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RESEARCH ARTICLE

Trends in Population Sex Ratios May be Explained by Changes in the Frequencies of Polymorphic Alleles of a Sex Ratio Gene

Corry Gellatly

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Abstract A test for heritability of the sex ratio in human genealogical data is reported here, with the finding that there is significant heritability of the parental sex ratio by male, but not female offspring. A population genetic model was used to examine the hypothesis that this is the result of an autosomal gene with polymorphic alleles, which affects the sex ratio of offspring through the male reproductive system. The model simulations show that an equilibrium sex ratio may be maintained by frequency dependent selection acting on the heritable variation provided by the gene. It is also shown that increased mortality of pre-reproductive males causes an increase in male births in following generations, which explains why increases in the sex ratio have been seen after wars, also why higher infant and juvenile mortality of males may be the cause of the male-bias typically seen in the human primary sex ratio. It is concluded that various trends seen in population sex ratios are the result of changes in the relative frequencies of the polymorphic alleles of the proposed gene. It is argued that this occurs by common inheritance and that parental resource expenditure per sex of offspring is not a factor in the heritability of sex ratio variation.

Keywords Sex ratio · Heritable variation · Human genetics · Polymorphism · Mortality · War

C. Gellatly (✉)
Evolutionary Biology Group, Newcastle University, 4th Floor William Leech Building, Newcastle upon Tyne NE2 4HH, UK
e-mail: corry.gellatly@ncl.ac.uk

Introduction

The sex ratio at birth, usually measured as proportion males, varies between human populations (Parazzini et al. 1998) and changes over time, with the change being autocorrelated between years (Gini 1955; Graffelman and Hoekstra 2000). This indicates that factors affecting the sex ratio are similar between years. It has been suggested that racial composition or age-structure of the population (Graffelman and Hoekstra 2000) and changes in sexual behaviour over time (James 1995) may explain autocorrelation. It might also be explained by inheritance of sex ratio variation. In studies that have looked for inheritance of sex ratio variation, Trichopoulos (1967) and Curtsinger et al. (1983) found a significant association between the sex ratio of a father's sibship and his offspring, but not a mother's sibship and her offspring, whilst Gini (1908) reported heritability of sex ratio variation from parents to offspring, though not specifically from father to son.

In England and Wales, the livebirth sex ratio changed considerably over the 20th century, increasing rapidly up to the mid-century then declining toward the end (Fig. 1). The increase from 1900 to 1960 resulted in approximately 2.8 extra males per 100 females born. It is interesting that this increase corresponds with peaks at the ends of the World Wars, also that a similar pattern occurs in the Belgian, French and German sex ratio data. It has been well established that these and other post-war sex ratio increases are statistically significant (Graffelman and Hoekstra 2000).

It has been hypothesised that the wartime peaks in the sex ratio are due to exceptionally frequent intercourse between returning soldiers and their partners (James 1971), resulting in earlier insemination within the menstrual cycle, which (due to hormonal changes over the cycle) may

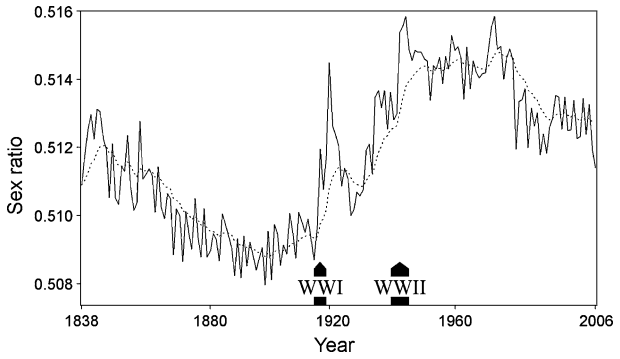

Fig. 1 Sex ratio of livebirths in England and Wales, 1838–2006. The annual data is represented by the continuous line (1st order autocorrelation = 0.898, $P < 0.001$) and the dotted line is a simple exponential smoothing line, which indicates the approximate trend. Source: Office for National Statistics, UK

increase the probability of a male birth. There have been mixed results from studies that have attempted to determine whether the timing of insemination affects offspring sex, with some reporting an effect (e.g. Harlap 1979; Perez et al. 1985; James 2000) and others not (e.g. Wilcox et al. 1995; Gray et al. 1998). It has also been suggested that the sex ratio may be stabilised by this effect, if individuals perceiving a bias in the adult sex ratio regulate their rate of copulation to increase their chance of having offspring of the rarer sex—who have a better chance of breeding (James 1995). A negative feedback loop would be expected from this type of behavioural response, resulting in autocorrelation and oscillations in the sex ratio over time; both of which have been observed (Gini 1955).

The wartime sex ratio increases have also been attributed to a finding that larger males are more likely to have male offspring (Kanazawa 2005) and are more likely to survive wars (Kanazawa 2007). A theoretical problem with this explanation, is that it implies a genetic link between male-size and sex ratio, which would be a constraint on the directional evolution of male-size and perhaps also on the maintenance of sex ratio equilibrium. Also, the statistical basis of the evidence in Kanazawa (2005) has been criticised (Gelman 2007; Denny 2008).

