Journal of Biosocial Science (2021), 53: 4, 639–642
doi:10.1017/S0021932020000413

CAMBRIDGE UNIVERSITY PRESS

SHORT REPORT

Genetic load and biological changes to extant humans

Arthur Saniotis[1,2]*, Maciej Henneberg[2,3] and Kazhaleh Mohammadi[4]

[1]Department of Anthropology, Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wroclaw, Poland, [2]Biological Anthropology and Comparative Anatomy Research Unit, Adelaide Medical School, University of Adelaide, Adelaide, SA, Australia, [3]Institute of Evolutionary Medicine, University of Zürich, Zürich, Switzerland and [4]Department of Medical Laboratory Science. Knowledge University, Erbil, Kurdistan Region, Iraq
*Corresponding author. Email: arthur.saniotis@adelaide.edu.au

(Received 09 March 2020; revised 08 May 2020; accepted 10 May 2020; first published online 11 August 2020)

Abstract
Extant humans are currently increasing their genetic load, which is informing present and future human microevolution. This has been a gradual process that has been rising over the last centuries as a consequence of improved sanitation, nutritional improvements, advancements in microbiology and medical interventions, which have relaxed natural selection. Moreover, a reduction in infant and child mortality and changing societal attitudes towards fertility have led to a decrease in total fertility rates (TFRs) since the 19th century. Generally speaking, decreases in differential fertility and mortality have meant that there is less opportunity for natural selection to eliminate deleterious mutations from the human gene pool. It has been argued that the average human may carry ~250–300 mutations that are mostly deleterious, as well as several hundred less-deleterious variants. These deleterious alleles in extant humans mean that our fitness is being constrained. While such alleles are viewed as reducing human fitness, they may also have had an adaptive function in the past, such as assisting in genetic complexity, sexual recombination and diploidy. Saying this, our current knowledge on these fitness compromising alleles is still lacking.

Keywords: Evolution; Genetic mutations; Relaxed selection

Extant humans are currently increasing their genetic load, and this is informing present and future human microevolution (You & Henneberg, 2016, 2017; Lynch, 2016). Genetic load may be defined as an accumulation of harmful genetic mutations in the gene pool. In other words, a population with a genetic load may have too many 'bad' genes in the gene pool in comparison to a 'standard' population with minimal deleterious genes. In theory, a standard population has the capacity to contain an optimal genotype. Since most random mutations are negative (fitness reducing) rather than positive (fitness enhancing) – the Probable Mutation Effect – there is a higher probability of genetic load accumulating in a human population where natural selection has been relaxed (Brace, 1964).

This is precisely what has been happening since the Industrial Revolution. The Industrial Revolution (*circa* 19th century) eventually led to the introduction of sanitation, public health measures, medical technologies and nutritional improvements. The last two centuries also saw many scientific and technological advancements and an understanding of the causation of infectious diseases. Consequently, natural selection, which had operated to 'weed out' non-fit individuals since the Paleolithic period, has reduced. This trend was enhanced in the 20th century with the advent of antibiotics in the 1940s. There is no doubt that antibiotics enabled millions of individuals to survive the onslaught of communicative diseases that had been the bane of countless generations of humans. A case in point is tuberculosis, which has interacted with human

