Cliff-edge model of obstetric selection in humans

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The strikingly high incidence of obstructed labor due to the disproportion of fetal size and the mother's pelvic dimensions has puzzled evolutionary scientists for decades. Here we propose that these high rates are a direct consequence of the distinct characteristics of human obstetric selection. Neonatal size relative to the birth-relevant maternal dimensions is highly variable and positively associated with reproductive success until it reaches a critical value, beyond which natural delivery becomes impossible. As a consequence, the symmetric phenotype distribution cannot match the highly asymmetric, cliff-edged fitness distribution well: The optimal phenotype distribution that maximizes population mean fitness entails a fraction of individuals falling beyond the "fitness edge" (i.e., those with fetopelvic disproportion). Using a simple mathematical model, we show that weak directional selection for a large neonate, a narrow pelvic canal, or both is sufficient to account for the considerable incidence of fetopelvic disproportion. Based on this model, we predict that the regular use of Caesarean sections throughout the last decades has led to an evolutionary increase of fetopelvic disproportion rates by 10 to 20%.

cephalopelvic disproportion | human evolution | natural selection | obstructed labor | obstetric dilemma

The incidence of obstructed labor in humans is strikingly high, in the range of 3 to 6% worldwide (1, 2). Most of these cases result from the disproportion of the newborn's head or shoulders and the mother's pelvic dimensions. Estimates of the incidence of cephalopelvic disproportion vary widely, depending on the criteria for diagnosis. In Africa, rates of cephalopelvic disproportion have been reported to range from 1.4 to 8.5% (3). US statistics suggest rates of 2.3% for infants weighing 3,000 to 3,999 g at birth, and 5.8% for those weighing 4,000 g or more (4). Without medical care, cephalopelvic disproportion often results in maternal and neonatal death or severe morbidity (5). Given this enormous—and in many parts of the world still persisting—selection pressure, it is puzzling why the pelvic canal has not evolved to be wider to reduce rates of obstructed labor.

At least 4 to 5 million years ago, bipedality evolved in the human lineage, long before brain size started to increase about 2 million y ago (6). The increasingly large-headed neonates thus had to be delivered through a pelvis that had earlier been adapted to bipedalism. It has been claimed that a wider pelvis would be disadvantageous for bipedal locomotion, hence constituting a selective force opposed to that of obstetrics ("obstetrical dilemma"; refs. 7–9). However, because the biomechanical benefit of a narrow pelvis presumably is small (10, 11), it remains unclear how a population's fitness loss due to the high rate of obstructed labor is outweighed by these minor advantages for bipedal locomotion.

Here we show that human obstetrics is subject to a particularly unusual selection scenario. The high proportion of mismatched individuals is a direct consequence of the inherently asymmetric fitness distribution of the size of the neonate relative to that of the mother's pelvic canal, even under weak directional selection.

The Obstetric Fitness Function. Successful labor requires the match of the neonatal head and shoulder dimensions with the dimensions of the maternal pelvic inlet, midplane, and outlet. Consider an idealized variable, D, that represents the difference between the size of the neonate and the size of the maternal pelvic canal. A negative value indicates a pelvic canal that can accommodate the newborn, whereas fetopelvic disproportion occurs if $D > 0$. In practice, this composite quantity cannot be inferred from the usual clinical measurements, but it is conceivable that D can be expressed as a function of a finite set of appropriate morphological measurements.

Neonatal size and maternal pelvic dimensions influence fitness (i.e., reproductive success) of the newborn and the mother in multiple ways. Undoubtedly, relative brain size had increased during human evolution in response to directional selection. Recently, it has also been suggested that the large human brain may be the result of runaway selection for the childcare of infants that are born prematurely because of their large brain (12). It is unclear whether any of this selection still persists after the slight decrease of brain size in the late Pleistocene. However, birth weight, which correlates with brain size at birth, is strongly positively associated with infant survival rate (13) and has also been reported to correlate negatively with the risk of multiple diseases (14). Reducing neonatal brain size by shortening gestation length seems to be equally disadvantageous: Delivery before term clearly increases the likelihood of impaired cognitive function in later life (15, 16). Grabowski and Roseman (17) identified a complex pattern of natural selection that has acted on the pelvis throughout hominin evolution, but no consensus has been reached about the actual benefit of a narrow pelvis for bipedal locomotion (7, 8, 10, 11). However, a narrow pelvic cavity might be advantageous for other reasons as well. During bipedal posture, the inner organs of the peritoneal

Significance

Compared with other primates, human childbirth is difficult because the fetus is large relative to the maternal pelvic canal. It is a long-standing evolutionary puzzle why the pelvis has not evolved to be wider, thus reducing the risk of obstructed labor. We present a mathematical model that explains the high rates of fetopelvic disproportion by the discrepancy between a wide symmetric phenotype distribution and an asymmetric, "cliff-edged" fitness function. Only weak selection for a large newborn, a narrow pelvis, or both is necessary to account for the high incidence of fetopelvic disproportion. Because the regular use of Caesarean sections has reduced maternal mortality, the model predicts an evolutionary response of fetal or maternal dimensions, increasing the rates of fetopelvic disproportion.

