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Can Embryo Selection Save the World?

Mingrui Wang[†*]

Abstract

In modern societies, purifying selection against deleterious mutations has been relaxed and the relationship between reproductive success and cognitive ability has reversed. Early 20th-century geneticists warned that the resulting genetic decline in cognitive and physical health poses a severe threat to civilization. Many today argue that reproductive biotechnologies—including polygenic embryo selection—offer a sufficient "technological fix" for the declining genetic baseline, but this premise raises serious scientific concerns. This paper synthesizes findings from psychometrics, quantitative genomics, evolutionary biology, immunology, and agricultural breeding to evaluate the systemic and biological limitations of these interventions. By examining the highly polygenic architecture of intelligence, the steady accumulation of *de novo* mutations, and the phenomenon of antagonistic pleiotropy, this review demonstrates that relying on current or anticipated future advancements in these technologies to engineer complex traits is fundamentally flawed. The analysis reaches four main conclusions: (1) Reproductive technologies can remove some severe mutations. (2) They cannot repair the deterioration of the genetic baseline caused by minor-effect rare variants and *de novo* mutations. (3) Aggressively targeting intelligence for genotypic selection risks severe unintended consequences, such as depleting historically preserved genetic diversity and compromising immune system resilience. (4) A "perfect" gene-editing system capable of eliminating *de novo* mutations would halt human evolution. This review urges caution regarding reproductive biotechnologies that aggressively aim to maximize specific polygenic traits.

Keywords: Genetic deterioration, Embryo selection, Mutational load, Antagonistic pleiotropy, PGT-P

1 Introduction

The direction of human biological evolution in the modern era has been a subject of intense concern for over a century. The concept of dysgenics—the genetic deterioration of a population—was formally articulated by Francis Galton, who argued that the relaxation of natural selection in industrialized societies would lead to the accumulation of harmful genes and a decline in heritable traits such as health and intelligence. The recognition that human biological capacity is not static, but changes across generations due to evolutionary pressures—or lack thereof—was the consensus among major geneticists in the late 19th century and the first half of the 20th century (Lynn, 1996). Historically, reproductive fitness favoured individuals with higher cognitive ability, maintaining a positive selective gradient for intelligence across pre-industrial societies (Meisenberg, 2010). However, the "demographic transition" fundamentally inverted this pattern. Modern industrialized societies now exhibit a persistent negative correlation between fertility and educational attainment or cognitive ability, a pattern observed at both the phenotypic and genotypic levels across multiple populations. We have, for example, genotypic evidence for this from the US, Iceland, and the UK (Beauchamp, 2016; Hugh-Jones & Abdellaoui, 2022; Kong et al., 2017; Sanjak et al., 2018).

For Galton and several other founders of modern genetics, this was not merely a matter of public health, but an existential threat to civilization itself. Because economic growth and societal maintenance rely on cognitive ability (Weede & Kämpf, 2002), the present trend is unsustainable over the long term. The cumulative genetic decline of population-level intelligence and health inevitably undermines the biological foundation required to sustain complex civilizations. The dysgenic effect is small in a single generation and therefore goes unnoticed by a society unaccustomed to multi-generational thinking, ultimately leading towards civilizational decline and collapse.

† Independent researcher, Beijing, China
* Corresponding author, email: mail@mingrui.wang

The seriousness of this "civilizational collapse" scenario is further illustrated by the interest in biological degeneration displayed by Karl Marx (Feuer, 1977, 1979). He wrote to the Russian translator of *Das Kapital* inquiring whether E. Ray Lankester's book *Degeneration* (1880) had been translated (Marx, 1881). In this book, Lankester used cross-species examples to demonstrate degeneration, asking: "Does the reason of the average man of civilised Europe stand out clearly as an evidence of progress when compared with that of the men of bygone ages? [...] In such respects we have at least reason to fear that we may be degenerate. Possibly we are all drifting, tending to the condition of intellectual Barnacles or Ascidians." Later, Marxist geneticists J. B. S. Haldane (co-founder of population genetics and proposer of mutation-selection balance) and H. J. Muller (who won the Nobel Prize for being the first to directly manipulate the genome via X-ray mutagenesis) further studied the accumulation of deleterious *de novo* mutations and were deeply concerned with "genetic load" and the long-term biological health of the species (Muller, 1950; Paul, 1984). For these red geneticists, eugenics was not a reactionary tool to justify capitalist inequality, but a crucial prerequisite to human emancipation (Paul, 1984). This consensus was clearly expressed in the 1939 "Geneticists' Manifesto", signed by Muller, Haldane, and other prominent geneticists, which declared that the genetic improvement of mankind could only be fully realized alongside major social changes that eradicate class prejudice and ensure economic equalization (Crew et al., 1939). Evolutionary theorist W. D. Hamilton mathematically formalized Haldane's conceptualization of kin selection (Hamilton, 1964) and further explored the biology of altruism—the conflict between the short-term, partial interests of the individual and the long-term, holistic interests of the group (Hamilton, 1967, 1975). Today, inclusive fitness theory is recognized as "the single most important theoretical revision of Darwin's theory of natural selection in the past century" (Buss, 2019). In his final manuscript, Hamilton (2000) reviewed Lynn's *Dysgenics: Genetic Deterioration in Modern Populations* and endorsed these foundational concerns, warning that acknowledging the objective reality of genetic deterioration is essential to avert future "painful catastrophes" for human civilization.

Methods proposed to counter these effects involved changing the relationship between trait value and fertility, a strategy Lynn (2001) termed "classical eugenics". However, in the second half of the 20th century, the pre-war prioritization of "social rights"—the collective right of the state to safeguard its future genetic quality—was superseded by the absolute priority of "individual rights", particularly regarding reproductive autonomy (Lynn, 1996, 2001). Consequently, the study of average population genetic levels was marginalized and classical eugenics, with its heavy emphasis on outcomes for society at large, became untenable in Western societies. In its place emerged medical genetics, sometimes called the "new eugenics" (Lynn, 2001), specifically novel reproductive biotechnologies aimed at disease prevention (e.g., predictive prenatal testing on early fetuses).

At the same time, the application of medical genetics to intelligence became confined to preventing severe, single-gene Mendelian disorders causing intellectual disability (Harper, 2019); the broader genetics paradigm was politicized and commercialized, and was overwhelmingly pushed towards the Mendelian school. In the first half of the 20th century, a scientific debate unfolded between the biometric school (led by Karl Pearson), which emphasized continuous, polygenic variation, and the Mendelian school (led by William Bateson), which focused on discontinuous variation and discrete inheritance (typically governed by one or a few genes of large effect). R. A. Fisher unified the two schools, showing that continuous variation naturally arises from the additive effects of multiple Mendelian loci. However, in the second half of the 20th century, the academic climate shifted. Politically, the study of continuous, polygenic variation was suppressed to discredit the eugenics of polygenic intelligence. Behind this marginalization was the moralistic fallacy—the flawed assumption that in order to achieve the social ideal of human equality, all individuals must possess identical innate biological capacities for socially valued traits.

