A role for epigenetics in economic analysis

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Abstract: *If DNA and the environment are looked at as inputs comparable to inputs in industrial production, transcription, translation, actions in the post-translational phase and epigenetic processes could be looked at as the corresponding productive processes. Given those inputs, their function is to produce and maintain organisms, where the epigenetic processes are the ones that react to the environment. The paper first briefly introduces epigenetic mechanisms, thereby highlighting their relevance with reference to the Flynn effect. It follows a digression on statistical methods and genetic models, needed to support the argument in the last section. There, on human grounds as well as on grounds of economic efficiency, a case is developed for strong support of children both before they are even born and during the very early years; this at the level of the family as well as at the level of the whole of society.*

Epigenetics is a new sub-discipline of biology that studies the processes taking place when genes are getting expressed. While ideas involving genetics have made it into economic analysis and even into prestigious economics journals, the insights of epi-genetics have so far barely been recognized. A quick JSTOR check of publications in the American Economic Review (June 2022) using the criterion 'genetic' garnered 254 hits, while the one using 'epigenetic' had only three.[1] Now, if one looks outside of economics, an enormous literature on the subject has emerged with contributions from fields as diverse as theoretical biology and applied medicine. Some of the more vocal authors of this literature (Lerner and Overton, 2017; Bjorklund, 2018) claim that epigenetics has replaced the gene-centric view of life, which if only in part true would also affect economic analysis. One objective of this paper is to be a stepping stone for insights from this field to make it into the analysis of economic issues. A vehicle for carrying out this task will be the Flynn effect, the observed secular increase in measured IQ scores in many countries, which by itself has relevance for economics. Another objective of the paper is to apply insights gained in the analysis of a particular economic issue.

The paper is organized as follows. The first section is a brief outline of what epigenetic processes are about. This is followed by an epigenetic assessment of explanations for the Flynn effect that are proposed in the literature, using for this a

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* Werner Neu is a consultant and researcher associated with WIK. The opinions expressed in this paper are not necessarily shared by WIK.

[1] True, in some quarters of (behavioral) economics, reasoning using epigenetics does take place (see Cory, 2021). The point made here is that studies published in the most prestigious economics journals stand for what style of economic reasoning is predominant in public discussions and in particular in circles where economic policy is formulated. As pointed out in Cunha & Heckman (2007) and Currie (2011), two papers in the AER thrown up by the JSTOR check, and as shown in the present paper, the insights from this new field have implications for public policy.

review of these explanations in an article by two psychologists from Vienna University. Then follows a digression aimed at providing methodological support for the analysis in the last section. This analysis consists of working out the implications of the insights generated regarding an issue involving human personality traits, including intelligence, in the context of societal and economic development.

1. An economist's understanding of epigenetics

Epigenetic mechanisms are of interest for economists (and other social scientists), because it is through them that (human) organisms react to environmental - among them economic and social - conditions. According to one of its definitions (Watson and Goodman, 2013) epigenetic phenomena are "gene-regulating activities that do not involve change to the base sequence (i.e., base-pairing is not altered)". This means that it does not need a mutation in the genomic code for changes to take place in the make-up of organisms and in their behavior; it suffices that there be an environmental change.

The interpretation of epigenetics adopted here is the one of molecular neuroscience, according to which epigenetic mechanisms play a role in the process of gene expression at the molecular level.[2] Before we comment on three particular forms of these phenomena, it is useful to note that the process of gene expression - the process by which the information contained in the genes is transformed into organisms - consists of several phases, broadly: transcription, translation and the post-translational phase. Through transcription, portions of DNA are transformed into messenger RNAs which subsequently are translated into proteins. In the post-translational phase, when the proteins are already created, further gene expression activities take place, the results of which then play a role in following cycles of gene expression. As already implied, epigenetic processes may interfere in any of these phases.

Three epigenetic mechanisms

Below we briefly comment on three epigenetic mechanisms, of which the first two are the most solidly researched while intensive research on the third started more recently though may prove to be the most revealing one. Other mechanisms not taken up are either not well researched or appear to be less important; for their coverage see Aristizabal et al. (2020). While most of the aspects discussed result from human studies, some result from - mostly mammalian - animal studies; this will in general not be pointed out, since when at the molecular level events and mechanisms affect homologous DNA regions, these are essentially the same across species.