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cavity are vertically aligned with the rectal and urogenital orifices; the pelvic girdle thus supports the inner organs and, secondarily, also the neonate. Whereas in quadruped mammals the pelvic floor muscles are vertically oriented and mostly involved with the motion of the tail, the connective tissue and muscles of the horizontal pelvic floor in humans support the abdominopelvic organs and resist intraabdominal pressure exerted from above (18, 19). Pelvic organ prolapse as well as multiple other pelvic floor disorders and connective tissue defects, such as premature rupture of fetal membranes or cervical insufficiency, are common in human females, especially during pregnancy and after vaginal birth (20–22), suggesting a system very sensitive to perturbations. It has been shown that a wide pelvic cavity increases the probability of disorders: The transverse diameter of the pelvic inlet is correlated with the rate of pelvic floor disorders, including prolapse (23, 24).

In terms of our model, a large neonatal brain and body as well as a narrow maternal pelvic canal both lead to a large value of D and are positively associated with individual fitness (neonatal or maternal). Opposed to that, a large neonate relative to the pelvic canal increases the risk of obstructed labor. It has been shown that Caesarean section rate and maternal morbidity is only weakly related to neonatal head circumference for normal size variation, but beyond a critical value (90th to 95th percentile) obstructed labor and morbidity increase drastically (25–28). In our model, fitness increases with D until it reaches a maximum at $D = 0$; beyond this threshold, the neonate does not fit through the mother's pelvic canal anymore and fitness drops to zero (here the model refers to the situation before the safe availability of Caesarean sections). Individual female fitness, plotted as a function of D (the blue curve in Fig. 1*A*), has the form of an asymmetric "cliff edge" (29, 30): It increases continually before it drops suddenly. In the simplest version of the model, as presented in Fig. 1*A*, individual absolute fitness increases linearly with slope β_A on the left side of the cliff edge. For modern human variation, this linearity is supported by the medical literature cited above. However, the fitness slope may be higher for the offspring than for the mother because of an inherent discrepancy in the optimal amount of fetal provisioning that arises from the effects on future offspring (31); the slope β_A thus represents the average fitness increase.

The success of labor is not only influenced by D but also by numerous other factors, including flexibility of the pelvic ligaments, orientation of the neonate, and efficiency of uterine contractions (4, 5). However, as long as these factors are statistically independent of the discrepancy between neonatal and maternal dimensions, the selection gradient and evolutionary trajectory of D can be modeled independently of other factors (32, 33).

Variation of Birth-Relevant Dimensions. In contrast to the highly asymmetric fitness function, the dimensions of the head and the pelvis tend to be approximately symmetrically distributed (34–36). The difference, D, between birth-relevant neonatal and maternal dimensions can thus be considered a polygenic and symmetrically distributed trait. Importantly, D is affected both by maternal and neonatal genes, where half of the alleles affecting neonatal size are of paternal origin and therefore independent of the alleles that influence the mother's pelvis. If neonatal size and pelvic canal size vary independently, their variances sum up to that of D (*Materials and Methods*). Whereas both head size at birth and pelvic dimensions show considerable genetic variation (34, 37), gestational age at birth is heavily influenced by environmental factors (38–40). Heritability of gestation length has been estimated to be only 0.3 (41), where about two-thirds of this genetic variation are of maternal origin and one-third is of fetal origin (42). Furthermore, female pelvic remodeling extends into late adulthood (43, 44); the dimensions of the pelvic canal thus are also influenced by the mother's age. For those reasons, phenotypic variation of D is large, highly polygenic, and has a strong environmental component. Recombination between maternal and paternal alleles—in addition to the environmental effects—is likely to maintain an approximately symmetric and wide trait distribution, despite the asymmetric fitness function.

A Model of Obstetric Evolution. The mean population fitness (i.e., the average number of offspring per individual in the population) is given by the integral of the product of the fitness function and the trait distribution of D. For the cliff-edged fitness function introduced above, Fig. 1*B* shows the mean population fitness for a range of mean phenotypes, μ_D, assuming constant standard deviation (SD), σ_D. Such a plot is referred to as an adaptive landscape (45, 46). It has been shown that in the standard case of adaptive evolution toward a single fitness maximum the population mean of a quantitative trait approaches the fitness peak, that is, the population moves uphill on the adaptive landscape (32, 45).