Commercially, the Mendelian paradigm flourished. This was initially due to the technological limitations of the era, which could map only discrete disease-causing mutations; the approach also aligned with the pharmaceutical industry's profitable, reductionist model of "one gene, one disease, one drug". The assumption that complex biology could be decomposed into isolated, targetable components became an economic priority. During the foundational decades of biotechnology, the intellectual property system permitted the patenting of isolated genes and single-locus diagnostics (L. L. Hill, 2003; Sherkow & Greely, 2015).

Even after subsequent legal reforms restricted the patentability of unaltered genomic DNA, commercial incentives continue to overwhelmingly reward discrete, single-target molecular mechanisms (Sherkow & Greely, 2015). In contrast, highly distributed polygenic networks do not offer single molecular entities that can be easily monopolized; thus, despite reflecting biological reality, they are commercially unattractive.

Today, with the advent of massively parallel genome sequencing, microarrays, and genomic datasets, the biometric school is effectively being "rediscovered". As Tautz et al. (2026) emphasized, the genotype-phenotype map is fundamentally polygenic, and purely Mendelian diseases are the exception rather than the rule. Even in conditions historically treated as monogenic, it is now understood that the polygenic background heavily dictates disease penetrance (Fahed et al., 2020). Nevertheless, the politicization and commercialization of science over the past decades have already embedded the Mendelian paradigm in the public consciousness and scientific funding. This paradigm has resulted in serious scientific failures (Duval, 2018; Hopkins, 2008; Ségalat, 2007), including the inability to identify the genetic etiology of the vast majority of cases of adult-onset neurodegenerative disorders that affect cognition, such as Alzheimer's disease (Frisoni et al., 2022) and Parkinson's disease (Blauwendraat et al., 2020).

As the broader scientific paradigm inevitably shifts back towards the polygenic reality—catalysed by milestone studies such as the first genome-wide association study (GWAS) for educational attainment (Rietveld et al., 2013)—the scope of new eugenics is once again expanding beyond severe single-gene disorders. Polygenic embryo screening has been proposed as a potential technological solution to the problem of genetic deterioration. Proponents suggest that once the technology matures, a "technological fix" will be sufficient to solve the problem. Lynn (2001) posited that the widespread, voluntary adoption of embryo selection could theoretically arrest and reverse genetic deterioration. Similarly, Dutton and Woodley of Menie (2018) characterized the modern era as a race between the accumulation of deleterious mutations (mutational load) and the development of genetic technologies capable of correcting them. More specifically, proponents argue that by screening embryos using polygenic scores derived from GWAS, we can select for higher intelligence (Shulman & Bostrom, 2014).

This paper argues that such technological optimism is misplaced. By examining the genetic architecture of intelligence—specifically the distinction between common and rare variants, the prevalence of *de novo* mutations, the phenomenon of antagonistic pleiotropy, and lessons learned from actual agricultural breeding programs—I demonstrate that reproductive biotechnologies are fundamentally constrained in their ability to improve genotypic intelligence. Natural selection weighs both common and rare variants when assessing overall biological fitness and preserves advantageous genetic novelty; artificial interventions, however, are myopic. They either target isolated traits—some of which historically underwent balancing selection for multiple alleles—or enforce strict genomic conservation, depriving the species of its evolutionary potential. Consequently, embryo selection and potentially more radical genetic technologies, such as large-scale genome editing, are incapable of resolving the long-term, population-level problem of genetic deterioration.

2 The genomic architecture of intelligence

Muller (1950) wrote: "Moreover, it is likely that, in man especially, the number and complications of genes having to do with mental traits is exceedingly great, so as to result in a comparatively high mutation frequency, one requiring a considerable compensatory selection for the mere maintenance of equilibrium." Decades later, modern genomic research has provided rigorous empirical validation for this hypothesis: Intelligence is a highly heritable and complex trait (Plomin & Deary, 2015). Its extreme polygenicity makes it especially vulnerable to rare, deleterious mutations. While GWAS and polygenic scores have successfully mapped the common variant landscape, they are blind to the rare mutational load that exerts a powerful drag on cognitive function. This distinction—between the visible common variants and the invisible rare load—is the critical prerequisite for understanding the mechanism of genetic deterioration. Population-level single nucleotide variants can be classified into three types:

1. Common variants with minor effects: Ancient variants detected by microarrays or sequencing, whose effects can be inferred in GWAS. They can be targeted by polygenic embryo screening (PGT-P).

2. Rare variants with major effects: Variants detected by sequencing, whose effects can be inferred by sequence-to-function models. These typically manifest as Mendelian diseases and are kept rare by purifying selection. These are the current targets of preimplantation genetic testing for monogenic defects (PGT-M).

3. Rare variants with minor effects: The continuous influx of highly polygenic, weakly deleterious *de novo* mutations. This category constitutes the invisible mutational load, whose combined contribution is likely responsible for much of the "missing heritability", yet it remains overlooked in most contemporary research.

Traditional family-based designs in behavioural genetics capture the heritability arising from the additive effects of all variant types. The long-standing consensus in behavioural genetics is that intelligence is highly heritable—often estimated between 60% and 80% in developed nations (Bouchard, 1998), or even up to 86% when isolating the latent *g* factor (Panizzon et al., 2014). The "shared" familial environment exerts only a transient childhood effect (Bouchard, 1998), while the remaining "non-shared" environmental variance is increasingly recognized as endogenous biological noise, such as stochastic developmental errors and somatic mutations (Plomin, 2024). Heritability studies often estimate only genetic effects that are additive. Using an extended twin-family design, Vinkhuyzen et al. (2012) examined non-additive (i.e., dominance and epistasis) genetic effects. They estimated that while additive genetic factors accounted for 44% of the variance in adult intelligence, non-additive genetic factors accounted for 27%. Using common SNP data from unrelated individuals, Hivert et al. (2021) found negligible non-additive effects.

A persistent challenge in contemporary genomics—and a central vulnerability in current predictive paradigms—is the sharp contrast between pedigree-derived heritability and the heritability captured by single-nucleotide polymorphisms (SNPs) in unrelated cohorts (e.g., estimated at 21% for cognitive performance by Lee et al. (2018) using LDSC, and 31% for verbal-numerical reasoning by Davies et al. (2016) using GCTA-GREML). Analytical frameworks such as LDSC and GCTA-GREML compute heritability directly from molecular data (Bulik-Sullivan et al., 2015; J. Yang et al., 2017); however, when applied to standard array data, they only capture the heritability explained by common variants. Consequently, estimates based on common SNPs act merely as a lower bound. The substantial "missing heritability" gap between these array-based estimates and family studies highlights that a high proportion of heritability is driven by evolutionarily recent, rare, or structurally complex mutations that are not captured by standard genotyping. When models like GREML-KIN reincorporated pedigree data to account for rare variants, the molecular heritability estimate surged to 54% (W. D. Hill et al., 2018). Wainschtein et al. (2026) used whole-genome sequencing (WGS) to evaluate the missing heritability of cognitive traits. They showed that the total WGS-based heritability was 34.7% for educational attainment, with rare variants (0.01% < MAF < 1%) accounting for approximately 43% of this explained variance. For fluid intelligence, the WGS-based heritability reached 32.8%. The impact of ultra-rare variants (MAF < 0.01%) and *de novo* mutations remains unaccounted for even in these estimates. This shows that the missing heritability resides within the rare mutational load—a domain systematically overlooked by conventional GWAS models and current polygenic embryo selection practices.