A link between higher male mortality and a male-biased primary sex ratio was first hypothesised by Fisher (1930), as a corollary to a wider theory of sex ratio evolution, based on an equal-investment principle. This is the principle that parents will invest their resources equally between each sex of offspring, because each sex supplies exactly half the genes of all future generations; as such, any genes that cause parents to invest unequally in the sexes will tend to be deselected. It is a reciprocal process, in which the investment that parents make in each sex is not only a function of the sex ratio, but the sex ratio is a function of the investment that parents make in each sex. If, therefore, one sex requires more parental resources up to the end of the period of parental care, the sex ratio of the species will become biased to compensate. In the case of the human sex ratio, males suffer higher mortality in infancy so require less parental care on average, which leads to a higher rate of male births to equalise parental investment in each sex. In itself, this principle does not explain the post-war sex ratio increases, because it relates to male mortality during parental care, whereas the soldiers that died in the wars had presumably become independent of their parents.

The equal-investment principle has become synonymous with frequency dependent selection, but frequency dependent selection as it relates to the sex ratio is actually a more general concept, first described by Darwin (1871). It is simply the idea that the probability of an individual being able to breed is dependent on the frequency of the opposite sex in relation to its own sex. A tendency to produce the rarer sex will be favoured by selection, because the rarer sex has more mating opportunities and will have more offspring. It is because of this, and because every offspring has one mother and one father, that a population sex ratio is typically expected to be 1:1. However, the sex ratio is not a typical trait, because it has no effect on the survival of an individual or on the survival of that individual's offspring, instead it affects the probability of an individual's offspring being able to breed. It is not immediately clear how natural selection can alter the sex ratio, when it does not act directly on the individuals that determine it. The equal-investment principle suggests that it occurs by affecting the resources expended by parents on offspring, which affects the transmission of parental genes to future generations.

Hypothesis

An alternative to the equal-investment principle is described here, to explain how selection acts on the sex ratio. It is proposed that the sex ratio is a variable and heritable trait, due to a polymorphic autosomal gene, which in humans and other mammals is expressed in males and affects the sex ratio through the male reproductive system, possibly by altering the ratio of X:Y sperm.

In the simplest case, there would be two polymorphic alleles occurring in the gene, an *m* allele coding for greater production of Y sperm and an *f* allele coding for greater production of X sperm. In a case where neither allele is dominant, *mm* males produce more Y sperm and have more sons, *ff* males produce more X sperm and have more daughters, whilst *mf* males produce equal X:Y sperm and will be equally likely to have sons or daughters (Fig. 2). In other cases, the alleles might be dominant and recessive or there may be a range of alleles coding for different levels

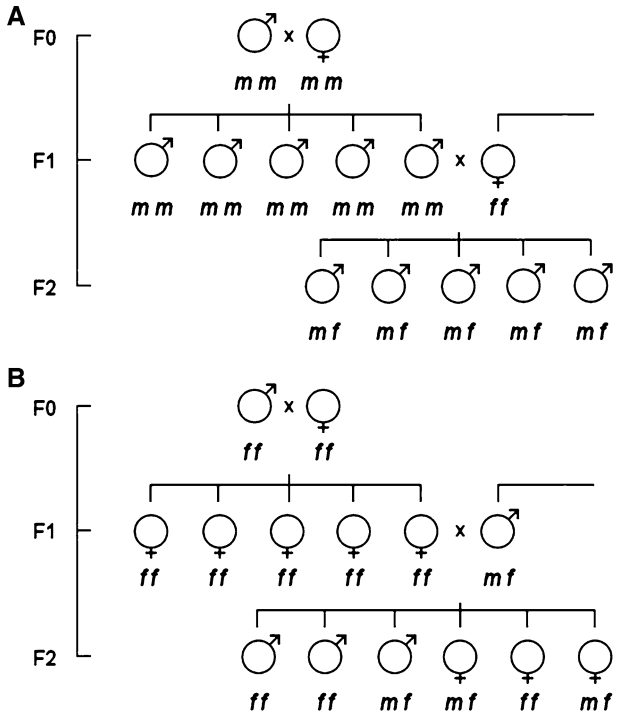

Fig. 2 These trees illustrate how the gene works in Sim. 1. In the first tree (**a**) the F0 male is *mm*, so all F1 offspring are male, they have an *mm* genotype because their father and mother were both *mm*, so produce all male F2 offspring. The F2 offspring have an *mf* genotype, because their father was *mm* and their mother was *ff*. In the second tree (**b**) the F0 male is *ff*, so all his offspring are female, they have an *ff* genotype because their father and mother were *ff*. The F1 female mates with an *mf* male, resulting in an equal number of male and female offspring, with *mf* and *ff* genotypes in the F2 generation

of X or Y sperm production, each with various dominances in the male phenotype.

The existence of this type of polymorphic gene would explain autocorrelation in human sex ratio data, because offspring inherit their sex ratio producing tendency from their parents. It is predicted that the apparent degree of heritability of the sex ratio by males will be low, because a male will inherit an allele from his mother as well as his father, but his mother will not have had any influence on the sex ratio of her offspring, because she did not express the gene. In effect, therefore, the inheritance of an allele from the mother dilutes the inheritance of the sex ratio from father to son, though it should still be possible to detect.

It is also suggested that the gene may explain how a higher rate of male mortality results in an increase in male births, both after wars and during peacetime. If it is assumed that male mortality is distributed to some extent evenly between families, then families with more sons ought to have relatively more sons still alive after the mortality. This should result in more males being born in the next generation, because males with more brothers inherit their fathers tendency to produce more males.