In these standard models, the fitness distribution is symmetric, and the trait mean that maximizes the population mean fitness thus is equivalent to the trait value with maximal individual fitness. This differs from the evolutionary scenario with an asymmetric fitness function. The symmetric phenotype distribution cannot match the cliff-edged fitness distribution well: The population optimum is shifted toward the flatter shoulder of

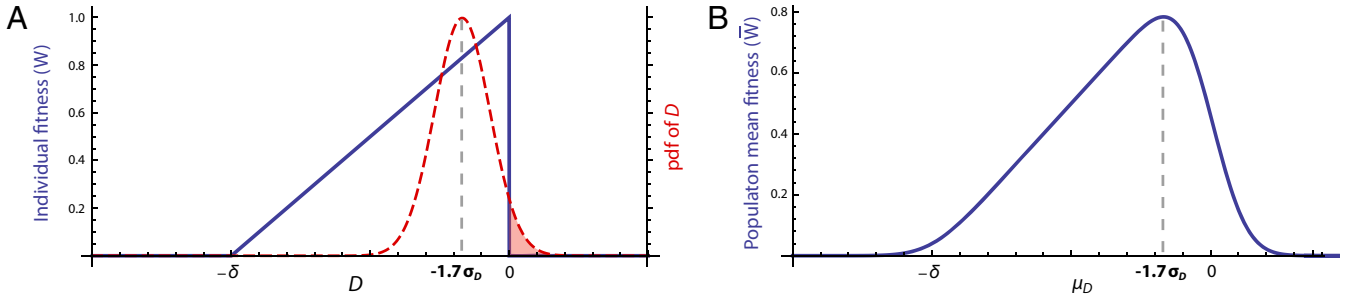

Fig. 1. The cliff-edge model of obstetric selection. (*A*) Model I: The discrepancy, *D*, between neonatal size and maternal pelvic canal size is approximately normally distributed in a population with mean μ_D and SD σ_D. The red dashed curve shows the probability density function (pdf) of *D*. Individual female fitness, *W* (blue curve), increases linearly with *D* to its maximum at $D = 0$; thereafter fitness drops to zero because of fetopelvic disproportion. In this example, the fitness function has a slope of $\beta_{A\sigma} = 0.1$ units absolute fitness per SD of *D*. (*B*) The corresponding adaptive landscape: population mean fitness, $\bar{W}$, plotted against μ_D, the population mean of *D*. Because of the asymmetric fitness function, the trait mean that maximizes population fitness deviates from the trait value with maximal individual fitness; in this example it is situated 1.7 SDs of *D* to the left. This optimal phenotype distribution entails a 4.5% rate of individuals with fetopelvic disproportion, that is, with $D > 0$ (the red area in *A*). This fraction neither depends on the maximum value of absolute fitness nor on the scale of *D*, only on the linear fitness increase per SD ($\beta_{A\sigma} = \sigma_D/\delta$).

the individual fitness curve (30, 47, 48). The mean of D that maximizes population fitness thus deviates from the individual fitness maximum at $D = 0$ (Fig. 1*B*). This also leads to the—seemingly paradoxical—situation where the optimal trait distribution involves a fraction of individuals falling beyond the "fitness edge," that is, with zero fitness (the red area in Fig. 1*A*). In other words, as long as the size of the neonate relative to that of the maternal pelvic canal is positively associated with reproductive success (increasing fitness for $D < 0$), the population will evolve a distribution of D that implies a constant fraction of individuals subject to fetopelvic disproportion.