Holland et al. (2020) estimated the "polygenicity" (as the proportion of causal variants in the genome) of many traits and showed that cognitive phenotypes are the most polygenic quantitative traits. Specifically, they estimated 35,000 and 24,000 independent causal variants among common SNPs (0.32% and 0.22% of all common SNPs) for educational attainment and intelligence, respectively. This estimate implies a massive "mutational target size" that extends beyond the specific common variants identified in GWAS. It suggests that a significant fraction of the functional genome is used for cognitive processes. In addition to the common variants, rare variants could impact the same elements of the genome and exert deleterious effects.

Huguet et al. (2021) further supported this by analysing copy number variants (CNVs), estimating that approximately 10,000 genes—roughly half of the protein-coding genome—modulate cognitive ability. However, focusing solely on coding regions (1-2% of the genome) underestimates the true vulnerability, as the expression of these genes is governed by regulatory elements (such as enhancers and promoters)

and potentially other genomic features whose functions are not yet fully understood. Theoretically, any deleterious *de novo* mutation disrupting the coding or regulatory sequences of these 10,000 genes will negatively impact intelligence. While some high-impact variants are individually detectable, the vast majority are minor-effect variants. Though their existence can be theoretically inferred and their collective load effect macroscopically observed, detecting them at the single-mutation level is exceedingly difficult. Because gene regulation exhibits a "many-to-one" architecture, a much larger proportion of the genome likely influences these 10,000 genes, and by extension, cognitive ability. Databases like GeneHancer (Fishilevich et al., 2017) and the ABC model demonstrate that regulatory elements encompass an area vastly larger than the coding exome, with single genes often regulated by multiple distal enhancers across different tissues and cell types (Nasser et al., 2021). Furthermore, the ENCODE Project Consortium (2012) revealed biochemical activity across much of the non-coding genome, suggesting the effective mutational target size is orders of magnitude larger than the exome alone.

The genomic era has witnessed an exponential growth in GWAS sample sizes, yet this approach has exposed the theoretical limits of common-variant prediction. For direct intelligence measures, Savage et al. (2018) leveraged nearly 270,000 samples to pinpoint 205 significant loci and 1,016 genes, confirming dense expression networks in the central nervous system (CNS). Using educational attainment as a highly correlated proxy, the field has dramatically increased cohort sizes from 126,000 (Rietveld et al., 2013) to an unprecedented 3 million individuals (Okbay et al., 2022). Yet the predictive variance of polygenic scores for these cognitive phenotypes in independent samples remains capped at 12-16%—a fraction of the 60-80% heritability—corresponding to a correlation of .35 to .40 between the trait and its predictive score. The theoretical upper limit of GWAS predictive power is the common SNP heritability (h^2_{SNP}), which has been estimated at 12% (Lee et al., 2018) and 21% (Davies et al., 2016) for educational attainment.

High polygenicity is not unique to intelligence. Although the legacy of the reductionist Mendelian framework continues to constrain genetics, common diseases are fundamentally polygenic in nature (Khera et al., 2018). While this review concentrates on cognitive health, physical health is governed by the same biological and evolutionary principles, suggesting that the mechanisms of genetic deterioration described here apply equally to non-cognitive traits. Beyond this parallel logic, there is a direct genetic interconnection: because of the extensive pleiotropy inherent in the genome, many mutations concurrently impair both cognitive and physical health, including immune resilience. Consequently, the relaxed purifying selection against variants deleterious to intelligence inevitably facilitates the accumulation of mutations that simultaneously degrade overall physical health. Therefore, the conclusions drawn in this review are likely to apply to the overall biological baseline of the human population.

3 The mechanism of genetic deterioration

Mutation-selection balance is the equilibrium in which the continuous influx of novel, predominantly deleterious mutations is offset by the purifying force of natural selection. Genetic deterioration (dysgenics) arises from two sources: the natural accumulation of *de novo* mutations, and reversed selection, which is characterized by a negative correlation between fertility rates and intelligence.

First, as early-life mortality dropped sharply in modern societies, purifying selection that historically removed deleterious mutations was significantly relaxed, allowing genetically impaired individuals to survive and reproduce. Darwin (1871) explicitly warned against this, noting that while savages quickly eliminated the weak in body or mind, civilized men built asylums and did their "utmost to check the process of elimination". Consequently, the natural accumulation of *de novo* mutations has accelerated. High-coverage whole-genome sequencing of parent-offspring trios estimated an average human mutation rate of approximately 1.2×10^{-8} per nucleotide per generation, which translates to roughly 70 new mutations in every newborn (Kong et al., 2012). Specifically, the paternal germline drives an increase of 1.51 *de novo* mutations per additional year of age at conception—four times the rate observed in the maternal germline, which accumulates mutations at 0.37 per year (Jónsson et al., 2017). This striking divergence stems from different mutagenic mechanisms in male and female gametogenesis. Recent studies show that paternal mutations are overwhelmingly replication-driven; maternal mutations primarily arise from the

accumulation of non-replicative DNA damage and meiotic recombination errors during the oocyte's decades-long developmental arrest (Halldorsson et al., 2019). Unlike the inactive oocyte pool, spermatogonial stem cells (SSCs) undergo continuous division throughout a male's life. This persistent mitotic activity subjects the male germline to compounding DNA replication errors and cumulative oxidative stress within the ageing testis (Aitken et al., 2020; Wood & Goriely, 2022). Furthermore, the paternal mutation rate is exacerbated by "selfish spermatogonial selection". In this micro-evolutionary process, certain spontaneous mutations confer a proliferative advantage to the SSCs themselves, facilitating the clonal expansion of mutant sperm populations over time. While advantageous to the individual stem cell, these mutations are deleterious to the resulting offspring, not only causing severe dominant genetic disorders (such as Apert syndrome and achondroplasia), but also exerting broader negative impacts on polygenic neurodevelopmental stability through the transgenerational accumulation of milder variants (Aitken et al., 2020; Wood & Goriely, 2022). This provides a micro-level illustration of the conflict between the short-term interests of the mutated cell and the long-term interests of the individual's lineage.

The consequences of this continuous mutational influx extend far beyond specific developmental disorders, negatively affecting overall human health. While current natural selection remains effective at removing catastrophic genomic errors through "ultraselection" on approximately 0.4-0.7% of the genome (Dukler et al., 2022), this focused pressure is insufficient to arrest the accumulation of widespread, weakly deleterious variants. Assuming a substantial relaxation of selection facilitated by modern medical intervention, Lynch (2016) estimated that recurrent mutational load drives a baseline fitness decline of roughly 1% (and potentially up to 5%) per generation. Similarly, Kondrashov (2017) estimated that the overall health of young people deteriorates by 2% to 5% per generation (p. 223). Given its massive mutational target size, the human brain is especially vulnerable to this systemic genetic erosion. Extensive population-level sequencing has confirmed that the collective burden of ultra-rare disruptive and damaging mutations exerts a negative effect on educational attainment and adult cognitive function (Chen et al., 2023; Ganna et al., 2016). This aligns with the finding of an inverse association between an individual's overall deleteriousness (and total count of minor alleles) and their educational attainment (Wang & Huang, 2023). The danger of this mutational influx is amplified by the fact that most deleterious mutations do not wait to become homozygous to do their damage. As Muller (1950) demonstrated, the great majority of seemingly recessive mutant genes act as "effective dominants", exerting their primary detrimental effects on the population through minor manifestations in the heterozygotes. Rather than presenting as clear-cut diseases, these accumulated mutations typically manifest as subtle, quantitative inadequacies—such as lowered physiological resilience or a reduced cognitive baseline.

