



A review of the established and suspected causes of variations in human sex ratio at birth



William H. James^{a,*}, Victor Grech^b

^a The Galton Laboratory, Department of Genetics, Evolution and Environment, University College London, United Kingdom

^b Department of Paediatrics, Mater Dei Hospital Medical School, Malta

ARTICLE INFO

ABSTRACT

The human sex ratio (proportion male) at birth (SRB) varies with many variables. Some of this variation has an established proximate cause. For instance, low SRB (more females) at birth are associated with various forms of stressful events or circumstances during or prior to pregnancy. These low SRB are almost certainly mainly caused by maternal-stress-induced male foetal loss. Other types of SRB variation are thought to be caused by hormonal variation in either or both parents around the time of conception. One or other of these two types of proximate cause seems to be responsible for most of the established variation of SRB. This will be illustrated here in respect of some selected forms of SRB variation. It seems likely that a clarification of the hormonal causes of SRB variation will also help explain the striking (apparent) inconsistencies in the results of reported tests of the influential Trivers-Willard hypothesis. It is further proposed that an appreciation of the evidence that parental hormones influence SRB may enhance understanding of several important pathologies (hepatitis B, toxoplasmosis, testicular cancer, prostate cancer and autism).

© 2017 Elsevier B.V. All rights reserved.

1. Introduction

In recent years, it has become customary to classify the causes of variation of sex ratio at birth (SRB) as either 'ultimate' or 'proximate'. Ultimate causes are those hypothesized to be adaptive (*viz.* to maximize reproductive success) and to have arisen via the processes of evolution and natural selection. The issue is complex since SRB varies with many variables. Furthermore, the various hypotheses positing ultimate causes are not necessarily in competition, as they make different and non-competing predictions. Interpretation of results designed to test such a hypothesis will necessarily simultaneously have to take account of adaptive hypotheses that make other predictions [1].

Proximate causes are those closest to an event and therefore immediately responsible for observed results. Some proximate causes may also appear to serve ultimate causes. However, a few proximate causes with regard to SRB (e.g. non-ionizing radiation) are non-adaptive.

Several adaptive hypotheses have been formulated [2,3]. However, the only ultimate cause hypothesis to be discussed here is the Trivers-Willard hypothesis (TWH). It will be treated together with its relationship with two proposed proximate causes *viz.* maternal-stress-induced

male-sex-selective spontaneous abortion and parental hormone levels at the time of conception.

National vital statistics of many countries have shown that SRB varies with maternal age, paternal age, birth order, social class and race: SRB is high in firstborns, and in births to young mothers, young fathers, parents of higher social class and to White parents [4]. Moreover, there are biased SRBs in infants later diagnosed with certain neurodevelopmental disorders and congenital malformations. Furthermore there is strong evidence that SRB exhibits variation across couples (Lexis variation) and variation within couples (Poisson variation) [4]. This Poisson variation has several identifiable components, some varying across a woman's whole reproductive life (as in the demographic variables of parental ages and birth order noted above). Another Poisson component is exemplified by the reported variation of SRB with time of conception within the menstrual cycle [5].

All of these forms of variation are apparently independent, and the cause/s of some are not well established. This is noteworthy because SRB has been studied extensively by demographers, geneticists (including evolutionary theorists), epidemiologists, statisticians, probability theorists, animal experimentalists and human reproductive biologists. SRB thus remains one of the most longstanding unresolved problems in the biological sciences. Indeed, an early writer on the topic was the first worker to draw a statistical inference using probability theory. Using this technique, he inferred that there is a very general tendency

* Corresponding author.

E-mail addresses: w.james@ucl.ac.uk (W.H. James), victor.e.grech@gov.mt (V. Grech).

for more boys than girls to be born (nearly 13 boys for every 12 girls), an SRB of 0.52 [6].

We suggest that it is of cardinal importance that this variation of SRB is addressed directly. What are its causes? The main purpose of the present paper is to focus on that question and to summarise how two forms of proximate explanation potentially account for most of this variation. An established cause of SRB variation will be discussed and we shall then indicate why it seems incapable of explaining all the reported forms of variation.

2. An established cause of SRB variation: maternal-stress-induced male-sex-selective foetal death

Given that the biological sex of a human individual does not change after conception, the SRB of a live cohort at birth logically depends on two factors, namely sex ratio at conception (SRC), and the modification of this ratio by sex-selective embryonic and/or foetal death (miscarriage and/or stillbirth).

For many years, it was thought by obstetricians and epidemiologists that maternal stress (of various sorts) is a cause of foetal death, and that male foetuses were more at risk than females. Without having been decisively demonstrated, this was generally supposed to be a cause of the variation of SRB with variables listed above (maternal age, etc.). In the past two decades, the credibility of this proposition has been greatly strengthened by the work of Catalano and his colleagues. Using time-series analysis, this group has shown that miscarriage is associated with many forms of stress e.g. the 9/11 terrorist attacks [7,8]; ambient temperature stress [9]; mass layoffs [10,11,12] and the Great East Japan Earthquake in 2011 [13]. It has also been shown that the miscarriages associated with such stressors are of small, frail male foetuses [8]. Others have identified further human stressors associated with low subsequent SRB (and thus, presumably, with male-sex-related miscarriage) e.g. parasite stress [14]; the sovereignty referendums in Canada [15]; the recession of 2007 in the U.S. [16]; severe preconceptional life events [17]; self-assessed early pregnancy stress [18]; maternal occupational stress [19]; a stressful lifestyle as identified by commute times ≥ 90 min [20]; and other earthquakes such as in Japan [21,22], Iran [23] and Chile [24]. Moreover, it has been reported that there was a decline in SRB in the UK 4–5 months after the death of Princess Diana in 1997 [25]. Lastly, it has been reported that pregnant Muslim women who observe the fast of Ramadan in early pregnancy have a low SRB [26].