The larger the slope of the fitness function on the flat shoulder, that is for $D < 0$, the faster will the trait distribution evolve toward the fitness edge and the closer toward the edge will the optimal population mean lie. This results in an increase of the fraction of individuals with $D > 0$ (Fig. 2*A*). In other words, the model predicts a higher rate of obstructed labor if the strength of selection for a large neonate, a narrow pelvis, or both is increased. The fraction of individuals with $D > 0$ for a given selection pressure can only be reduced by reducing phenotypic variation, the dispersion of D. The wider the phenotype distribution, the larger the number of individuals affected by obstructed labor (Fig. 2*A*; see also ref. 48). In other words, for a population with a mean phenotype close to the edge, the fitness function imposes a stabilizing selection gradient on D. But in the case of obstetric evolution the variation of the composite trait D, with its complex genetic structure and strong environmental component, cannot easily be reduced by stabilizing selection on either maternal or fetal dimensions separately. However, positive correlation between fetal size and maternal pelvis dimensions can reduce the variance of D (*Materials and Methods*). Indeed, neonatal head size and maternal pelvis shape have been found to covary (36), presumably via pleiotropic genetic effects. Furthermore, size and weight of the newborn are correlated with maternal stature and pregnancy weight (39, 49, 50). This correlation is partly driven by the genes shared between the mother and the fetus (51), but the fetus also develops under the influence of the maternal environment. For example, data from in vitro fertilizations with egg donation have shown a correlation of infant birth weight and head circumference with the height of the genetically unrelated mother (52). Although this integration of neonatal and maternal dimensions may have evolved as an adaptation to the specific obstetric selection scenario, there is still independent variation: The discrepancy, D, varies considerably more than fetal and maternal dimensions separately.

The simplest version of the cliff-edge model as presented in Fig. 1 (linear fitness increase and normally distributed D) has a single parameter only: $\beta_{A\sigma}$, the absolute fitness increase per SD of D (*Materials and Methods*). When $\beta_{A\sigma}$ is divided by the population mean fitness, the resulting parameter expresses the increase of relative fitness per SD of D, which equals the well-known standardized directional selection gradient, β_σ (53). This relationship allows us to infer the directional selection gradient on D for a given rate of fetopelvic disproportion. For example, a population with a 4.5% rate of disproportion at its population optimum (evolutionary steady state) implies $\beta_{A\sigma} = 0.1$ units increase of absolute fitness per SD of D and $\beta_\sigma = 0.12$ (Fig. 2*A*; see *Materials and Methods* for more details). Considering the wide range of reported incidences, disproportion rates of 2 to 6% translate into absolute fitness slopes of 0.05 to 0.13 and standardized selection gradients of 0.06 to 0.16. Studies of numerous morphological and life-history traits in animals have shown that standardized selection gradients typically are rather modest (median 0.15, mean 0.2 of absolute values) but with a long tail of larger values (54–56). According to our model, the current rates of fetopelvic disproportion thus suggest the persistence of moderate directional selection on D toward larger size of the neonate relative to that of the maternal pelvic canal. However, it is not clear from our model whether selection is acting on the neonate, on the maternal pelvic canal, or on both.

The cliff-edge fitness function in Fig. 1 can also be described as consisting of two opposing directional selection regimes: linear selection with slope β_A favoring larger D, and truncation selection favoring smaller D with the threshold at $D = 0$, where truncation selection is known to be the most efficient form of selection (57, 58). At the evolutionary steady state, that is, for the mean phenotype with maximal population fitness, these two directional selection gradients cancel. If phenotypic variance stays constant, the remaining stabilizing selection gradient leads to a constant fraction of cases with fetopelvic disproportion, which equals the tail of the phenotype distribution beyond the fitness threshold.

Selection on birth-relevant pelvic dimensions may not necessarily originate only from obstetrics. Due to the developmental and structural integration of the pelvis, other selection regimes, including thermoregulation (59–61), can have an indirect effect on the pelvic canal (17, 33, 62). The directional selection gradient on D may also comprise effects other than actual selection, such as plastic responses to environmental changes. The balance between maternal and fetal interests depends on the environment in which it is negotiated; it may be disrupted