Methods

Population Genetic Model

A computer model was designed to run simulations, in which variants of the hypothesised gene controlled the sex ratio at birth in a population. It was an individual-based model (IBM), with a finite number of individuals in each generation, each having a specific genotype and phenotype. IBM's, as defined by Uchmanski and Grimm (1996) differ significantly from classical equational models, including for example, the model used by Shaw and Mohler (1953), on which most subsequent sex ratio models have been based (Seger and Stubblefield 2002).

The main reason for using an IBM was to build a family structure into the population, to allow mortality simulations where males were removed from each family. It was recognised in preliminary modelling that a simulation where males are removed from the population at random, is of no interest, because genotypes are simply removed in the same relative frequencies with which they occur, causing no change in the genetic structure of the population and no change in the sex ratio. It would have been very difficult to incorporate a family structure into a classical equational model, because these models calculate the frequencies of specific genotypes or phenotypes as fractions of all those in the population, rather than those that belong to specific individuals whose families can be identified.

The model consisted of a database, in which the diploid genotype, phenotype and familial relations of each individual in each generation were stored. Iteration of each generation was managed by code written with the PHP scripting language. The generations were discrete and offspring were formed by monogamous breeding, except for some males, who were selected at random to father a second family when there was an excess of females in the population. All randomisation was determined by the PHP 'rand' function, which generates random integers within a chosen range. The carrying capacity of the population was 10,000 breeding pairs and the number of offspring produced by each breeding pair varied at random between one and seven, so at full carrying capacity approximately 40,000 offspring were born in each generation. In each generation, 10,000 males and 10,000 females were randomly selected from the offspring and randomly paired (unless they were brother and sister) to parent the next generation.

The genotype of every individual consisted of one of the four possible combinations of alleles from their parents,

determined at random. In this way, the model simulated random segregation of parental alleles in meiosis and random union of their gametes through sex, to form diploid offspring. An individual's sex was determined by their father's genotype. If the father's genotype was that for producing equal sons and daughters, for example, then there was an equal random likelihood of his offspring being either sex.

In each simulation there were either *m* and *f* alleles, or *m*, *f* and *i* alleles in the population. The *m* allele coded for production of male offspring, the *f* allele for production of female offspring and the *i* allele for production of equal male and female offspring. In Sim. 1, 2 and 3 there were only *m* and *f* alleles in the population. In Sim. 1 the alleles were expressed with incomplete dominance, so *mf* males were equally likely to have sons or daughters, whilst *mm* males produced only sons and *ff* males only daughters. In Sim. 2, the *m* allele was dominant and the *f* allele recessive, so *mf* and *mm* males produced only sons and *ff* males only daughters. In Sim. 3, the *f* allele was dominant and *m* allele recessive, so *mf* and *ff* males produced only daughters and *mm* males only sons. In Sim. 1a, 2a and 3a, the dominance relationship between the *m* and *f* alleles remained the same as in Sim. 1, 2 and 3, respectively, but an *i* allele was introduced in each simulation, which was dominant in all genotypes, so *mi*, *fi* and *ii* males were all equally likely to produce sons and daughters.

In Sim. 4, the effect of persisting higher male mortality was examined, by removing a single pre-reproductive male offspring from each family in every generation, in a simulation otherwise identical to Sim. 1. Sim. 5 aimed to test the effect of a single episode of higher male mortality, as would occur in a war, by removing either 0, 1 or 2 pre-reproductive male offspring from each family in generation 500 of Sim. 1, then allowing the following 10 generations to reproduce without any mortality occurring.

Genealogical Meta-Database

To look for evidence of heritable variation in the human sex ratio, a database was designed to hold data extracted from GEDCOM [Genealogical Data Communications] files. These files are widely used to store and exchange family tree data, and many are posted online by amateur and professional family tree researchers. The purpose of the database was to calculate the sex ratio of each individual's offspring and to compare the sex ratios produced by related individuals. It was technically a meta-database, because each family tree extracted from a GEDCOM file was effectively a sub-database that could be added or removed.

The GEDCOM files were mostly downloaded from The Genealogy Forum (GenealogyForum.com 2008). The majority were North American family trees—many with European roots, whilst the rest were mostly European. A rigorous process was used to select only those files that contained the most accurately compiled family trees. A family tree was not included in the database if it contained any of the following errors or potential sources of error: relationships to unlisted individuals; individuals related to more than two parents; stated number of offspring in a family not matching actual number; individuals listed as offspring of one sex and parents of another sex; time between dates of birth precluding possibility of the stated relationship between individuals; low mean number of offspring per family due to inclusion only of the author's direct ancestors and not their ancestor's siblings; family connection to very ancient or fictional persons. In total 927 family trees were included in the database, containing a total 556,387 individuals and 34 to 8,931 individuals per tree. It was not possible to check the factual accuracy of the family histories in any of the trees, but it is likely that the trees included in the database represent a higher standard of genealogical research, because they did not contain the errors detected in the other family trees.

The analysis of sex ratio inheritance included up to three generations of a family. In subsequent discussion, the grandparents of a family are referred to as the F0 generation and their offspring are the F1 generation, whilst the proportion of the F1 generation that are male is the F1 sex ratio. Likewise, the offspring of the F1 generation are the F2 generation and the proportion of the F2 generation that are male constitutes the F2 sex ratio.