Modern demographic fertility trends further exacerbate this phenomenon. Because highly educated individuals increasingly delay childbearing—if they choose to reproduce at all—the rate at which *de novo* mutations accumulate in the population gene pool is further amplified by parental age effects. Given the well-documented monotonic increase of *de novo* mutations with paternal age, researchers have attempted to leverage paternal age as a proxy to infer the speed of mutation-driven cognitive deterioration (Woodley of Menie, 2015). While estimating the exact magnitude of this cognitive decline has traditionally been confounded by the correlation between parental IQ and reproductive timing, Wang (2023) introduced a methodological framework that leveraged micro-molecular constants to calibrate macro-demographic data. By utilizing the biological asymmetry between male and female *de novo* mutation rates as a quantitative anchor, the study attempted to isolate the parental age effect independently of parental genotypic differences. It estimated a -2.0-point (95% CI: -3.7 to -0.3) change in offspring IQ per decade of paternal age when unadjusted for birth order. After further adjustment for birth order, this estimate was attenuated to a -0.6-point change (95% CI: -2.6 to 1.6). Adjusting for birth order risks over-controlling due to its high collinearity with paternal age, which would attenuate the true effect. Conversely, not adjusting for it leaves the estimate vulnerable to confounding from potential non-genetic birth order effects. The true magnitude of the effect likely lies somewhere between these two estimates.

However, the decline driven by *de novo* mutations is ignored by some contemporary authors. For instance, Bratsberg and Rogeberg (2018) observed that the phenotypic IQ rise and subsequent decline in Norway occurred within individual families, rather than being driven by demographic shifts between different

families. They asserted that this indicated no genetic involvement in the decline of population intelligence, treating dysgenic fertility (a between-family difference) as the sole mechanism for genetic deterioration. Astonishingly, a study published in the *Proceedings of the National Academy of Sciences* (PNAS) attempting to debunk genetic deterioration completely ignored the *de novo* mutation mechanism that most concerned early geneticists like Muller—ironically, it was in the very same journal in which Muller (1928) both published his Nobel Prize-winning proof that environmental radiation actively generates *de novo* mutations and laid the foundational mathematical framework for quantifying human mutational damage (Morton et al., 1956). The *de novo* mutational load is dictated by fundamental biological laws and causes within-family changes. Even if the true effect were only a fraction of the unadjusted 2.0-point estimate—such as the 0.6-point change observed when controlling for birth order—it would still represent a decline larger than typical estimates predicted by dysgenic fertility. Because this mutational source is within-family, Bratsberg and Rogeberg's data are actually consistent with mutation-driven genetic deterioration. The observed rise and fall in IQ perfectly align with a continuous underlying genetic decline caused by mutation load that was temporarily masked by finite environmental improvements, becoming visibly manifest only after those environmental gains plateaued.

The second cause of genetic deterioration is reversed selection. This contemporary fertility pattern contrasts sharply with the selection pressures of pre-industrial societies. Historical and demographic analyses indicate that prior to the "demographic transition", there was a positive correlation between cognitive ability and reproductive fitness, which effectively maintained a positive selective pressure for intelligence (Meisenberg, 2010). However, the onset of the "demographic transition" reversed this pattern. As early-life mortality decreased and modern reproductive patterns emerged, the historical positive correlation vanished, decoupling cognitive ability from reproductive success.

Modern society exhibits a robust negative correlation between fertility and highly heritable traits such as intelligence and educational attainment (Lynn, 1996). This negative correlation has become an almost universal phenomenon, particularly evident in developing nations as shown by World Fertility Surveys for educational attainment (Bongaarts, 2003).

To quantify this dysgenic trend, researchers employ two primary methodologies to measure selection differentials (Lynn, 1996). The first is the *offspring method*, which calculates the selection differential from the covariance between adults' intelligence and their number of children. The second is the *sibling method* (Lentz, 1927), which infers the selective pressure of the preceding generation via the covariance between individuals' cognitive ability and their number of siblings. An analysis using population-representative data in China explicitly compared these two methods, yielding very similar estimates of the selection differentials (Wang et al., 2016).

Phenotypic evidence of this dysgenic fertility trend has been documented globally. A recent international meta-analysis of differential fertility incorporating data from 65 countries revealed that individuals with higher intelligence consistently reproduce at below-replacement rates, estimating a decline in genotypic IQ of 0.4 points per decade (Jensen et al., 2025). Note, this estimate reflects the population-weighted decline exclusively *within* countries; it excludes between-nation IQ differences, as cross-national heritability is difficult to quantify. Large-scale genomic analyses provide molecular evidence of an underlying genetic deterioration. Genetic data from cohorts in the US, Iceland, and the UK support the trend (Beauchamp, 2016; Hugh-Jones & Abdellaoui, 2022; Kong et al., 2017; Sanjak et al., 2018). However, a recent demographic analysis suggested that the negative relationship between female education and fertility has disappeared in Western Europe and related countries (Cheng et al., 2022).

For decades, massive environment-driven gains in phenotypic intelligence have masked genetic deterioration. Historically, this phenomenon—widely known as the Flynn effect—yielded rapid population-level gains (e.g., Lynn, 1982; Wang & Lynn, 2018). Recently, however, the trend has reversed, and average phenotypic IQ scores have begun to fall across many countries (Dutton et al., 2016).

4 Non-germline medical interventions

When confronted with the accumulation of deleterious germline mutations, the standard medical response relies on the optimistic assumption that continuous therapeutic advancements will neutralize these genetic defects. However, Muller (1950) dismantled this argument over seven decades ago: “Furthermore, may we not confidently expect that, with continued advances in general technology, living standards and medicine, the genetic burden will be further lightened and kept very small indeed? [...] The great trouble with this method is that [...] each successive generation will have not only the mutant genes which have in this way been passed along to it but also its own new crop of mutations.”

Today, advanced gene therapies utilizing CRISPR or viral vectors can manage specific monogenic pathologies. However, they are powerless against the polygenic degradation of baseline cognition driven by minor-effect mutations. Regarding physical interventions, the advancement of neurotechnologies raises the possibility that such tools could eventually enhance human cognition and prevent deterioration. Much research effort has been devoted to the treatment of neurodegenerative disorders that cause adult cognitive decline, such as Alzheimer’s and Parkinson’s diseases. Neuromodulation techniques—such as transcranial magnetic stimulation (TMS) and deep brain stimulation (DBS)—can only provide clinical relief. Their utility is also constrained: DBS requires invasive neurosurgical implantation, while the effects of non-invasive TMS are short-lived. Following a standard TMS treatment course—typically 2 to 4 weeks—cognitive improvements in Alzheimer’s disease generally last for only 1 to 3 months (Chou et al., 2020), whereas in Parkinson’s disease, such benefits typically last for only 1 month and completely disappear by the 3rd month (Y. Yang et al., 2024). As neurodegenerative diseases inevitably advance, these interventions eventually lose their efficacy.