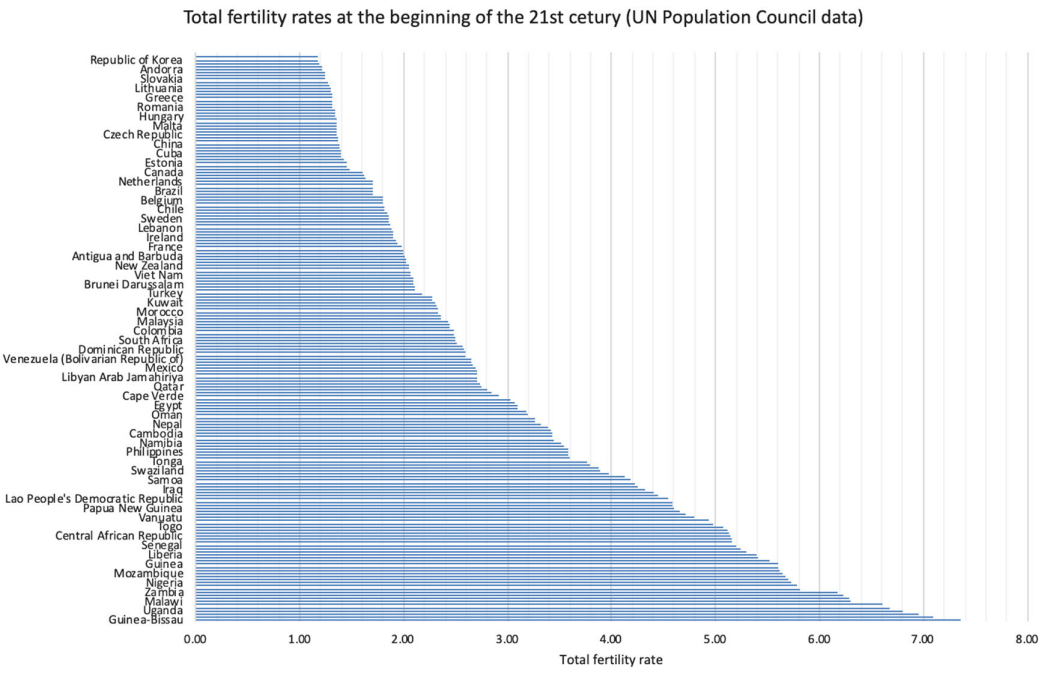

Figure 1. Total fertility rates at the beginning of the 21st century. Source: UN Population Council data.

populations for at least 5000 years (Holloway *et al.*, 2011) and produced major morphological malformations (Armocida *et al.*, 2016).

Unfortunately, the great influenza pandemic of 1918–1919, which killed ~20–40 million individuals, was a stark reminder of the ever-looming presence of the microbial world. The modern phenomena of Avian Flu, Ebola, Zika Disease and COVID-19, and the rise of antibiotic-resistant strains of tuberculosis, exemplify our inescapable 'arms race' with pathogens.

Reduction in infant and child mortality, coupled with increased consumption of industrially produced goods, have changed attitudes to fertility, reducing the numbers of children born to women during their lifetime: the total fertility rates (TFRs) in industrial countries fell from around 7 in the mid-19th century to less than 2 in a third of countries in the world at the beginning of the 21st century. Effective birth control reduced differential fertility in two ways: a small number of offspring for normally fecund people, and promoted by assisted reproduction techniques, fertility of individuals or couples who are naturally infecund.

Figure 1 shows the TFRs of a selection of countries at the beginning of the 21th century. In many countries the premature death of infants and toddlers has declined considerably. From 4 Ma ago to the Middle Ages the odds of neonates surviving to adulthood and reproducing were ~0.20–0.30. It was only at the close of the 20th century that the odds of neonates surviving into adulthood and reproducing reached around 0.99 (Saniotis & Henneberg, 2011). This meant that nearly all individuals in developed nations could reach adulthood and experience an extended post-reproductive period. Generally speaking, decreases in differential fertility and mortality have meant that there is less opportunity for natural selection to eliminate deleterious mutations from the human gene pool. Although there exists some opportunity for natural selection this is probably <1% in the developed world, compared with ~ 50% in the pre-industrial age.

Figure 2 shows the change in the opportunity for selection in *Homo sapiens* over time. It has been hypothesized that the average human may carry ~250–300 mutations, most of which are

https://doi.org/10.1017/S0021932020000413 Published online by Cambridge University Press