All F1 individuals used in the analyses had a name and accurate date of birth, which allowed for duplicate records to be removed based on a match of that information. It is clear that family trees become less complete further back in time, so it was decided to include only F1 individuals born after 1599 in the analyses. This is after the establishment of parish records for births, marriages and deaths in the 16th century, e.g. in England, Germany and the Netherlands, where many of the family trees originate.

Results

Population Genetic Modelling

Frequency Dependent Selection

In Sim. 1 (Figs. 3, 4a), a dynamic equilibrium developed between the sexes, resulting in a sex ratio close to parity over 500 generations (Mean = 0.501, SD = 0.01). This occurred because the rarer sex had a better chance of being randomly paired with the opposite sex to breed, whilst the rarer sex were more likely to have inherited and so pass on

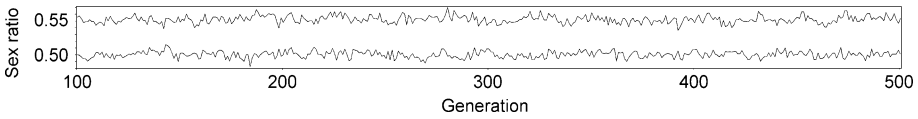

Fig. 3 Sex ratio of births in generation 100–500 of Sim. 1 (lower line) and Sim 4. (upper line)

the allele for production of the rarer sex, causing more of that sex to be born in the next generation. The increase in one sex due to its lower frequency in the population caused it to become more frequent, so the opposite sex then became the rarer sex and began to increase; and so on. It is clear that frequency dependent selection is occurring in the model, whether or not this genetic mechanism exists in nature.

Autocorrelation

In Sim. 1, the sex ratio was significantly autocorrelated between generations (1st order autocorrelation = 0.708, $P < 0.001$). This occurred because the sex ratio produced by the parents in any generation was the result of the alleles that they had inherited from their parents, causing the sex ratio to change gradually and non-randomly from one generation to the next.

A Dominant m or f Allele

In Sim. 2 and 3 (Fig. 4b and c) the *m* and *f* alleles were dominant or recessive, whereas in Sim. 1 neither allele was dominant. It was seen that an equilibrium sex ratio still occurred in these simulations, because frequency dependent selection was operating on the individual phenotypes, i.e. the sex of each individual, which determined the probability of those individuals being able to breed. It can be seen in Fig. 4 and Table 1 how the frequency of genotypes and alleles was readjusted by the 'requirement' of selection for males or females to be born, so that a sex ratio equilibrium was maintained regardless of the dominance of alleles.

A Dominant i Allele

The aim of introducing a dominant *i* allele was to test whether selection would eliminate the variant *m* and *f* alleles in favour of the *i* allele, because it is well known that frequency dependent selection will draw the sex ratio toward an equilibrium value. It can be seen in Table 1, that regardless of the dominance relationship between the *m* and *f* alleles, over 500 generations a dominant *i* allele does not exclude the other alleles.

Increased Male Mortality in all Generations

In Sim. 4, the removal of a male offspring from each family in all generations resulted in a Mean sex ratio of 0.553 over 500 generations, which is significantly different from

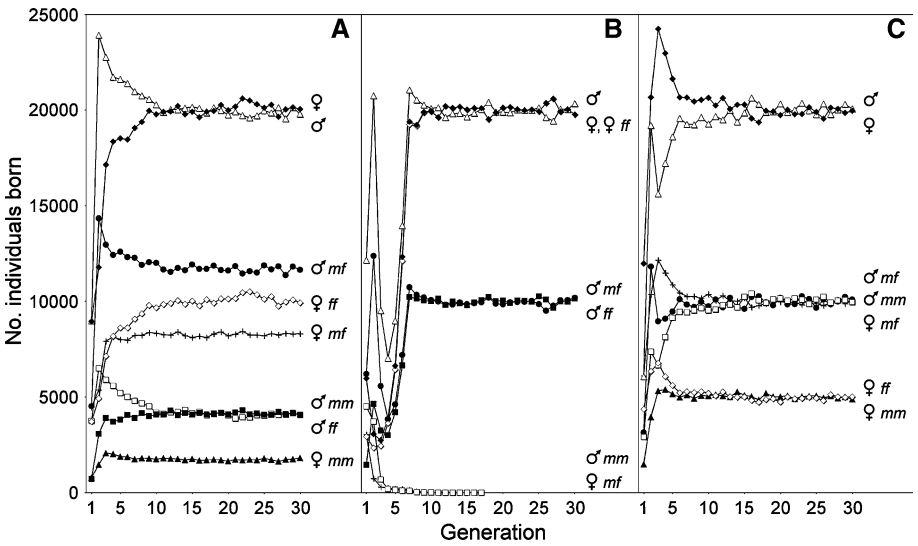

Fig. 4 The sexes and genotypes of offspring born in the first 30 generations of Sim. 1 (**a**), Sim. 2 (**b**) and Sim. 3 (**c**). In each case an equilibrium state has been reached by F30 and each sex and genotype remain at a similar frequency through to F500. The simulations all started with 1,500 individuals of each genotype and sex. In Sim. 2 (**b**) *mm* females were never born, because males with the dominant *m* allele produced only sons, this caused *mf* females to disappear by F18 and all females were *ff* thereafter, causing *mm* males to disappear in F19 because sons could not inherit an *m* allele from their mothers. In Sim. 3 (**c**) *ff* males were never born, because all males with the dominant *f* allele produced only daughters, though all other genotypes were maintained at stable frequencies