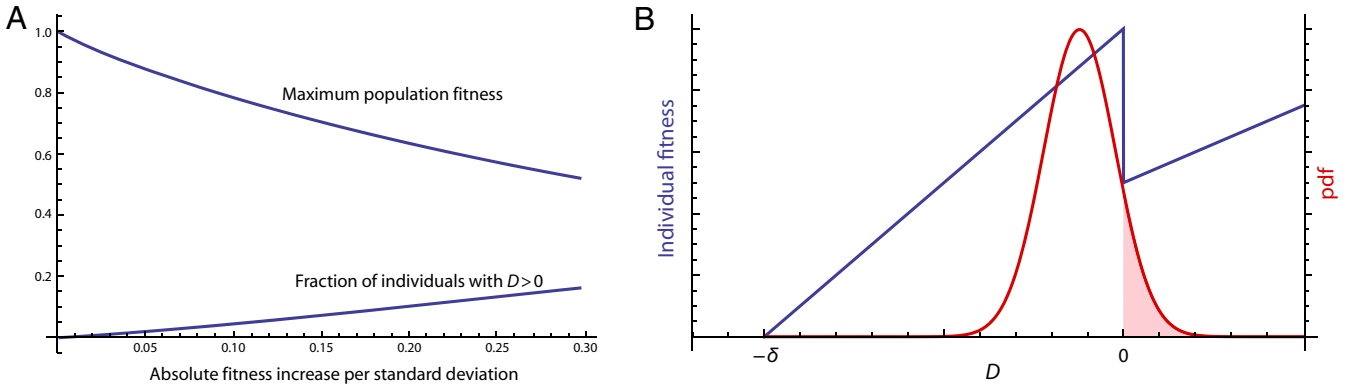

Fig. 2. (*A*) Effect of fitness increase on the rate of individuals beyond the "fitness edge." If $\beta_{A\sigma}$, the absolute fitness increase per SD of *D*, increases, the maximum population fitness decreases and the fraction of individuals beyond the fitness edge (i.e., with $D > 0$) increases. (*B*) Model II. Individual fitness, averaged over both sexes, increases linearly with *D*, until it drops to zero at $D > 0$ for females but continues to increase for males. Assuming a sex ratio of 1/2 and a fitness increase of $\beta_{A\sigma} = 0.1$ per SD, a mean of $\mu_\sigma^* = -1.2\sigma_D$ maximizes the population mean fitness across both sexes, entailing a disproportion rate of 11.1%, which is more than twice as much as in model I.

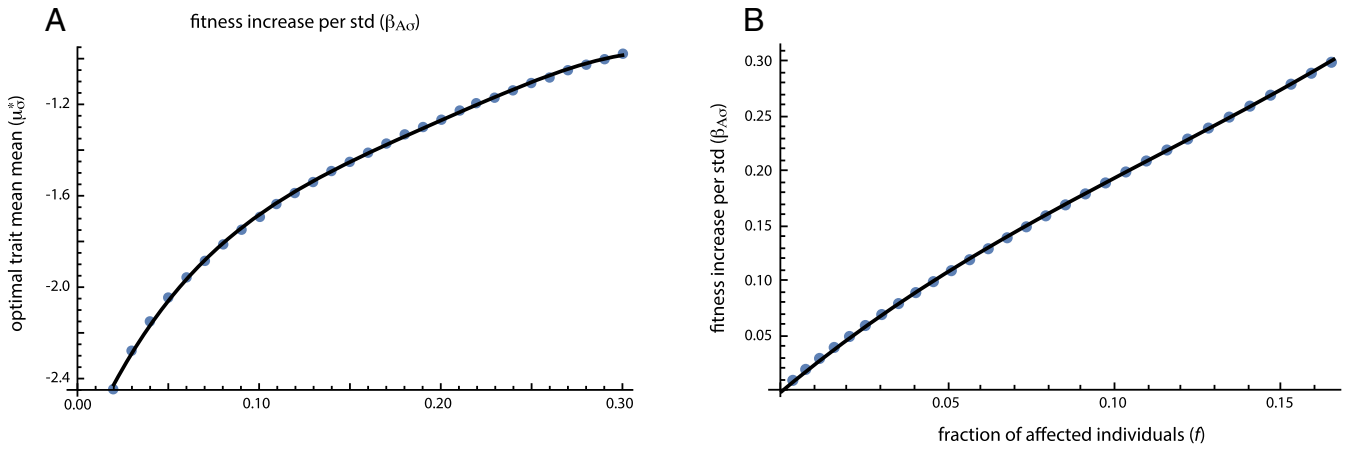

Fig. 3. Polynomial approximations of Eq. 3 for μ^*_σ (A) and $\beta_{A\sigma}$ (B) within the interval $0.02 < \beta_{A\sigma} < 0.3$. The dots are computed by the actual formulas, and the curve is the polynomial approximation.

if the environment changes (16, 63). For example, mothers born and raised in third-world countries tend to have short stature and narrow pelvic dimensions; they experience marked risk of cephalopelvic disproportion and shoulder dystocia after migrating as adults to the United States, where a change to a high-protein diet putatively causes an increase in birth size (64). Similarly, the unequally strong investment in the fetal brain, which is maintained even under maternal starvation, protects the fetus under conditions of food scarcity. However, when nutritional conditions change substantially, as they did in the last century, this overproportional investment in the fetus may lead to a mismatch of neonatal brain size and maternal pelvic dimensions.