In summary, whether molecular or neuromodulatory, these therapies remain fundamentally identical to the conventional medicine Muller criticized: They are somatic interventions, not germline repairs. Because they exclusively target somatic cells to cure the individual phenotype, they leave the germline (sperm and eggs) untouched. Consequently, the deleterious mutations are preserved and passed on to the next generation. This ensures that each subsequent generation of descendants will inherit the uncorrected ancestral load alongside a newly acquired crop of *de novo* mutations. This creates multiple interacting biological deficits, forcing future generations into an ever-expanding medical dependence where exponentially more treatments will be required simply to maintain baseline human function. As Muller (1950) warned, it would inevitably lead to the complete disintegration of our natural biological organization. In such a scenario, Muller predicted that “everyone would be an invalid, with his own special familial twists”, requiring highly individualized, continuous medical intervention merely to survive.

5 GWAS-based embryo selection

Embryo selection is currently recognized within the public discourse as a prospective method to enhance offspring intelligence. The standard protocol involves fertilizing multiple embryos *in vitro*, sequencing their genomes, evaluating polygenic scores for cognitive and health traits based on population-level GWAS data, and implanting the most promising candidate. However, this approach suffers from important limitations.

Firstly, the predictive power of polygenic scores is limited. Current polygenic score models for cognitive traits rely almost exclusively on common variants derived from population-level data. Even those constructed from cohorts of millions account for only a small fraction of phenotypic variance (7–10% in Lee et al., 2018). Though predictive power will grow as sample sizes increase, it cannot exceed the SNP heritability ceiling. This leaves the vast majority of the biological architecture—particularly rare and *de novo* variants—invisible to the selection process. While conventional preimplantation genetic testing (PGT) can be effective at screening out major chromosomal abnormalities (aneuploidies and structural rearrangements, including large-scale copy number variations; PGT-A/SR) and specific monogenic or simple oligogenic disorders (PGT-M), such interventions only eliminate catastrophic errors. Moreover, PGT-M relies on prior knowledge—parents must already know they carry a pathogenic mutation (e.g., after having an affected child). It is ineffective against true *de novo* mutations. Untargeted fetal screening for

pathogenic *de novo* mutations is unfeasible because of the false-positive paradox: when conducting mass screening for rare events, errors yield far more false alarms than true discoveries, rendering the screening impractical. GWAS-based embryo screening (PGT-P) is powerless to detect or halt the silent accumulation of minor-effect *de novo* point mutations—the diffuse, polygenic genetic load that constituted the primary concern of early geneticists like H. J. Muller.

This blind spot is not merely a matter of insufficient data that can be resolved by scaling up sequencing efforts. Even if we could hypothetically obtain perfect whole-genome sequencing (WGS) data and precise intelligence testing for the entire global population, methods like GWAS would still fail to accurately estimate the effects of rare and *de novo* variants. Multiple adjacent variants in linkage disequilibrium (LD) might exert independent causal effects—sometimes in opposing directions—on the phenotype. Association studies cannot estimate the effects of these physically linked variants.

Secondly, embryo yield is limited; the power of selection depends on the pool size. In standard *in vitro* fertilization, couples typically produce only 3 to 8 viable embryos (cited in Karavani et al., 2019). Under these clinical constraints, the expected phenotypic gain is minimal; Karavani et al. (2019) demonstrated that selecting the "best" of 5 embryos yields an expected average gain of merely ~2.5 IQ points, based on the predictive power available at the time (r^2_{pgs}=4.3%). Due to high unexplained variance, the highest-scoring embryo frequently does not develop into the offspring with the highest actual phenotypic value. The research suggested that the simulated gain increases proportionally to the square root of the proportion of the variance explained by the predictor. Even if the polygenic score's predictive power were to reach the common SNP heritability ceiling ($h^2_{SNP}\approx$21%) for cognitive performance, the simulated gain for 5 embryos would only increase to ~5.5 IQ points ($2.5 \times \sqrt{\frac{21\%}{4.3\%}}$). Even if future technology allowed a couple to choose from a pool of 1,000 embryos, the average gain would still be only ~5.1 IQ points under the 4.3% predictive power model, and would barely reach ~11.3 points even with 21% predictive power. Moreover, if embryos were simultaneously screened for multiple health traits alongside intelligence, the selection pressure would be divided, causing the potential for cognitive enhancement to decrease significantly.

The within-family predictive power of polygenic scores is lower than population-level (between-family) estimates, driving the realized utility down even further due to inherent range restriction among siblings and the compounding effects of assortative mating (Turley et al., 2021). Current estimates of the within-family penalty rely on additive models and likely underestimate the true extent of this predictive decay. In population-level studies using common variants, non-additive genetic variance appears statistically negligible (Hivert et al., 2021; Zhu et al., 2015) because purifying selection keeps deleterious dominant mutations at extremely low frequencies. However, every couple transmits rare inherited deleterious variants, and every embryo acquires *de novo* mutations. Because polygenic scores rely exclusively on common additive variants, they are blind to this mutational load. Family-based studies reveal substantial non-additive genetic variance, accounting for up to 27% of the variance in intelligence (Vinkhuyzen et al., 2012), suggesting that neurodevelopment is a non-linear biological system where deleterious mutations act as an asymmetric downside risk that can override a high additive score. Consequently, linear models artificially inflate the expected accuracy of embryo selection. This phenomenon is well-documented in agricultural genomics, where traditional models that ignore non-additive interactions consistently overestimate the accuracy of genetic predictions among full-sibling families (Muñoz et al., 2014; Nadeau et al., 2023; Pante et al., 2002).

6 Sequence-to-function models

Recent advancements in artificial intelligence have introduced "sequence-to-function" deep learning models. Unlike GWAS, which rely on statistical correlations, these models learn the syntax of the genetic code, enabling them to directly estimate the molecular consequences of variants (Avsec et al., 2021, 2026). The continued research and development of these tools could enable the identification of high-impact *de novo* mutations even within the non-coding genome—variants invisible to GWAS yet often responsible for severe neurodevelopmental disorders. Theoretically, this would allow for the effective eradication of Mendelian cognitive deficits and catastrophic biological errors from the gene pool, thereby reducing the most severe manifestations of mutation load.

However, the ability to screen out the most severe mutations does not equate to the ability to reverse genetic deterioration. A fundamental limit remains: the accumulation of weakly deleterious variants. Because deep learning models are trained to recognize deviations from evolutionary conservation (Brandes et al., 2023), they can identify major functional disruptions but remain insensitive to the subtle, cumulative effects of weakly deleterious variants. Given the extreme polygenicity of cognitive traits, the effects of the vast majority of deleterious *de novo* mutations are incredibly small—falling far below the threshold at which conservation-based AI models can reliably detect them.