Table 1 Mean sex ratio, genotype and allele frequencies in each simulation

Sim	Allele dominance	Sex ratio	Genotype frequencies (%)						Allele frequencies (%)		
			mf	*mm*	*ff*	*mi*	*fi*	*ii*	*m*	*f*	*i*
1	$m = f$	0.501	♂ 29.34	♂ 10.45	♂ 10.34				39.76	60.24	
			♀ 20.7	♀ 4.29	♀ 24.88						
2	$m > f$	0.502	♂ 25.14	♂ 0.1	♂ 24.96				12.7	87.3	
			♀ 0.05	♀ 0	♀ 49.75						
3	$m < f$	0.499	♂ 24.96	♂ 24.9	♂ 0				62.41	37.59	
			♀ 25.06	♀ 12.5	♀ 12.58						
1a	$i > (m = f)$	0.502	♂ 13.76	♂ 5.72	♂ 5.53	♂ 10.51	♂ 10.28	♂ 4.4	29.94	40.53	29.53
			♀ 11.17	♀ 2.93	♀ 10.64	♀ 7.15	♀ 13.51	♀ 4.4			
2a	$i > (m > f)$	0.504	♂ 7.11	♂ 0.94	♂ 7.65	♂ 7.09	♂ 17.7	♂ 9.86	11.59	44.03	44.38
			♀ 3.41	♀ 0.26	♀ 11.61	♀ 3.17	♀ 21.33	♀ 9.87			
3a	$i > (m < f)$	0.498	♂ 9.79	♂ 10.54	♂ 0.92	♂ 16.35	♂ 6.19	♂ 6.01	41.63	23.74	34.63
			♀ 10.66	♀ 6.47	♀ 4.37	♀ 12.45	♀ 10.24	♀ 6.01			
4	$m = f$	0.553	♂ 32.0	♂ 13.39	♂ 9.88				44.19	55.81	
			♀ 19.79	♀ 4.9	♀ 20.04						

All simulations ran for 500 generations and started with 1500 individuals of each genotype and sex

equality, using chi-square to compare the average proportion of each sex ($\chi^2 = 444.23$, d.f. = 1, $P < 0.001$), unlike Sim. 1, which was a comparable simulation without any mortality occurring and where the sex ratio did not deviate significantly from equality ($\chi^2 = 0.24$, d.f. = 1, $P > 0.8$). It can be seen that there was a higher frequency of the *m* allele and a higher frequency of the *mm* genotype in relation to the *ff* genotype in the population (Table 1), which was the cause of the higher sex ratio.

Increased Male Mortality in a Single Generation

In Sim. 5, the removal of one or two pre-reproductive males from all families in F500 caused a sudden peak in the sex ratio in F501, which, in the case of two males being removed, was also followed by a raised sex ratio for several more generations (Fig. 5). A chi-square test was used to test whether the sex ratio in each generation differed from a null expectation of equality. It was seen that no generations differed from equality for 0 males removed; F501 ($P < 0.001$), F507 ($P < 0.01$) and F510 ($P < 0.05$) differed for 1 male removed; and F501–507 ($P < 0.001$) differed for 2 males removed.

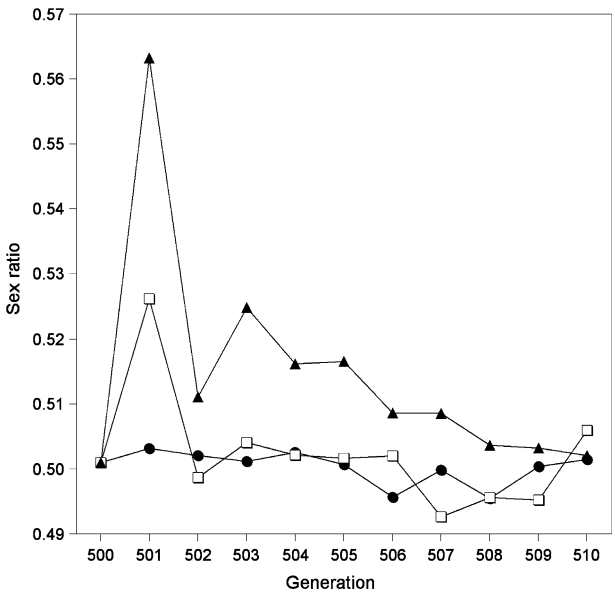

Fig. 5 The result of removing 0 (*circles*), 1 (*squares*), or 2 (*triangles*) pre-reproductive males from every family in generation F500, on the sex ratio of offspring born in the following 10 generations

Genealogical Database

Test for Association of F2 and F1 Sex Ratio According to F1 Sex, Using Regression Analysis

To test whether the sex ratio produced by individuals of either sex was correlated with that produced by their parents, a regression analysis was carried out with the dependent variable as Mean F2 sex ratio produced by >1 F1 full-siblings of the same sex, where each sibling had >4 offspring. The independent variables were F1 sex ratio and F1 sex. The results of this test indicate that together F1 sex and F1 sex ratio are significantly related to F2 sex ratio ($F_{2,\ 1808} = 5.588$, $P < 0.004$), explaining 0.5% of the variation, whilst F1 sex itself is a significant predictor of F2 sex ratio ($F_{1,\ 1809} = 7.076$, $P = 0.008$), explaining 0.3% of the variation. A separate regression analysis was then conducted for each F1 sex using the same data, which showed

that F2 sex ratio is significantly associated with F1 sex ratio when produced by F1 male offspring ($n = 1224$, $t = 2.584$, $P = 0.01$), with F1 sex ratio explaining 0.5% of the variation in F2 sex ratio. In contrast, no association with F1 sex ratio was detected when the F2 sex ratio was produced by F1 females ($n = 587$, $t = 0.269$, $P = 0.788$).