The presented model can be extended in various ways (see ref. 48 for a comprehensive mathematical treatment of asymmetric fitness functions). For instance, taking into account that not all cases of fetopelvic disproportion are lethal for the mother, or that she had offspring from earlier pregnancies, slightly increases the rate of affected women. More importantly, the above model (model I) describes only female phenotypes and assumes no genetic correlation between the sexes. However, because neonatal head size and pelvic morphology are controlled by genes that are expressed in both sexes, the traits are expected to coevolve in males and females (65). Both sexes may be subject to similar nonobstetric selective forces, yet obstructed labor primarily affects the mother's fitness; the father's lifetime reproductive success is much less influenced by it. We therefore extended the previous model by including both sexes (model II, with a sex ratio of 1/2). We assumed complete genetic correlation (coevolution) between the sexes, and an unconstrained fitness increase for males, whereas female fitness drops to 0 at $D > 0$ (Fig. 2*B*). For a slope of absolute fitness $\beta_{A\sigma} = 0.1$, the inclusion of males pushes the optimal mean to $\mu_D = -1.2\sigma_D$, with 11.1% of females experiencing disproportion (note that a constant sexual dimorphism does not influence this rate). Incidences of 2 to 6% correspond to standardized directional selection gradients ranging from 0.02 to 0.07—considerably lower than those for model I. This implies that genetic correlation between the sexes severely aggravates the risk of obstructed labor for women. The biological and social factors determining fitness and genetic correlation in the sexes differ across populations; the actual selection scenarios specific to different populations thus may vary between models I and II.

Caesarean Sections. In industrialized countries, Caesarean sections have minimized maternal mortality due to obstructed labor. Although the obstetric selection pressure has been relaxed, the directional selection on D may persist and induce an evolutionary change. Theory shows that the expected evolutionary change of a mean phenotype resulting from directional selection equals the product of the additive genetic variance (the heritable part of phenotypic variation) and the directional selection gradient (32, 45). Heritabilities of most pelvic dimensions have been reported to range from 0.5 to 0.8; the heritability of biischial breadth (the only birth-relevant dimension reported) is 0.56 (34). A twin study reported a heritability of 0.73 for intracranial volume at gestational week 40 (37), but this estimate does not take into account the plasticity of gestational length. The heritability of intracranial volume at the time of birth may thus be considerably lower (39). As a conservative estimate, let us assume a 3% incidence of fetopelvic disproportion before the availability of Caesarean sections and a heritability of 0.5 for D. This implies a standardized selection gradient of $\beta_\sigma = 0.080$ for model I and of $\beta_\sigma = 0.037$ for model II. The predicted average change of D after the emergence of Caesarean sections is 0.040 and 0.018 SDs per generation for the two models, respectively. For the time range that Caesarean sections have been regularly and safely conducted in industrialized countries (since the 1950s and 1960s, i.e., roughly two generations), our model predicts a 20% increase of the incidence of fetopelvic disproportion for model I and a 9% increase for model II. Note that these are predictions about the actual disproportion rate, not Caesarean section rate, which has increased much more rapidly for other reasons; the obstetric literature typically considers the actual disproportion rate constant.

Conclusion

In an attempt to model the evolutionary dynamics underlying the obstetric dilemma, we identified three distinct characteristics of human obstetric selection that jointly produce the high rates of obstructed labor. First, the size of the neonate relative to the birth-relevant dimensions of the maternal pelvis has a highly asymmetric, cliff-edged fitness distribution. Second, the genetic structure of this trait is particularly complex. It involves maternal and paternal genes distributed across two generations and is superimposed by a strong environmental component. This causes a wide and approximately symmetric variation of the discrepancy between fetal and maternal dimensions. Third, obstetric selection affects only the female half of the population, but female and male dimensions are genetically correlated and subject to similar nonobstetric selection. The tight fit of the neonate through the maternal birth canal thus is aggravated by the influence of the genes selected in males.

We demonstrated that due to these three properties weak directional selection favoring large neonates relative to the maternal pelvic dimensions is sufficient to account for the high

incidence of fetopelvic disproportion in human populations. Our model does not specify the origin of these selective forces, but we found evidence in the medical literature for a reproductive advantage of both large neonates and women with a narrow pelvis, independent of putative biomechanical advantages. We predict that this weak directional selection has led to a 10 to 20% increase in the rate of fetopelvic disproportion since the regular use of Caesarean sections.

