelian inheritance, based on parental phenotypes and the genetic model. Multiplying these three matrices produces corrected offspring probabilities for each parental mating type.

Correcting families with multiple children

McManus did not provide an explicit correction method for families with more than one child, but he noted that the triplet approach could be extended. Following this suggestion, we generalized the matrices under the assumption that the same misclassification process applies independently to each child. In this case, the offspring transition matrix *P* expands to represent the joint probability of observing a set of measured handedness outcomes $\{H_{1m}, H_{2m}, \ldots, H_{Nm}\}$

given their true states $\{H_{1t}, H_{2t}, \ldots, H_{Nt}\}$. Misclassification is again assumed to occur in only one direction.

$$p(\#\text{measured left handers} = \text{k}|\#\text{ true left handers} = \text{n}) = \begin{cases} p(R_m|R_t)^{N-n}\binom{n}{k}p(L_m|L_t)^k p(R_m|L_t)^{n-k} & k < n \\ \binom{N-n}{N-k}p(R_m|R_t)^{N-n}p(L_m|R_t)^{k-n}p(L_m|L_t)^n & k > n \\ p(R_m|R_t)^{N-k}p(L_m|L_t)^k & otherwise \end{cases}$$

The transmission matrix *T* for multiple children describes the distribution of true left-handed offspring counts within a family of size *N*, conditional on the parental phenotypes. Each column of *T* corresponds to a specific number of true left-handed children, and probabilities are derived directly from the binomial distributions described in Appendix 2. The corrected probabilities of observed outcomes are then obtained by multiplying *P* and *T*, together with the appropriate parental correction matrix *Q*.

Correcting for twins

Twin datasets differ from family data in that parental phenotypes are not reported. As a result, only the offspring transition matrix *P* and the transmission matrix *T* are required. The transition matrix *P* for twins is equivalent to that used for families of size two, reflecting possible misclassification of either twin's handedness.

$$P = \begin{pmatrix} p(R_m \times R_m|R_t \times R_t) & p(R_m \times L_m|R_t \times R_t) & p(L_m \times L_m|R_t \times R_t) \\ p(R_m \times R_m|R_t \times L_t) & p(R_m \times L_m|R_t \times L_t) & p(L_m \times L_m|R_t \times L_t) \\ p(R_m \times R_m|L_t \times L_t) & p(R_m \times L_m|L_t \times L_t) & p(L_m \times L_m|L_t \times L_t) \end{pmatrix}, T = \begin{pmatrix} p(R_t \times R_t) & p(L_t \times R_t) & p(L_t \times L_t) \end{pmatrix}$$

The transmission matrix *T* must be built separately for monozygotic (MZ) and dizygotic (DZ) twins. For MZ pairs, the two offspring share the same genotype and thus have correlated phenotypic probabilities, while for DZ pairs, the two offspring are considered siblings with independently sampled genotypes. The detailed derivation of these probabilities is shown in Appendix 2. Combining *P* and *T* provides corrected predictions for the observed distribution of twin handedness.

$$M = T \cdot P = \begin{pmatrix} p(R_m \times R_m) & p(L_m \times R_m) & p(L_m \times L_m) \end{pmatrix}$$

Appendix 2: Probabilities

This appendix derives the genotype-to-phenotype probabilities used in our likelihood functions. These probabilities describe how parental genotypes give rise to offspring handedness, and how these extend to families with multiple offspring and to twin datasets. All derivations assume Mendelian inheritance under McManus' (1985) single-locus, two-allele model.

Probabilities of handedness in progeny:

Under Mendelian inheritance, the probability of each genotype in the offspring depends on the parental genotypes $G_1 \times G_2$. These genotype probabilities are then mapped to phenotypes according to McManus' assumptions. Therefore, the probability that two parents with genotypes G_1 and G_2 produce a left-handed child is:

$$p(H|G_1 \times G_2) = \sum_{G \in \{DD,DC,CC\}} p(H|G) \cdot p(G|G_1 \times G_2)$$

Subsequently, by applying the binomial distribution, we can calculate the probabilities of n offspring within a family of N exhibiting left-handedness.

$$p_N(n|G_1 \times G_2) = \binom{N}{n} p(L|G_1 \times G_2)^n p(R|G_1 \times G_2)^{N-n}$$

Thus, based on the phenotypes of the two parents, the probability that they will have n out of N offspring exhibiting left-handedness is calculated by:

$$p(n|H_1 \times H_2) = \sum_{G1 \in \{DD,DC,CC\}} \sum_{G_2 \in \{DD,DC,CC\}} p(G_1|H_1)p(G_2|H_2)p_N(n|G_1 \times G_2)$$