Sex Ratio Heritability Estimate

An estimate of heritability (h^2) can be derived from the value of the partial regression coefficient [b] in a mid-offspring on mid-parent regression, in which case heritability of the sex ratio by males is 0.057 ± 0.022.

Test of the Absolute Difference between F2 and F1 Sex Ratio According to F1 Sex, Using a Paired t-Test

A paired t-test was carried out to compare the absolute difference from the F1 sex ratio of the Mean F2 sex ratio (| Mean F2 sex ratio − F1 sex ratio |) between F1 male and F1 female siblings from the same families. All F1 and F2 families had >4 offspring and F1 families had at least one male and one female offspring. It was found that the difference between Mean F2 and F1 sex ratio was less for male (0.1704 ± 0.0103, 99% c.i., $n = 1098$) than female (0.1851 ± 0.0109, 99% c.i., $n = 1098$) siblings ($t = 2.738$, $P = 0.006$), which indicates that males produce a sex ratio more similar to that produced by their parents.

Test for Association of F2 and F1 Sex Ratio According To F1 Sex, Using a Generalized Linear Model

The regression and t-test analyses used only families with >4 offspring, which reduced error because larger family sizes give a better indication of the true sex ratio producing tendency of the parents, but this also reduced the sample size. In order to include a greater proportion of the available data, a generalized linear model with binomial errors was used (R statistical package), which tested whether the total proportion of F2 males and F2 females (grandchildren) descended from F0 parents (grandparents) was dependent either on F1 no. offspring or F1 sex ratio, where the F2 offspring were produced either by F1 males or F1 females. The response variable was the untransformed proportional data of the F2 males and F2 females, whilst F1 sex ratio and F1 no. offspring were included as explanatory variables in separate tests for F1 males and F1 females. All records included >1 offspring in each family. The tests indicate that F2 sex ratio is significantly associated with the F1 sex ratio when it is sired by F1 males ($F_{1,\ 13420} = 4.403$, $P = 0.035$), but not when it is sired by F1 females ($F_{1,\ 10987} = 0.004$, $P = 0.947$). F1 no. offspring was not significant in either case, neither was the interaction between F1 no. offspring and F1 sex ratio.

Discussion

It has been shown with a large genealogical dataset, sourced mostly from North America and Europe over the last four centuries, that there is a heritable component in the human sex ratio. It is seen that males tend to produce a sex ratio like that produced by their parents, whereas females do not. This confirms the findings of Trichopoulos (1967) and Curtsinger et al. (1983). It also corroborates the findings of Morton et al. (1967) and Khoury et al. (1984) from interracial crosses, which showed that the sex ratio of offspring is closer to that which is typical of the father's, rather than the mother's race.

A possible problem with the genealogical data used in this study, is that much of it was collated by amateurs researching their own family trees. Although the family trees were filtered for errors and it can be argued that family members are the best people to research their own trees, some of them are still likely to contain incorrect family connections and incomplete families. This is apparent from the above expected excess of males in the database, which is probably due to males being more easily traced through the family name. It is unlikely, however, that this excess recording of males could have affected the results of the study. In all of the tests of the data, the sex ratio produced in one generation was tested for association with the sex ratio produced by sons or daughters in the next generation. It was found, not only that males with more brothers had more sons, but males with more sisters had more daughters, which would not be expected if the results were simply due to excess recording of males.

Another problem with genealogical data, is that the accuracy of male parentage is hard to know. In particular, this has a bearing on the estimate of heritability of the sex ratio by males, which may well be higher than the value of 0.057 ± 0.022 reported here. If it is reasonably assumed that female parentage is more accurate in genealogical data, then if females do inherit the sex ratio from their parents it will be easier to detect than in males. In fact, it was not detected in females, which suggests that females either do not inherit or do not express a sex ratio gene.

A Male-Expressed, Autosomal Gene

A pattern of inheritance in which males demonstrate greater heritability of the parental sex ratio has been shown in experimental populations of the crustaceans *Branchipus schaefferi* (Beladjal et al. 2002) and *Tigriopus californicus* (Voordouw et al. 2005), also the polychaete worm

Ophryotrocha labronica (Premoli et al. 1996). Of the hypotheses that have been offered to explain this pattern of inheritance, a meiotic-drive gene on the Y chromosome (Beladjal et al. 2002) might explain the pattern in humans. Except, the human data shows continual variation in heritability, so males with more sisters have a tendency to produce more daughters, which cannot be due solely to a Y chromosome gene, because such a gene would be diminished by producing daughters. If the female-producing tendency were due to separate genes that suppress the meiotic-drive gene then continual variation would not be seen. Variable dosage of a sex-determining supernumerary B chromosome has been suggested to explain male-specific inheritance and continual variation in *B. schaefferi* (Beladjal et al. 2002), but supernumerary chromosomes are unusual in humans and often associated with malformations (Fuster et al. 2004). Another hypothesis is that a polygenic system gives the father zygotic control over sex, so after fertilisation the equal sex ratio imposed by a major sex-determining gene in the mother is modified (Premoli et al. 1996), but this idea has been criticised on the basis that the polygenic system would presumably also be transmitted through females (Voordouw et al. 2005). A male-expressed, autosomal gene of the type proposed here, is capable of explaining the sex ratio patterns observed in the polychaete worm and crustaceans, it is also the most parsimonious explanation, because it involves common inheritance and a single gene, rather than intragenomic conflict and polygenic effects.