Materials and Methods

The Cliff-Edge Model. Let z denote a phenotypic trait, such as D introduced earlier, with a population distribution $P(z)$, and write $W(z)$ for the absolute fitness of an individual, with a population mean of $\bar{W} = \int W(z)P(z)dz$. The relative fitness, w, of an individual with phenotype z is $w(z) = W(z)/\bar{W}$. For model I, let the cliff-edged function of absolute individual fitness be $W(z) = \beta_A(z + \delta)$ if $-\delta \le z \le 0$ and 0 otherwise, where δ is the interval of z in which absolute fitness increases with slope β_A (Fig. 1*A*). The linearity can be considered a local approximation to a nonlinear function; the arguments in this paper also extend to a wider class of functions (30, 47, 48). The range from $-\delta$ to 0 likewise is no restriction of generality, because any variable z may be translated to fit this requirement. As a further idealization, let the phenotypic distribution within a population be $P(z) = P(z, \mu_z, \sigma_z) \sim N(\mu_z, \sigma_z)$. Again, our arguments do not strictly require a normal distribution of trait values, only an approximately symmetric distribution with finite variance. Our model further assumes constant variance over time; the only evolving parameter is the population mean of the trait, μ_z. The population mean fitness is then given by $\bar{W} = \int_{-\delta}^{0} \beta_A(z + \delta)\, P(z)dz$, and the adaptive landscape is the curve of $\bar{W}$ over μ_z (Fig. 1*B*). In the standard models of adaptive evolution, the population mean moves uphill on the adaptive landscape until the maximum population fitness has been reached (32, 45, 46). Assuming constant σ_z, we thus seek the value μ_z^* for which $\bar{W}$ is a maximum:

$$\mu_z^* = \arg\max_{\mu_z} \int_{-\delta}^{0} \beta_A(z + \delta)\, P(z, \mu_z, \sigma_z)dz. \quad [1]$$

Because of the cliff-edged individual fitness function, μ_z^* will be less than—but close to—the individual fitness maximum at $z = 0$ whenever $\sigma_z > 0$ (48). As long as $\beta_A > 0$, the population maximum always involves a fraction of individuals beyond the fitness edge (i.e., individuals with zero fitness). This fraction is given by

$$f = \int_{0}^{\infty} P(z, \mu_z^*, \sigma_z)dz. \quad [2]$$

The three model parameters have a single degree of freedom only; we can thus reduce them to one new compound parameter, $\beta_{A\sigma}$. The fraction f is independent of population size and the total number of offspring (the areas under the probability density function and fitness curve in Fig. 1*A*). Thus, without loss of generality, we set the maximum individual fitness at $z = 0$ to 1, so that $\beta_A = 1/\delta$, and express δ in terms of SDs, δ/σ_z. Then the model has a single parameter only: absolute fitness increase per SD, $\beta_{A\sigma} = \sigma_z/\delta$. Because $\beta_{A\sigma}$ is unit-free, the fraction f is independent of the scale of z. Eqs. **1** and **2** can be expressed in terms of this new model parameter:

$$\mu_\sigma^* = \arg\max_{\mu_\sigma} \int_{-1/\beta_{A\sigma}}^{0} \beta_{A\sigma}(z + 1/\beta_{A\sigma})\, P(z, \mu_\sigma, 1)dz, \quad [3]$$

$$f = \int_{0}^{\infty} P(z, \mu_\sigma^*, 1)dz,$$

where $\mu_\sigma^* = \mu_z^*/\sigma_z$ is the optimal trait mean expressed in units of SDs.

For model I, with the fitness slope set to $\beta_{A\sigma} = 0.1$, the maximal mean population fitness of $\bar{W} = 0.78$ was achieved by a mean trait value of $\mu_\sigma^* = -1.7\sigma_z$, with $f = 0.045$. This was computed by numerical integration in Mathematica 10.0 (Wolfram Research, Inc.).

In Fig. 2*A*, the maximal population fitness $\bar{W}$ and the ratio f were computed for standardized fitness slopes, $\beta_{A\sigma}$, ranging from 0 to 0.3 based on Eq. **3**. The resulting plot is equivalent to a plot with fixed SD, σ_z, and varying absolute fitness slope, β_A, as well as to a plot with varying σ_z and fixed β_A, using Eqs. **1** and **2**.

Model II in Fig. 2*B* was based on the fitness function $W(z) = \beta_A(z + \delta)$ if $-\delta \le z \le 0$ and $W(z) = \beta_A(z + \delta)/2$ if $z > 0$, reflecting that fitness still increases for the male half of the population with slope β_A beyond $D > 0$, whereas the female half has zero fitness. Obviously, the male fitness increase for positive values of D can be linear only in the near vicinity of $D = 0$ because, among other reasons, of the altered sex ratio. However, this limitation does not affect our calculations because the estimated trait means are clearly negative.

Phenotypic Variation. Write N for an idealized measure representing neonatal size and C for the mother's pelvic canal size. The variance of the difference $D = N - C$ can be expressed in terms of the variances and the covariance of N and C:

$$\mathrm{Var}(D) = \mathrm{Var}(N) + \mathrm{Var}(C) - 2\mathrm{Cov}(N, C).$$

This well-known theorem implies that if N and C were uncorrelated, their variances would add up to the variance of D. Any positive association between them would reduce variation in D, which in turn would reduce the fraction f (Fig. 1*B*).