7 Foreseeable technological advancements

To overcome the mathematical limits of embryo yield, proponents of genetic enhancement have set their sights on the development of "stem-cell-derived gamete" technology. As Shulman and Bostrom (2014) proposed, if viable human sperm and eggs could be reliably derived from induced pluripotent stem cells, the biological limits on natural egg retrieval would be effectively abolished. This technology could enable the creation of hundreds or thousands of embryos for a single couple, vastly expanding the selection pool and dramatically increasing the expected phenotypic gain. Furthermore, Shulman and Bostrom (2014) hypothesized the possibility of "iterated embryo selection"—extracting cells from these generated embryos to derive new gametes, thereby allowing an even higher diversity of combinations. Biological barriers remain for such technologies. Generating gametes from stem cells risks epigenetic imprinting errors similar to those seen in mammalian reproductive cloning. More importantly, gametes derived from induced pluripotent stem cells are expected to harbour more *de novo* mutations than natural gametes, because natural germline cells have uniquely efficient DNA repair mechanisms compared to somatic cells.

Proponents of such technologies draw parallels to successful long-term selection experiments in agriculture, such as the breeding of commercial broiler chickens, which have increased in size more than four times since 1957 (Hsu, 2014), and the Illinois maize experiment for protein and oil content. However, these successes were driven by phenotypic selection rather than genotypic selection. Phenotypic selection captures and propagates both standing common variation and *de novo* mutations that continuously arise in the population (Mulder et al., 2019). In a recent review, Floriani and Lipka (2025) highlighted that rare variants are critical for driving yield improvements and stress resistance in staple crops such as maize and soybean. They noted that empirical studies in yeast demonstrate that such rare alleles often exhibit larger effect sizes and explain more than half of the additive genetic variance. In contrast, GWAS-based selection relies on predefined common SNP markers, meaning favourable *de novo* mutations would not be selected and would be lost.

Beyond embryo selection, the rapid advancement of gene-editing technologies could theoretically offer a more direct way to halt genetic deterioration. Visscher et al. (2025) theorized that with advancing understanding of causal variants, CRISPR-like technologies could evolve to permit heritable polygenic editing—the simultaneous, high-throughput editing of tens or hundreds of loci across the genome. As previously mentioned, trait-associated variants identified in GWAS frequently occur in clusters; nearby variants are co-inherited in the population and are in strong linkage disequilibrium (LD) with one another. The authors predicted that if we could identify the causal variant within an LD block and edit ten such loci with the largest effects, the lifetime prevalence of Alzheimer's disease could be reduced from 5% to 0.6%, type 2 diabetes from 10% to 0.2%, and coronary artery disease from 6% to 0.1%.

This calculation rests on the premise that there is only one causal variant ("lead SNP") per LD block, implying that editing these specific single nucleotides would reverse the entire phenotypic effect observed for those LD blocks in the population. This assumption is invalid. Experimental and statistical research demonstrates that a single independent GWAS signal is often driven by multiple functional variants aggregating within a strong LD block (Long et al., 2025). Experimentally, Abell et al. (2022) used high-throughput functional assays to reveal that 17.7% of eQTLs contain multiple active SNPs in tight LD. At the *FTO* locus, Sobreira et al. (2021) showed that a single risk haplotype harbours at least four distinct enhancers coordinately regulating downstream genes. Furthermore, Chatterjee et al. (2021) showed that

disrupting multiple linked enhancer SNPs at the *RET* locus causes a synergistic, rather than merely additive, reduction in target gene expression.

Even assuming that in the future, technologies such as stem cell-derived gametes, heritable polygenic editing, and sequence-to-function predictive models achieve a threshold of clinical reliability—reaching a point where their practical utility outweighs their cost and technical risks—a fundamental biological barrier remains: the extensive interconnectedness of the human genome.

8 Antagonistic pleiotropy

The implicit assumption for the use of embryo selection to offset genetic deterioration is that since overall cognitive capacity can be elevated by aggressively selecting for advantageous common variants identified by GWAS, the underlying *de novo* mutational load can be neutralized. In other words, the logic presumes that the diffuse burden of minor-effect *de novo* mutations can simply be compensated for by aggregating advantageous common variants. However, this palliative strategy is biologically problematic because the genome exhibits widespread antagonistic pleiotropy—where an allele confers a functional advantage for one trait while increasing susceptibility to adverse outcomes in another. For example, genetic variants promoting high educational attainment correlate with increased risks for psychiatric conditions like autism spectrum disorder and bipolar disorder (Anttila et al., 2018).

This pervasive biological trade-off poses a fundamental challenge to the very premise of polygenic embryo selection and genome editing. Because these reproductive technologies aim to unilaterally maximize desired phenotypes, such as cognitive capacity, they unintentionally co-select for antagonistically linked deleterious traits (Turley et al., 2021; Visscher et al., 2025). Unlike natural phenotypic selection—which assesses overall evolutionary fitness by simultaneously acting on common and rare variants across numerous traits—current polygenic selection only screens common variants, and only for specific or isolated phenotypes. Yet, the "harmful common variants" for these phenotypes might be the pleiotropic alleles that natural selection has maintained in long-term balance because they are beneficial to other phenotypes.

A theoretical technological workaround to this global pleiotropy might involve using local genetic correlation frameworks, such as LAVA (Werme et al., 2022), to isolate and exclude specific genomic regions exhibiting antagonistic effects, while selecting for alleles in regions free of pleiotropic conflict. However, this detailed approach reveals a deeper layer of complexity. Even when the global genetic correlation between two traits appears neutral, extensive localized antagonistic pleiotropy often persists across the genome. While current tools have identified a subset of these conflicting regions, the extreme polygenicity of cognitive traits dictates that countless local antagonistic effects remain undetected due to statistical power limitations.

Recent comprehensive analyses support the ubiquity of this biological trade-off. Bian et al. (2024) identified extensive pleiotropic conflicts covering approximately 11.4% of LD blocks in the human genome, noting that these antagonistic variants are enriched for intermediate allele frequencies and exhibit strong signatures of balancing selection[1].

Note, because this estimate primarily captures conflicts between macroscopic phenotypes, we can expect this antagonism to be even more pervasive at a microscopic level. Cognition is a highly complex trait underpinned by a large number of biological substrates (endophenotypes / intermediate phenotypes). Antagonistic pleiotropy likely operates not only for macroscopic traits like intelligence but also between different endophenotypes. Wang (2025) explored this possibility, suggesting that the same set of genetic predispositions may exert conflicting effects on different endophenotypes of the same behavioural phenotype. The same genetic predisposition might be beneficial to the brain-structural mechanisms of educational attainment, yet detrimental to its brain-functional mechanisms.