An indication that inheritance is via an autosomal gene, is the low h^2 value observed. If the gene were on the Y chromosome, then male offspring would inherit the same sex ratio producing tendency as their fathers and h^2 would be higher. A male-expressed, autosomal gene would also explain why, even though bulls and boars seem to have a tendency to produce more of one or other sex (Chandler et al. 1998), it has not been possible to select for a sustainable sex ratio bias in these males. It would be because male offspring inherit an unknowable allele from their mothers, which causes them to produce a different sex ratio from their fathers.

Mechanism

A segregation distorter acting at some stage in spermatogenesis, is the most obvious potential heritable mechanism by which males may affect the sex ratio. In humans, a correlation between greater production of X or Y sperm and paternity of exclusively or predominantly female or male children was shown by Bibbins et al. (1988) and Dmowski et al. (1979), though not by Irving et al. (1999), whilst it has been shown quite conclusively in bulls and boars (Chandler et al. 1998). Graffelman et al. (1999) screened approximately 200 spermatozoa from 176 men using FISH analysis. An average of 50.3% of sperm were Y-bearing, which is lower than the secondary sex ratio of 51.3% and leads to the conclusion that the male-bias in live births cannot be ascribed to a systematic semen sex ratio bias. It is a reasonable conclusion, except it is based on the assumption that there is a normal distribution around a mean value of 51.3% Y-bearing sperm. If, in fact, there is a polymorphism in the population, with perhaps 20% of men producing either more X or more Y, as predicted by the present hypothesis, then there would have only been about 35 males with biased sperm in this sample, more of which may have been X-biased by chance.

A number of studies have shown a negative correlation between the sex ratio and paternal age (e.g. Ruder 1985; James and Rostron 1985; Jacobsen et al. 1999), which indicates that there is some paternal control over the sex ratio. It is possible that this is due to facultative or age related changes in a segregation distorting mechanism acting in spermatogenesis, though it could also be due to behavioural changes associated with ageing, e.g. reduced rate of copulation (James and Rostron 1985). The analysis of heritability in this study did not control for age of parents, though it is thought unlikely that it is an explanatory factor in the result, because this would require the age of fatherhood to be significantly correlated between fathers and sons.

Male Mortality

In Sim. 4, the removal of one pre-reproductive male from each family in every generation caused a permanent male-bias in the sex ratio (Fig. 3, Table 1). This occurred because the mortality resulted in a greater relative decline in sons from families with less sons, which were the males most likely to have inherited the *mf* and *ff* genotype and so produce female offspring. It is possible to think of this in terms of the percentage of males removed from each family; removing a single son from a family with two sons removes 50% of their sons, whilst from a family with five sons, it removes 20%. Across a population, this translates to a greater loss of males from families with less sons.

In Sim. 5 (Fig. 5), the mortality in generation F500 caused a sudden peak in the sex ratio of F501, for the same reason described above. The reason the sex ratio drops off in F502, is because the fathers of that generation inherited half their alleles from their mothers, who were unaffected by the mortality and so passed a normal complement of alleles to their sons. The sex ratio rises in the following generations, because of the overall decline in *f* alleles caused by the mortality, which is only reversed by frequency dependent selection several generations later. The resemblance of the response to mortality is similar to the

WWI peak in Fig. 1. However, Fig. 1 is based on annual sex ratio, whilst the simulation is by generation. The sex ratio peak after WWI (Fig. 1) was highest in 1919 (0.5144) and dropped off quite quickly in the following years, falling below the 1918 (0.5117) value in 1923 (0.5108). Sim. 5 does not explain why the sex ratio dropped off within the space of a few years, rather than in the next generation. It is suggested that this occurred, because males who had been too young to fight in the wars began reach sexual maturity and father children in the years after the war.

It should be recognised that the distribution of male mortality in Sim. 4 and Sim. 5 was unrealistically simple. It is obvious, for example, that male mortality was not distributed completely evenly between families during the wars, as it was in the simulations; nonetheless, it also seems that it did not occur completely at random. A search of British Army WWI service records (1914–1920), recently made available online (Ancestry.com 2008), shows that for 711,547 soldiers aged 16–60 in 1920, their mean age in 1914 at the outbreak of war was 26.78 and modal age was 18. 50.3% of these soldiers were born within 12 years of each other (1888–1899) and 95.3% were born between within 29 years of each other (1872–1900). It seems that soldiers were drawn from a fairly narrow age cohort, which quite possibly caused them to be fairly evenly distributed between the nation's families, though further work is required to confirm this.