[2] Stilling et al. (2014) point out that there is an excessive use of the term 'epigenetics' in the current scientific vocabulary. After reflecting on several uses of the term, they nevertheless conclude that, irrespective of the particular interpretation adopted, the molecular machinery mediating these seemingly different effects is indistinguishable in all interpretations.

DNA methylation

This mechanism is the most studied one. It involves chemical elements ('marks') attached to specific DNA sites which - depending on the situation - are established, interpreted or removed by factors especially created for this purpose (Nicholson et al., 2015; Yoon et al., 2017). One important aspect is that at the very beginning of life, around the time of fertilization of the egg, most of the parents' marks are erased and then - in accordance with an embedded program - newly established (Issa, 2002). Thus epigenetic marks are needed for the development of the organism and its stability throughout life. In case that - say due to an environmental event later in life - a DNA site is *de novo* methylated, this site is closed to being transcribed, and, conversely, in case an initially methylated site is de-methylated, this one becomes open to transcription. What then precisely happens, whether the effect is beneficial, harmful or neutral, will depend on the type, strength and persistence of the signals received.

Histone modifications

Histones are large molecules around which DNA is wrapped; they provide the structure for the DNA sequence. When DNA is wrapped 'loosely' around this structure, it is open to transcription; when DNA is wrapped 'tightly', it is not. Histone modifications are interventions by which chemical elements ('marks'), similar to those in the case of methylation, get attached to protrusions ('tails') sticking out from the histones through which the tightness or looseness of the histones is changed. Such modifications usually take place post-translationally, thus be able to influence following cycles of gene expression. Like methylation, histone modifications occur through specific marks that are brought into place by factors that are also especially created for this purpose. It is mentioned (de Lima Camillo & Quinlan, 2021) that there may be more than 1,000 different histone modifications possible in the human body.

Non-coding RNA

Non-coding RNA (ncRNA) differs from messenger RNA in that it is transcribed but not translated into protein; it rather performs structural (non-epigenetic, cell viability maintaining) and regulatory (epigenetic related) functions (Sadakierska-Chudy and Filip, 2015). It seems that ncRNA is the most pervasive of the epigenetic mechanisms as it interferes directly or indirectly at all three levels of gene expression, at transcription and translation as well as during the post-translation phase. At the transcriptional and post-translational levels, it takes part in the processes that bring the various marks into place (Malecová and Morris, 2010. At the translational level, its role has been referred to as 'fine-tuning' gene expression (Sevignani et al., 2006; Loukas et al., 2021), in that ncRNA molecules are able to react rapidly and in a 'sophisticated, efficient and cost-effective' way to external factors (Pecoraro et al., 2022; O'Dea et al.. 2015). In case this fine-tuning gets awry, for example when there is some harmful environmental impact, then ncRNAs are

also involved in the causation of diseases, in particular cancer (Diamantopoulos et al., 2022).

Further comments concerning epigenetic mechanisms

The comments take up aspects that are of particular interest in the context of this paper.

- When shortly after conception parents' marks have mostly been erased and the embryonic genome is epigenetically reprogrammed, this process may already be influenced by environmental factors. Both, the enzymes that attach the new marks to DNA and histones as well as the marks themselves, are susceptible to environmental influences, be they stressors or beneficial ones. This environmental influence, potential and real, continues through the lifespan of the organism (Breton-Larrivée et al., 2019; Kanherkar et al., 2014).

- As implied by the description so far, epigenetic effects are carried over into cells created through successive rounds of cell division. This is heredity by cell division whereby epigenetic marks, unless their effects are overruled by the effects of some new environmental influence, persist and continue to exert their influence during the organism's life span. It is also the case that epigenetic marks on parents' DNA are retained when that DNA is passed on to the next generation; in this case we have what is called imprinting (Jaenisch and Bird, 2003; Skvortsova et al., 2018).

- Imprinted genes will differ depending on whether they come from the father or the mother. It is then relevant which ones are passed on to become part of the offspring's genome, which scientists say is determined by an epigenetic parental tug of war (Moore and Haig, 1991; Creeth et al., 2018). The outcome of this conflict, whether more in the interest of the mother or that of the father and thereby the embryo(s)[3], may in turn be influenced by environmental conditions (King et al., 2015; Bonduriansky and Chenoweth, 2009).