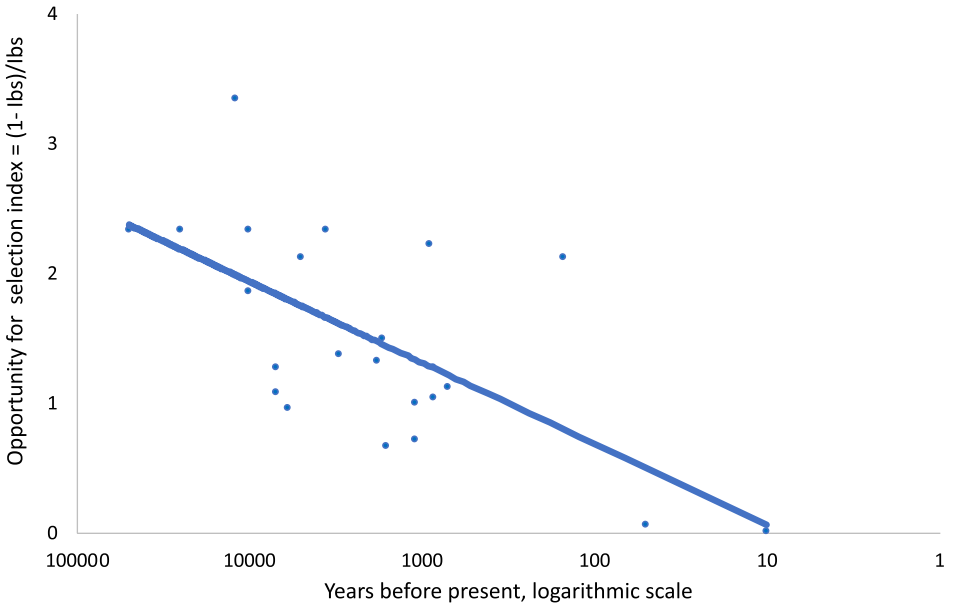

Figure 2. Changes in the opportunity for selection in *Homo sapiens*. The index is taken from You and Henneberg (2016), as applied to data originally used for Figure 3 in Saniotis and Henneberg (2011).

deleterious, as well as several hundred less-deleterious variants (Agrawal & Whitlock, 2012). These deleterious alleles in extant humans means that our fitness is being constrained (Agrawal & Whitlock, 2012). While such alleles are viewed as reducing human fitness, they may also have had an adaptive function in the past, such as assisting in genetic complexity, sexual recombination and diploidy (Otto & Goldstein, 1992; Keightley & Otto, 2006; Agrawal & Whitlock, 2012).

Little is known about these fitness-compromising alleles. However, initial studies of all countries of the world ($N \cong 190$) by You and Henneberg (2016, 2017) have suggested a deleterious effect of the accumulation of such mutations due to relaxed selection, by showing a negative correlation between a country's opportunity for natural selection and the prevalence of type 1 diabetes and the incidence of fifteen basic types of cancer.

Conflicts of Interest. The authors have no conflicts of interest to declare.

Ethical Approval. No research involving human subjects was conducted by the authors.

Funding. This research received no specific grant from any funding agency, commercial entity or not-for-profit organization.

References

Agrawal AF and Whitlock MC (2012) Mutation load: the fitness of individuals in populations where deleterious alleles are abundant. *Annual Review of Ecology, Evolution, and Systematics* **43**, 115–135.

Armocida E, Böni T, Rühli FJ and Galassi FM (2016) Does acromegaly suffice to explain the origin of Pulcinella? A novel interpretation. *European Journal of Internal Medicine* **28**, e16–e17.

Brace CL (1964) The probable mutation effect. *American Naturalist* **98**(903), 453–455.

Holloway KL, Henneberg RJ, de Barros Lopes M and Henneberg M (2011) Evolution of human tuberculosis: a systematic review and meta-analysis of paleopathological evidence. *Homo* **62**(6), 402–458.

Keightley PD and Otto SP (2006) Interference among deleterious mutations favours sex and recombination in finite populations. *Nature* **443**, 89–92.

Lynch M (2016) Mutation and human exceptionalism: our future genetic load. *Genetics* **202**(3), 869–875.

https://doi.org/10.1017/S0021932020000413 Published online by Cambridge University Press

Otto SP and Goldstein DB (1992) Recombination and the evolution of diploidy. *Genetics* **131**, 745–751.
Saniotis A and Henneberg M (2011) Medicine could be constructing human bodies in the future. *Medical Hypothesis* **77**(4), 560–564.
You W and Henneberg M (2017) Cancer incidence increasing globally: the role of relaxed natural selection. *Evolutionary Applications* **11**(2), 140–152.
You WP and Henneberg M (2016) Type 1 diabetes prevalence increasing globally and regionally: the role of natural selection and life expectancy at birth. *BMJ Open Diabetes Research & Care* **4**(1), e000161.

Cite this article: Saniotis A, Henneberg M, and Mohammadi K (2021). Genetic load and biological changes to extant humans. *Journal of Biosocial Science* **53**, 639–642. https://doi.org/10.1017/S0021932020000413