Genomics research frequently grapples with the "portability problem"—the observation that European-derived polygenic scores perform sub-optimally when predicting phenotypes in non-European populations (Lupi et al., 2024). But a more important evolutionary question is: why do these genotype-phenotype associations, for complex traits like intelligence, remain shared across different human races that diverged

[1] Balancing selection refers to the evolutionary processes that actively maintain multiple alleles at the same locus.

tens of thousands of years ago? Based on this widespread pleiotropy, I propose a hypothesis: The very fact that genetic variants linked to intelligence detected in common-variant GWAS are shared across different races strongly implies the existence of antagonistic pleiotropy. If the common variants negatively associated with a highly fitness-relevant trait like intelligence had been exclusively detrimental, ancestral variants would have been purged by natural selection over the extensive evolutionary time since human races diverged. Under such a scenario, the "low-intelligence" variants identified by contemporary GWAS would primarily consist of mildly deleterious mutations that had arisen independently in different races and drifted to higher frequencies. However, their persistence as common variants across races implies they have instead been actively maintained by balancing selection.

Directly contradicting the independent local drift hypothesis, empirical analyses suggest that GWAS signals are highly replicable across races (Marigorta & Navarro, 2013). This variant-level sharing proves they are not deleterious mutations that occurred after human divergence, but rather deeply conserved ancient variants. These trade-offs have ancient evolutionary roots; genomic evidence reveals that certain disease-associated polymorphisms, including major genomic deletions, have been actively maintained by balancing selection for hundreds of millennia—predating even the divergence of modern humans and Neanderthals (Aqil et al., 2023)—sometimes because they confer early-life developmental and reproductive advantages at the cost of late-onset disease and senescence (Rodríguez et al., 2017). Thus, the detrimental effects of these variants on specific cognitive or physical phenotypes are linked to biological benefits elsewhere in the physiological network or lifespan. The attempt to "correct" these ancient variants to unilaterally maximize a single trait could disrupt this biological equilibrium.

The side effects of such unilateral selection are illustrated by commercial agricultural breeding. For instance, intensive artificial selection in broiler chickens over the past half-century has yielded unprecedented increases in growth rate, feed efficiency, and breast meat yield, with modern commercial strains growing to more than four times the mass of unselected strains from 1957 (Zuidhof et al., 2014). However, this massive phenotypic enhancement was accompanied by severe unintended consequences driven by antagonistic pleiotropy (Rauw et al., 1998; van der Most et al., 2011). The extreme selection for rapid muscle accumulation unintentionally compromised the birds' overall physiological equilibrium, resulting in widespread skeletal deformities and cardiovascular vulnerabilities (Julian, 2005). Most critically, it significantly depressed their immunological resilience. Qureshi and Havenstein (1994) demonstrated that modern broilers selected almost exclusively for maximum muscle growth exhibited impaired adaptive immunity compared to a 1957 random-bred control line: while their innate immune system (such as macrophage function and inflammatory recruitment) remained largely intact, the metabolically expensive adaptive system was severely compromised.

9 Genetic diversity and immunity

Perhaps the most catastrophic risk of employing large-scale embryo selection or genome editing to stop genetic deterioration lies in the depletion of genetic diversity and its effects on immunocompetence. Host resistance to rapidly evolving pathogens is dependent on high levels of genetic variation, particularly heterozygosity (Penn et al., 2002). For instance, heterozygote advantage at the major histocompatibility complex (MHC)—the highly polymorphic genomic region governing immunological recognition—allows individuals to recognize and clear a vastly broader spectrum of pathogenic strains. Conversely, inbreeding-induced depletion of genome-wide diversity has been shown to depress cell-mediated immune responses and overall immunocompetence in wild birds (Reid et al., 2003, 2007).

This immune system vulnerability is directly linked to cognitive ability because the genomic architecture of the human immune system is tightly interwoven with the CNS. The brain is integrated with immune functions anatomically via recently discovered meningeal lymphatic vessels (Louveau et al., 2015) and molecularly through genetic pleiotropy. Some of the core genes that dictate advanced cognitive functions and neural wiring are dual-purpose immune genes. For example, MHC class I molecules, classically responsible for antigen presentation, are also essential for regulating neurite outgrowth, synaptic plasticity, and the activity-dependent refinement of cortical connections during brain development (Elmer & McAllister,

2012). Similarly, the classical complement cascade—specifically complement component 4 (C4) located within the MHC locus—mediates the precise elimination of synapses (synaptic pruning) in the developing brain, a process whose dysregulation is implicated in cognitive wiring abnormalities and schizophrenia (Sekar et al., 2016).

Furthermore, cross-disorder genomic analyses demonstrate that the genetic overlap between brain-behavioural phenotypes and immune-mediated diseases is a genome-wide phenomenon. For example, widespread genetic correlations between psychiatric conditions and immune phenotypes persist robustly even after the entire extended MHC region is statistically removed from the analysis (Tylee et al., 2018). Shared genetic risk variants frequently operate through diverse, non-MHC pathways that guide both neuronal migration and immune regulation, such as the *EPHB4* gene linking schizophrenia and Crohn's disease (Pouget et al., 2019). Because cognitive and immune functions share this deeply integrated, genome-wide architecture, they cannot be uncoupled. Attempting to preserve immune diversity by algorithmically excluding known immunity-related regions from genomic cognitive enhancement is biologically infeasible.

The root of the problem is that nature optimizes traits in a fundamentally different way than biotechnology does. Natural selection operates on the phenotype. It evaluates only the final outcome, allowing diverse genetic pathways to reach the same phenotypic destination (Barghi et al., 2020). Through convergent evolution, this "many-to-one mapping" of genotype to phenotype ensures that necessary adaptations are achieved while leaving a vast reservoir of genetic heterogeneity intact. This phenomenon is widely observed, from diverse morphological forms mapping to identical mechanical functions (Wainwright et al., 2005) to distinct genetic mutations enabling human lactase persistence (Tishkoff et al., 2007) and mammalian high-altitude adaptation on the Tibetan Plateau (Lyu et al., 2022). By achieving the same phenotypic target through heterogeneous genetic blueprints, natural selection protects variation. This preserves the genetic diversity essential for future adaptations and fending off novel pathogens. Genotypic selection, however, enforces a standardized molecular blueprint. By optimizing for a specific set of predefined markers, it systematically eradicates the underlying variance that phenotypic selection would otherwise tolerate. This molecular overlap establishes an evolutionary trap. By standardizing the brain, we unknowingly standardize the immune system. This antagonism with immunity represents a unique form of pleiotropy: traits like intelligence are typically directionally selected in natural selection (where higher capacity is favoured); the immune system relies on genetic diversity itself to combat rapidly evolving pathogens. Importantly, once this immunological diversity is compromised, we cannot rely on *de novo* mutations to restore it. The extreme polymorphism of the major histocompatibility complex—the genomic region governing adaptive immune responses—is maintained through ancient balancing selection favouring multiple alleles, rather than a rapid turnover of new mutations. This ensures a deep reservoir of protective alleles (Özer, 2023). As explained by Fisher's geometric model, an organism's phenotype exists within a highly complex, multi-dimensional space. When a population is well-adapted and located at or near its fitness optimum, random genetic changes are much more likely to move the organism away from this peak. This is especially true for complex organisms like humans. As organismal complexity increases, random mutations become overwhelmingly likely to disrupt crucial biological functions rather than enhance them (Lin et al., 2025). Consequently, while future biotechnology might succeed in halting cognitive deterioration, the irreversible loss of immune diversity could ultimately lead to human extinction.