- All the factors that make up epigenetic mechanisms originate from non-coding DNA, which is the part that does not code for the proteins used to construct the organism.4 The Encode Project Consortium (2012) estimated that the protein coding part of DNA makes up less than 2% of all DNA, which means that the non-coding part makes up more than 98%. They also estimated that more than 80% of this non-coding DNA is functional, most of it in the sense that it codes for regulatory factors. While this claim has been contested (Kellis et al., 2015), it is

[3] The 'interest' expressed by the mother's genes consists in conserving resources for future pregnancies, while that expressed by the father's and the offspring's genes consist in having as much as possible of maternal resources devoted to the current offspring.

[4] Note the difference of the term 'non-coding' in respect of non-coding RNA (discussed earlier) and non-coding DNA. The former are molecules that unlike messenger RNA do not translate into protein; the latter is that part of DNA that does not code for proteins but for other functional factors, among them non-coding RNA.

nevertheless accepted that the number of these factors is by far greater than the number of proteins (Mattick and Amaral, to be published 2023). This insight is important, since environmental influences, including most mutations, become effective by way of the actions of such factors (Aznaourova et al., 2020; O'Dea et al., 2015).

- Epigenetic effects are in general reversible. Actual reversals would depend on suitable changes in behavior or environment or appropriate external intervention. Reversibility has empirically been demonstrated in medical science through the development of so-called epigenetic drugs that through reverse mechanisms aim to neutralize the disease triggering processes (Ganesan et al., 2019; Liang & Turcan, 2022).

In social science research, epigenetic mechanisms and processes[5] become relevant because of their potential of throwing light on how environmental circumstances may get translated into changes in people's physical condition and personality traits. Such a causative role of environmental influences has, however, been questioned with the argument that the observed statistical associations could represent mechanisms of causation running in the other direction. The findings of a recent study (Kong et al., 2018) are a compelling antidote to this position. In this study a correlation was established between 'the frequencies of sites in the DNA of people that the children of these people did *not* inherit' and the 'educational attainments of those children at a later age'. A significant positive correlation between educational attainment and the frequencies of those sites in parents' DNA was established. Given that the part of parents' genes not transmitted is considered to have contributed to establishing the environment in which the children were raised, the conclusion is that there is an indirect effect on offspring, and the next insight, based on what we know by now, is that instrumental in bringing about the indirect effect are epigenetic processes. This conclusion allows social scientists to argue with confidence that personality traits are the product of the joint action of genes and environment, an insight which in respect of diseases - also complex traits - had been demonstrated much earlier (Croce, 2009).

In respect of reversibility, we mentioned above the successful development of so-called epigenetic drugs that are able to counter the effects of disease caused by epigenetic reactions to a toxic environment (Ganesan et al., 2019; Liang & Turcan, 2022). The successes in this field point to the potential that may lie in policies through which the harmful consequences of adverse circumstances on social outcomes might be remedied.

[5] The terms 'mechanisms' and 'processes' are used here interchangeably; they differ insofar, as the former refers to epigenetic factors as the things that drive change, while the latter refers to the taking place of such change.

2. Establishing the relevance for the Flynn effect

The Flynn effect stands for secular increases of up to three IQ points per decade in many countries during the last century (Flynn, 1987). Given that the effect is familiar to most social scientists, we will use it here to help making epigenetic mechanisms more concrete and vivid. Kaminski et al. (2016), who take a position similar to the one in this paper, point out that the Flynn effect is too strong to have been caused by evolutionary changes in the genetic code. They therefore reason that other causes should be identified and they invoke environmental as well as epigenetic mechanisms, before embarking on their own investigation. They are thus consistent with what is the theme of this paper, that when environmental conditions influence the expression of genomes, epigenetic processes are engaged, thereby altering the corresponding phenotypes. Since intelligence as a trait is obviously part of the phenotype, changes in intelligence brought about by environmental factors must necessarily have undergone these epigenetic processes. Having said this much, we could close this section, given that it has become clear that epigenetic processes always have this role of mediator between an environmental event and a change in a trait of the organism. There is, however, more to be learned by examining the particular ways in which such factors impinge on the organism, and what the results in terms of intelligence may have been.

In the following we will approach this by taking up the article by Pietschnig and Voracek (2015) (henceforth P&V), in which the authors provide a meta-analysis of studies assessing the Flynn effect. Their analysis includes a review of suggested explanations for the effect, which based on their table 2 are listed in Table 1. We will take up five of these explanations, which were selected because of the particular aspects of epigenetic mechanisms they allow us to highlight. Thus, the emphasis of this check will lie on elucidating the working of these mechanisms, not on discussing in detail the findings of P&V's review. In this review the authors mention epigenetic factors a couple of times but do not dwell on it.