A Stable Polymorphism

It was shown in the model simulations (Figs. 3, 4) that selection acting on the proposed gene will cause the frequency of each sex born to continually oscillate from an excess of one sex to the other, as the sex ratio is maintained near to equality in a dynamic equilibrium. It is notable that previous authors have described oscillations in the human sex ratio, occurring with approximately 30 year amplitude and within remarkably restricted ranges (Gini 1955; James 1995), which can be explained by this result.

It is interesting that when the *m* or *f* allele was dominant, the sex ratio was still maintained near to equality. It shows how brood sex ratios can be exclusively male or exclusively female, whilst the population sex ratio can be 1:1, which is a pattern that has been observed in the freshwater snail *Pomacea canaliculata* (Yusa and Suzuki 2003).

It is interesting that the dominant *i* allele did not become fixed in the population, even though this would have caused all males to father equal male and female offspring. It suggests that for some reason selection does not cause the sex ratio to level out into a stable equilibrium, but causes it to persist in a dynamic equilibrium. There are two important aspects to understanding why this happens:

Firstly, consider the simple sex ratio model of Shaw and Mohler (1953), which showed that '[w]henever the primary sex ratio of a population is not 0.5, selection favors sex ratio genes whose increase in frequency will cause a shift closer to 0.5… [but when] the population sex ratio is already 0.5 there is no selection for sex ratio genes no matter what the direction or magnitude of their effects' (Shaw and Mohler 1953). There is no selection occurring when the sex ratio is at 0.5, because all individuals have an equal chance of being able to breed. This explains why the dominant *i* allele did not exclude the *m* and *f* alleles in Sim. 4. If the sex ratio of the breeding population is biased toward one sex, frequency dependent selection will cause individuals who produce offspring of the more frequent sex to pass on less of their genes. As the population sex ratio gets closer to 0.5, the strength of selection gets progressively weaker, until at 0.5 it doesn't matter what sex ratio of offspring is produced, because all individuals have an equal chance of breeding, and any sex ratio biasing alleles cannot be deselected.

Secondly, it needs to be understood why the sex ratio deviates from equality once selection has returned it to equality. Consider an F1 generation where the sex ratio at birth has become equal after being male-biased in the F0 generation. Individuals born in the F1 generation have inherited their genotype from the F0 generation, in which males were the more frequent sex and where females had a greater chance of reproducing. As a consequence, F1 individuals were more likely to inherit the tendency to produce female offspring, which means that when the F1 males breed (and every individual has an equal chance of breeding when the sex ratio is equal) the sex ratio of the F2 offspring will be female-biased. It is because selection effectively acts to reverse biases in the sex ratio, but there is no selection when the sex ratio is equal, that the sex ratio perpetually oscillates from an excess of one sex to other. It is a homeostatic type process.

Sex-Allocation

Sex ratio theory that is based on the equal-investment principle is often described as sex-allocation theory, because it is based on the concept that resources are allocated toward the production of either sex. In his account of sex-allocation theory, Charnov (1982) explains that higher male mortality in childhood causes an increase in the primary sex ratio, because it frees parental resources for investment in other offspring, which causes selection to favour overproduction of males to substitute for those that die. A difficulty with this explanation, is that the actual details of selection are not made clear and it is not explained how selection causes differentials in parental resource expenditure to affect the genes that parents pass to

their offspring. It is true that sex-allocation theory explains many sex ratio phenomena in terms of facultative adjustment, but it is not clear that Charnov (1982) or indeed Fisher (1930) were describing selection acting on a facultative mechanism to bias the sex ratio in response to male mortality. If the mechanism is not facultative, then for parental resource expenditure to affect the genes that parents pass to offspring, it must affect the genes that are passed into the gametes during meiosis, which would entail non-random, non-Mendelian segregation. In fact, non-Mendelian segregation due to the action of meiotic-drive genes has been hypothesised to explain male or female biased broods in various species, as well as greater heritability of the parental sex ratio by male *B. schaefferi* (Beladjal et al. 2002). It should be pointed out, however, that the evidence for meiotic-drive genes is tentative, because no genetic markers have been found and the existence of the genes is inferred from the brood sex ratios of crosses (Pomiankowski and Hurst 1999).

In contrast to a meiotic-drive type mechanism, the genetic mechanism proposed in the present study functions by Mendelian, random segregation of alleles, which is typical of genetic systems. It can explain how frequency dependent selection regulates the sex ratio, how increased male mortality causes the sex ratio to rise and why autocorrelation and oscillations occur. It also suggests that the recent declines in male births in many countries is due to frequency dependent selection readjusting the sex ratio downwards after the high reached in the generations after the World Wars, because of the massive loss of young men and their genes, during the conflicts.

It is argued here that the sex ratio is ultimately under genetic control, with selection acting at the interface between the individual and the population, through the probability of an individual finding a member of the opposite sex to breed with. It does not act directly on the ratio of X:Y sperm or the ratio of sons to daughters, this is indirectly affected by the probability of those sons and daughters being able to breed and thereby pass on the alleles that caused them to be either male or female. A deviation in the sex ratio of the population is not corrected by a physiological response in the parents, although this is what seems to happen with the immediate increase in male births after wars. It is important to make the distinction between the genetic mechanism described here and facultative mechanisms of sex ratio control, which are physiological responses, in which the sex ratio of offspring is adjusted by a parent in response to the prevailing conditions, in order to enhance the probability of their offspring surviving and reproducing.

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