Evolutionary Prediction. Under the idealized assumption of no genotype–environment interactions, the phenotypes can be decomposed into an additive genetic component and an independent environmental component. In the absence of environmental changes between generations and changes due to recombination or mutation, the mean phenotypic change, $\triangle\mu_z$, from one generation to the next can be modeled as the product of the additive genetic variance, G, and the directional selection gradient, β (32, 45):

$$\triangle\mu_z = G\beta.$$

The directional selection gradient is the slope of relative fitness on the trait,

$$\beta = \frac{\partial w(z)}{\partial z} = \bar{W}^{-1}\frac{\partial W(z)}{\partial z} = \frac{\beta_A}{\bar{W}}.$$

The standardized directional selection gradient (53), β_σ, is expressed in terms of SDs and equals the standardized slope of absolute fitness divided by the population mean fitness: $\beta_\sigma = \beta_{A\sigma}/\bar{W}$.

We assumed a heritability of 0.5 for D, that is, the genetic variance of D equals half the phenotypic variance. Thus, when expressing D in units of SD, $G = 0.5$. We further assumed a conservative estimate of 3% incidence of fetopelvic disproportion before the use of Caesarean sections. Choosing $f = 0.03$ in Eq. **3** gives $\beta_{A\sigma} = 0.070$ and an optimal population trait mean $\mu_\sigma^* = -1.88\sigma_D$ for model I.

Caesarean sections remove the fitness threshold so that fitness can be assumed to increase linearly even for small positive values of D. The mean fitness, $\bar{W}^*$, of the population right after the emergence of Caesarean sections, that is, still centered at μ_z^*, but with relaxed fitness threshold, is thus given by

$$\begin{aligned}\bar{W}^* &= \int_{-\delta}^{\infty} \beta_A\,(z + \delta)P(z, \mu_z^*, \sigma_z)dz \\ &= \int_{-1/\beta_{A\sigma}}^{\infty} \beta_{A\sigma}\,(z + 1/\beta_{A\sigma})P(z, \mu_\sigma^*, 1)dz \\ &\approx 1 + \mu_\sigma^*\beta_{A\sigma} = 0.868 \quad \text{for } \beta_{A\sigma} < 0.3. \end{aligned} \quad [4]$$

The standardized directional selection gradient is then $\beta_\sigma = \beta_{A\sigma}/\bar{W}^* = 0.081$, and the predicted evolutionary change per generation is $\Delta\mu_\sigma = G\beta_\sigma = 0.040\sigma_D$. Because the population mean of D was estimated to be $\mu_\sigma^* = -1.88\sigma_D$, a response to selection over two generations shifts the mean to $-1.80\sigma_D$, which in turn is associated with a predicted disproportion rate of $f = 0.036$—a 20% increase of incidence.

For model II, an incidence of 3% translates into $\beta_{A\sigma} = 0.035$ and $\mu_\sigma^* = -1.88\sigma_D$. Given a heritability of 0.5, the corresponding $\beta_\sigma = 0.037$ after Caesarean sections shifts the mean to $-1.84\sigma_D$ after two generations, which gives $f = 0.0326$—a 9% increase of incidence.

In both models, higher initial rates of disproportion lead to higher increases due to Caesarean sections; the presented figures thus are conservative estimates. In any case, because of the idealizations and approximations in the model and the uncertainty of the published incidences, our predictions are merely meant to represent orders of magnitudes. Prediction of long-term evolution is even more difficult because changes in variational properties and selective forces are hard to foresee. Medical treatment may relax some of the selective forces, whereas fetal development and maternal metabolism may constrain the response to selection (10, 16).

Polynomial Approximations. The dependences of the optimal trait mean, μ_σ^*, and the fraction, f, on the absolute fitness increase, $\beta_{A\sigma}$, are given by Eq. **3**, expressed in terms of SDs of z. These relationships cannot be expressed in closed form, but we found that for $0.02 < \beta_{A\sigma} < 0.3$ they can be approximated very well by the following polynomials (Fig. 3):

$$\mu_\sigma^* \approx -2.76 + 18.53\beta_{A\sigma} - 109.49\beta_{A\sigma}^2 + 360.3\beta_{A\sigma}^3 - 452.2\beta_{A\sigma}^4$$

$$\beta_{A\sigma} \approx 2.55f - 8.51f^2 + 25.15f^3$$

Together with the approximation in Eq. **4**, these polynomial representations allow for the application of the model without computing the actual maximizations over the integrals.

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