Table 1: Types of explanation for the Flynn effect suggested by P&V article

Education	Genomic imprinting
Exposure to technology	Nutrition
Family size	Pathogen stress
Test taking behavior	IQ variability
Hybrid vigor	Social multipliers - arising out of a more advantageous environment*
Blood lead levels	Life history speed

* The wording 'arising out of a more advantageous environment' added to indicate the underlying reason for the multipliers.

Assessing explanations reviewed by P&V in the light of epigenetics

Below we will take up five of the explanations listed in Table 1 and assess them applying what we know of epigenetic processes.

Education

The statistical results cited by P&V are mixed so that P&V need a long discursive argument for in the end being able to conclude "that there is little doubt that education plays a role in explaining the Flynn effect". Actually, the mixed results should cause little surprise. It is necessarily difficult to disentangle the effects of education on intelligence from the effects of intelligence on education. This latter influence must also exist. For example if education as explanatory variable is measured in number of years in school, this variable will tend to be larger for children that are more intelligent to start with, so relating intelligence to education would be relating it in part to itself.

As regards the point of interest here, Hill et al. (2019), in a statistically based study establishing the degree of heritability of intelligence, found that more than 90% of the base pair variants associated with intelligence came from the non-coding region of DNA. Since the molecular elements that play a role in transcription and epigenetic regulation are an output from this part of DNA, which is readily susceptible to environmental influence, this means that the degree of intelligence would also be affected by the environment as experienced for example in schools and through the education provided.

Given that during a large part of the last century living conditions improved and schools became better, it follows that - mediated by epigenetic mechanisms - education had a better chance of increasing intelligence with consequent increases in average IQ scores. These IQ increases in turn helped to further improve living conditions (Rindermann, 2018; Hanushek and Woessmann, 2020) which in turn helped to increase IQ scores, and so forth.

Blood lead (pb) levels and Pathogenic stress

The two conditions are closely related. Actually *pb* exposure is considered to be a xenobiotic stress (Metryka et al., 2018) with similar kinds of effects as those of pathogenic stress, which in the P&V discussion is represented by infectious diseases. These kinds of stress encompass many other toxic pollutants; psychological stress has been added more recently (Ellis et al., 2006). As P&V point out regarding lead, there is clear evidence that these kinds of stress can have a detrimental effect on development during pregnancy and childhood. More concretely, psychological stress could affect the expression of the gene for the 'brain-derived neurotropic factor' (BDNF) with long-term consequences for children through impaired learning, memory formation, maturation and functioning of the frontal cortex in general (Sapolsky, 2017; Frías-Lasserre et al., 2018). Further these stresses could exert their influences over the whole lifespan (Šrám et al. 2005; Bishop et al., 2020; Ding et al., 2021).The point is that there are stressors of different kinds which, however, have the one aspect in common that their effects are being mediated by epigenetic mechanisms, whether in respect of intelligence or more broadly in respect of other developmental issues. Regarding the negative

impact on intelligence, Rygiel et al. (2021) show this for lead and Kaminski et al. (2018) for psychological stress.

Now, as regards the Flynn effect, what was pointed out above regarding the improvement of living conditions holds in reverse for all the types of stress just mentioned. As over time their levels have on average been reduced through better hygiene, less lead and fine particles in the air and less poverty and more security, concurrent epigenetically mediated positive effects in human development and thereby on IQ scores took place.

Genomic imprinting

P&V present imprinting as a hypothesis which in principle would be suitable to explain IQ but to which they then give little credence. Now, like epigenetic processes, imprinting is not a cause but a means by which some actual causes are transmitted to the organism. Imprinted genes, as pointed out earlier, are epigenetically modified genes that a child has inherited as such from its parents; they may thus transmit environmental influences that the parents earlier in their lives were exposed to and thus could qualify to have an impact on the intelligence of the offspring. The actual impact would then depend on the type and significance of environmental influences which parents would over time have exposed to. In other words, it would also depend on effects of education, more or less stress etc., but as experienced by the parents and not the individuals in question. If then effects through imprinted genes did contribute to the cognitive potential of children, given that conditions would over time also have improved for parents, it follows that the mechanism of imprinting would also help in explaining the Flynn effect.