It must be acknowledged that some of these ecological studies were not replicated (or replicable), and may have been subject to publication bias. Moreover, in others, the timing of the stressor was not closely monitored. Thus, the proposition that stress in early-to-mid pregnancy leads to male-biased miscarriage was not decisively tested in those studies. We suggest nevertheless that there remains sufficient evidence cited above for one to infer that, in general, this proposition is true. In further partial support of this proposition, there is evidence that psychiatric or other treatment reduces the probability of a further miscarriage to women who have had previous miscarriages [27,28]. It is therefore likely that male-sex-biased maternal-stress-induced miscarriage is the explanation for the established variation of SRB with the variables listed above.

The credibility of this argument is increased by the strong evidence that a major proximate cause of miscarriage is known to be a high level of stress-induced maternal adrenal androgens [29]. The argument is further strengthened by the fact that all such stress-related variation would be in conformity with the TWH. It is established in many species (including man), that males in good condition outreproduce females in good condition, and that females in poor condition outreproduce males in poor condition. For this reason, TWH predicts for adaptive reasons (to maximize the numbers of grandchildren), that females in good condition would produce a high proportion of sons, and that females in poor condition would produce a high proportion of daughters. The definition of 'condition' in this context is treated later here. However, it

may be assumed that women who miscarry are in poorer 'condition' than those who do not.

The theme that maternal-stress-induced male-sex-related foetal loss is adaptive was developed by Catalano's group who noted that "human gestation provides as much opportunity for natural selection as for maturation because at least 60% of conceptions spontaneously abort" [12]. These authors added that much medical literature attributes components of sub-optimal reproduction to 'dysregulated' gestation: "We offer the alternative view that natural selection conserved well-regulated, though non-conscious decisional biology that predicts the reproductive fitness of women by spontaneously aborting gestations that would otherwise yield frail infants, particularly small males" [30]. They further predicted and gave evidence that such strategic gestation (as opposed to dysregulated gestation) would ensure the prolongation of gestations that are stressed at 36–37 weeks. Their rationale for this prediction was that "additional time in utero would allow additional maturation and growth that could help an infant contend with stressors that extend into the neonatal period" [31]. Lastly, they found that the numbers of spontaneous and non-clinically-indicated induced abortions correlate positively in conception cohorts, suggesting that "risk aversion affects both the conscious and non-conscious mechanisms that control parturition" [32].

Thus, maternal-stress-induced spontaneous abortion of small, frail male foetuses may be interpreted as an established proximate cause, serving the adaptive function that women in good condition bear sons, and that those in poor condition bear daughters. Women who do not abort are adaptively served by it (because they are both more likely to have been in good condition and to have boys). Moreover, reproductive advantage also accrues to those women who do have a stress-induced male-biased abortion. This is because by aborting, ex hypothesi they do not waste time and energy on rearing an infant who will not later adequately compensate them reproductively by passing on their genes. However, as noted above, there are several other sorts of SRB variation which male-sex-related miscarriages cannot readily explain, as will now be shown.

3. Variation of SRB which may not be explained by male-sex-biased miscarriage

3.1. Biased SRB associated with pathology in fathers (testicular cancer and prostate cancer)

There seems no compelling reason to believe that the biased sex ratios reportedly associated with pathology in fathers would be caused by maternal stress-induced sex-biased miscarriages. The reported effects of prostate cancer and testicular cancer on SRB are treated later.

3.2. High SRBs

Male sex-biased miscarriages cannot readily explain high SRB at birth. Moreover, there are no known environmental circumstances under which female sex-biased foetal loss occurs. However, it is established that there are a number of parental conditions (both pathological and non-pathological) which are associated with high SRB. First, women recently infected with toxoplasmosis reportedly have a high SRB [33,34], as do women with pre-eclampsia [35]. Second, several studies have shown that parents of both sexes infected with hepatitis B (HBV) have a higher SRB than uninfected controls [36]. Third, SRB in South Africa reportedly rose nine months after the 2010 FIFA World Cup there [37]. Similarly there was a rise in the UK SRB in 1983 following the birth of Prince William in 1982 [25]. Fourth, though wars are stressful, SRB generally rose during and just after the two World Wars in the belligerent countries, but not the non-belligerent countries [38, 39]. In times of war, an adult sex ratio imbalance prevails, with more males being away from their homes. This has been claimed to result in sexual excesses, "actions [that] were viewed as understandable

Download English Version:

<https://daneshyari.com/en/article/5691124>

Download Persian Version:

<https://daneshyari.com/article/5691124>

[Daneshyari.com](https://daneshyari.com)