10 Hypothetical perfection: Prediction and editing

Modern genomic research fundamentally pursues two ultimate objectives: (1) understanding—the accurate functional mapping of the genome, enabling the perfect prediction of how any mutation (from common SNPs to *de novo* variants) affects protein structure, regulation, and phenotypic development; and (2) manipulation—the technological capacity to precisely edit and control the human genome.

If these goals were fully realized, it would be technically possible to precisely pinpoint every *de novo* variant compromising physical and cognitive health, and systematically correct each such mutation in the germline.

Yet, if this "perfect" technological solution were uniformly implemented, human evolution would effectively cease. Genetic variation is the fundamental source of evolution. Although the vast majority of non-neutral *de novo* mutations disrupt biological systems, particularly in highly complex organisms (Lin et al., 2025), advantageous mutations occasionally arise. These rare variants are the indispensable raw materials driving evolution, allowing the species to continuously adapt to the environment and elevate its physical and mental potential.

Furthermore, there is a fundamental theoretical limitation in using computational models to predict complex macroscopic phenotypes. Even at the molecular level, state-of-the-art protein structure prediction models are not forward simulations deducing outcomes using physicochemical rules; rather, they depend heavily on historical evolutionary data, such as multiple sequence alignments. If predicting a single protein is so challenging, predicting a highly complex trait like intelligence from genomic novelty is exponentially more difficult. This difficulty is rooted in computational irreducibility (Wolfram, 2024), which means that the developmental process cannot be mathematically bypassed; the exact outcome can only be known by allowing the biological system to actualize itself *in vivo*. The dependence of such models on known evolutionary history to evaluate mutations limits their ability to predict evolutionary novelty. For example, algorithms trained on historical data often fail to predict the physical consequences of new, individual missense mutations (Buel & Walters, 2022). When the biological system does not follow a fixed historical rule, the algorithm's predictions collapse. Consequently, sequence-to-function algorithms would only act as conservative filters, systematically removing unverified genetic variations to preserve the known norm. In doing so, this technological filter would eradicate the rare, advantageous *de novo* mutations that serve as the indispensable raw material for adaptation, unintentionally imposing an artificial ceiling on human potential and freezing the species in a state of permanent evolutionary stagnation.

11 Conclusions

This paper has critically evaluated the potential of reproductive biotechnologies to counter the trend of human genetic deterioration. Based on the analysis of genomic architecture, mutational load, evolutionary mechanisms, and current technological capabilities and their future development, four fundamental conclusions emerge:

1. Reproductive biotechnologies represent a useful tool in mitigating some severe mutations. These technologies warrant development and widespread application after rigorous scrutiny, with a specific ethical obligation to ensure equitable access, lest genetic inequality between socioeconomic groups be exacerbated.

2. Current biotechnologies are—and will likely remain—insufficient to fully offset the genetic deterioration driven by *de novo* mutations and negative fertility correlations. Due to the massive mutational target size of cognitive (and likely physical) health and the continuous influx of *de novo* mutations, simple genetic selection strategies cannot fully counteract these forces.

3. While screening embryos using polygenic scores may indeed increase the intelligence of offspring, widespread adoption carries the risk of reducing population-level genetic diversity. Unlike natural selection, which acts holistically on overall organismal fitness across all variants, polygenic scores target isolated phenotypes using common variants only. This short-sighted homogenization could deplete the population of protective alleles maintained by conflicting selection pressures and erode the biological resilience necessary to survive novel pathogens.

4. Theoretically, a "perfect" system of prediction and genome editing could halt genetic deterioration and stabilize physical and cognitive health. Yet, by correcting every deviation to fit a normative, conserved model, such a system would differ from the mechanics of natural selection, which preserves and relies on rare, advantageous *de novo* mutations. This technological filter would simultaneously eliminate the raw material of variation required for future adaptation, freezing our species in a state of static optimization and rendering it incapable of further evolution.

Despite the existential importance of understanding these issues for humanity, they are frequently marginalized in contemporary mainstream academia. The increasing politicization and commercialization of science severely challenge research into these questions. Langbert (2018) revealed severe political homogeneity within elite American liberal arts colleges, noting that among those registered with a major political party, 95% of biology professors, 94% of psychology professors, and 100% of anthropology professors identify as Democrats. This ideological hegemony inevitably shapes research agendas, creating blind spots on topics that conflict with specific political narratives. Democratic elites strategically encourage mass immigration to serve their interests: economically utilizing it as a reserve army of labour to suppress domestic wages for the working class, and politically leveraging it as a voting bloc to maintain state power—thereby subjecting research at the "population genetic level", with consequences that might be detrimental to their special interests, to unprecedented ideological pressure (Wang, 2026).

The suppression of science has historical precedent. When the National Academy of Sciences (NAS) faced pressure from a letter demanding the suppression of research regarding racial differences in intelligence, the co-discoverer of DNA structure, Francis Crick (1971) wrote: "[The letter] neither gives nor refers to any scientific arguments, but makes unsupported statements of opinion. This [. . .] is politics, not science." He threatened to resign as a foreign associate of the NAS to defend such research. In 2007, James Watson, another co-discoverer of DNA structure, boldly cited Richard Lynn's study on the subject, fearless of political persecution (Lynn, 2001). While the study of genetic deterioration within a population is distinct from the study of racial differences, the suppression of the latter has created a "chilling effect" that discourages rigorous investigation into the former. Such suppression betrays the legacy of Karl Marx and the founders of molecular biology. If open debate continues to be suppressed by political taboos, we risk failing to solve the problem of genetic deterioration while potentially exacerbating it through ill-conceived interventions that could trigger unforeseen health crises.

Furthermore, the commercialization of reproductive technologies introduces a distinct source of bias. While commercialization is frequently celebrated as a powerful engine for technological innovation and dissemination, its alienating and distorting effects on scientific objectivity remain vastly underappreciated (Wang, 2026). As Karl Marx famously observed, social existence determines social consciousness, a principle that applies as much to researchers as to any other group. Evolutionary biologist Robert Trivers (2011) expanded on this with his theory of self-deception, arguing that self-deception is an evolved trait of human nature, designed to allow individuals to more effectively deceive others by first deceiving themselves, ultimately serving their own special interests. Science, as a human enterprise, is not immune to this instinct. Both politicization and commercialization fuel this self-deception. When a scientific hypothesis aligns with a researcher's political ideology or financial interest, the brain readily constructs a biased narrative, filtering out contradictory evidence to maintain a coherent, self-serving worldview.

Unlike conventional medical research—which typically prioritizes short-term, partial outcomes by evaluating immediate efficacy and direct adverse effects on individual patients—large-scale embryo selection or gene editing for polygenic traits operates on an entirely different scale. While it attempts to integrate partial, immediate interests (such as parental reproductive choices) with long-term population interests, its unintended "side effects" are transgenerational, systemic, and holistic in nature. Because these long-term, population-level risks are easily overshadowed by the immediate gratification of political or commercial incentives, the only antidote to our evolved tendency for self-deception is rigorous, adversarial, and open debate. Considering that genetic quality is of paramount importance to humanity, I urge researchers to place the long-term, holistic interests of the human species above short-term, partial political and commercial interests, and above their own special interests in academic career advancement.

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