As to the likelihood that this happens, note first that imprinted genes make up a small subset of all genes. That these may, however, be quite potent in conveying particular traits to offspring is for example demonstrated by two studies: Li et al. (2020), examining 244 genes that were identified as imprinted (representing ca. 1% of the total of genes), show that in autistic individuals the genetic indicators of the disease were correlated with these genes; House et al. (2018) show that a Mediterranean diet is associated both with altered methylation of imprinted genes and favorable offspring behaviors.[6]

Social multipliers arising out of a more advantageous environment

Behind this term hides an approach proposed in Dickens and Flynn (2001), hence an approach to which Flynn himself contributed. It is a portmanteau explanation that encompasses all those discussed by P&V and, in its generality, is the most convincing of all the approaches so far suggested. Although it makes no use of epigenetic arguments, these could, as suggested below, easily and naturally be integrated. The model argument runs roughly as follows: Say an individual is born

[6] The two articles do not address the question whether their findings are consistent with the parental conflict or parental tug-of-war hypothesis.

that due to a genetic mutation or some environmental improvement has a better genetic endowment for intelligence than would otherwise have been the case. In the course of her/his life this individual will have an intelligence-increasing impact on her/his environment, initially being restricted to family but later extending to society at large. Provided that due to this exogenous event, newly born individuals are on average better endowed and in this way contribute positively to society, that improved environment will feed back onto the whole of the population and, in particular, on all subsequently born. An important insight from this is that the improvement of intelligence is a collective phenomenon.

We take up P&V's discussion regarding this explanation in some detail. They point out that most observations from their analysis fit well to the social multiplier theory but that similar to previous empirical investigations, their analysis could not provide a direct test of social multiplier effects; social multipliers would likely be able to explain portions of the observed gains, but evidence from a direct test of this theory would still be needed. This assessment is too casual and off the point in two aspects. First, it ignores that social multipliers are not initial impulses themselves that lead to change but constitute a set of intermediate mechanisms that, not unlike epigenetic mechanisms, come into play whenever there is an initial impulse having a positive effect in relevant areas. By not taking this explicitly into account P&V miss the pervasive applicability of this explanation. Second, from a macro point of view, it is not necessary that such multiplier effects be directly observed for them to be recognized as existing, even if further research may be needed to flesh out the details. Consider for example initial impulses like public policies to install a sewer system in a big city (first in London, see Chapra, 2011) or to establish compulsory schooling (first in Prussia and Austria, see Eckstein and Zilcha, 1994). There is no doubt that the one entails better hygiene, which entails healthier development of children, who are now cognitively better equipped to learn in school to which, as a consequence of the other, parents are now obliged to send them. Together with these effects, more and better schools lead to young adults that enter the workforce being equipped with at least the most fundamental skills (Stephens and Yang, 2014) and, being more productive than otherwise, help in increasing national income which again sets in motion new rounds of positive effects. All such effects have individually been established empirically, including the chain reactions according to which the one is followed by the other (Heylighen & Bernheim, 2000; Hanushek and Woessmann, 2008; many others too many to cite here). The developments just described apply to the improvement of many human traits, among them general intelligence. Since these traits have directly and indirectly over many paths been affected by material and societal improvements, with epigenetic mediation playing an active role in it, it follows that the multipliers of the Dickens/Flynn model - actually in an extended version - are an important part of the explanation for the Flynn effect.

Upshot

From the above discussion we extract three messages, (a) it is environmental events together with the program inherent in genes that mold human traits, (b) when

environmental factors have an impact on the make-up and behavior of an organism, whether this is also due to a change in the DNA itself or not, it always involves mediation by epigenetic processes, and (c) while the Flynn effect has explicitly been established for intelligence, many observations made in passing, as well as good reasons, speak for it that an effect like this applies to other human traits as well.

3. A digression on statistical methods and models

With 'statistical methods' we mean approaches in genetic research that establish the statistical associations between traits and variations in the DNA of organisms. With 'models' we mean particular conceptions regarding the type and profile of these associations and the kind of implications that can be drawn from them. Of the various statistical approaches applied in epigenetics, two relevant ones will be characterized briefly. The model we will focus on has great promise of becoming a leading one. In the discussion of this model the issue of causality will in particular be addressed.

Statistical methods

Of the two statistical approaches to be briefly discussed, the first is that of 'genome-wide association studies' (GWAS) that since the completion of the Human Genome Project in 2003 (Ikegawa, 2012) has routinely been applied to identify the degree of association between variations in DNA base pairs and variations in human traits. The second more recent one is an extension of GWAS which - since there are several versions - will here simply be dubbed GWAS+. We focus on the development from the first to the second approach to make clear why for our purposes GWAS+ is the more appropriate one. Neither of the two approaches is specifically epigenetically oriented, but each is applied to all the regions of DNA, thus also those that code for transcriptional and epigenetic factors.