Probabilities of handedness in twins

Twin datasets differ in that parental phenotypes are not observed, and outcomes must be modeled separately for dizygotic (DZ) and monozygotic (MZ) twins. For DZ twins, genotypes are sampled independently given the parental genotypes. The probability of a twin pair with handedness outcomes H_1, H_2 is therefore:

$$p\left(H_1, H_2 \middle| G_{p_1} \times G_{p_2}\right) = \sum_{G_1, G_2 \in \{DD,DC,CC\}} p\left(G_1 \middle| G_{p_1} \times G_{p_2}\right) p\left(G_2 \middle| G_{p_1} \times G_{p_2}\right) p(H_1|G_1) p(H_2|G_2)$$

For MZ twins, the situation differs because the pair always shares the same genotype. In this case, the probability of a handedness outcome H_1, H_2 is calculated by summing over the possible shared genotypes.

$$p\left(H_1, H_2 \middle| G_{p_1} \times G_{p_2}\right) = \sum_{G \in \{DD,DC,CC\}} p\left(G \middle| G_{p_1} \times G_{p_2}\right) p(H_1|G) p(H_2|G)$$

Therefore, the probability of having twins with phenotypes H_1, H_2 given the parental phenotypes $H_{p1} \times H_{p2}$ is:

$$p\left(H_1, H_2 | H_{p_1} \times H_{p_2}\right) = \sum_{G_{p_1}, G_{p_2} \in \{DD,DC,CC\}} p\left(G_{p_1} \middle| H_{p_1}\right) p\left(G_{p_2} \middle| H_{p_2}\right) p\left(H_1, H_2 \middle| G_{p_1} \times G_{p_2}\right)$$

Thus, the probability of having a twin couple with phenotypes H_1, H_2 is:

$$p(H_1, H_2) = \sum_{H_{p_1}, H_{p_2} \in \{R,L\}} p\left(H_1, H_2 \middle| H_{p_1} \times H_{p_2}\right)$$

Appendix 3: Likelihood functions

This appendix provides the explicit likelihood functions used to estimate the parameters $p(L_t)$, which represents the true population rate of left-handedness, and $p(L|DC)$, the probability of left-handedness among heterozygotes. Each dataset type—triplets, families with multiple children, and twins—contributes its own likelihood, which are then multiplied to determine the total likelihood for model fitting. The probabilities in these functions are derived from the framework outlined in Appendix 2 and are further refined using the correction matrices described in Appendix 1.

Triplet datasets

For datasets reporting offspring and their two parents, the likelihood is based on the observed counts of left- and right-handed children in each mating category. If $n_H(H_1 \times H_2)$ denotes the number of offspring with phenotype H (right if $H=R$, left if $H=L$) from parents with phenotypes $H_1 \times H_2$, then the likelihood for a given dataset is

$$L_{triplets} = \prod_{H_1,H_2 \in \{R,L\}} \prod_{H \in \{R,L\}} [p(H \mid H_1 \times H_2)]^{n_H(H_1 \times H_2)}$$

where $p(H \mid H_1 \times H_2)$ is the probability of observing phenotype H given the parental phenotypes, as determined by the genetic model and correction matrices.

Families with multiple offspring

For datasets that record the distribution of the number of left-handed children within families, the likelihood reflects the multinomial structure of the data. Let $n_s(n|H_1 \times H_2)$ be the number of families of size s with n left-handed offspring from parents of type $H_1 \times H_2$. If $p_s(n \mid H_1 \times H_2)$ is the probability of such an outcome under the model and correction matrices, then

$$L_{families} = \prod_{s} \prod_{n=0}^{s} \prod_{H_1,H_2 \in \{R,L\}} [p_s(n \mid H_1 \times H_2)]^{n_s(n|H_1 \times H_2)}$$

This formulation considers all possible family sizes and outcomes, weighting them according to their observed frequencies.

Twins

For twin datasets, parental phenotypes are not recorded, and the likelihood is based on the observed distribution of twin pairs. Let $n(H1, H2|Z)$ represent the number of twin pairs of zygosity type Z (MZ or DZ) with phenotypes H_1 and H_2. If $p(H_1, H_2|Z)$ is the model probability of observing such a pair, then the likelihood is

$$L_{twins} = \prod_{Z \in \{MZ,DZ\}} \prod_{H_1,H_2 \in \{R,L\}} [p(H_1, H_2 \mid Z)]^{n(H_1,H_2|Z)}$$

Total likelihood

The overall likelihood function for the entire dataset is obtained by multiplying the contributions of the three data types:

$$L_{total} = L_{triplets} \cdot L_{families} \cdot L_{twins}$$

This total likelihood was maximized using the procedures described in the Methods section, providing estimates of $p(L_t)$ and $p(L|DC)$. The same framework also served as the basis for likelihood-ratio tests comparing model fit to perfect-fit baselines.