For both types of methods, panels of a large number of study subjects are needed, running up to hundreds of thousands. In GWAS, their sequenced DNA is partitioned into windows of a certain number of them, for example 250,000 or 1 million, from each of which a sample is selected to carry out statistical tests. Given that the human DNA consists of 3.2 billion base pairs, such samples can still contain observations of several thousands. Typically a test consists of determining the association between particular traits of the study subjects (for example a particular disease, obesity, degree of intelligence) and frequencies of variations in base pairs (variants) at the selected loci of DNA. Tests based on GWAS to determine this way the degree of heritability of intelligence usually come up with percentages of up to 30%. One of the apparently most thorough studies of this type, Hill et al. (2019), already referred to, arrived at a heritability estimate of 25.44%, which means that the variation in the frequencies of base pairs identified as establishing this heritability, relative to the variation in a measure of probands' intelligence, corresponded to that percentage. Now, more than 90% of these base pairs came from non-coding DNA (intergenic, intronic, ncRNA, see fgure 1b on study page 174). This implies that the

variants establishing the 25.44% heritability are predominantly from this DNA region and thus code for transcription and - most relevant here - epigenetic factors, where the latter are then responsible for allowing environmental signals to influence the eventual expression of genes.

As we have seen, the focus of GWAS is on the strength of association between a trait of interest and variants at particular loci of DNA. Stringent confidentiality criteria are usually applied to prevent frequent false positive declarations. It was soon recognized that this approach carries the other risk of leaving out relevant variants that although by themselves not meeting the statistical criteria may in sum have a substantial effect. That led to the development of various approaches to overcome this problem. According to Yang et al. (2010, 2011), developers of one of the new approaches, the task is to estimate "the variance explained by *all* the variants on a chromosome or on the *whole* genome for a complex trait rather than testing the association of any particular variant to the trait" (italics added). A more concrete statement by Wen and Stephens (2010), developing one of the other approaches, is: "In this paper we consider the following form of imputation problem. We assume that data are available on *p* variants in a reference panel of data on *m* individuals sampled from a population, and that a subset of these variants is measured on a further study sample of individuals taken from a similar population. The goal is to estimate data at unmeasured variants in the study sample, using the information on the correlations among measured and unmeasured variants that is contained in the reference panel data".[7] The GWAS+ approaches have since been applied and developed further, as witnessed by the more than 4,000 times that according to Scholar Google (July 2022) the 2010 Yang et al. study was cited since publication, i.e. on average ca. 340 times per year.

Models

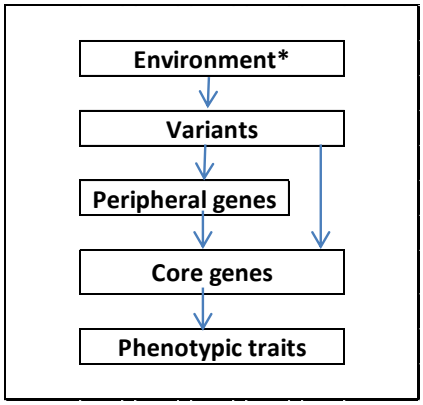
GWAS, GWAS+ and other statistical approaches provide information about associations between traits and genetic variants. One needs then explanatory models to properly interpret this information. At first models were used in which the effects of genetic variants were assumed to contribute linearly to the total effect on a trait, i.e. that this total effect would be obtained by summing up individually measured ones and that there would be no interaction between them. These models were in general only able to explain a low fraction of the total variance in a trait. In contrast to that, Boyle et al. (2017) introduced the 'omnigenic' model which posits that many more variants than identified by these early models influence a complex trait, in particular many of those that on the basis of conventional statistical criteria would not be taken into account. The model's hypothesis is that among the genes that determine a trait, one has to distinguish core genes and peripheral genes, that among the total number of these genes, peripheral genes by far outnumber the core genes, and that when all over a regulatory network interconnected genes determine

[7] In both quotes the terms 'variants', 'measured' and 'unmeasured', already familiar to the reader, have replaced the technical terms 'SNP', 'typed' and 'untyped' that were used in the sources.

the phenotype, the peripheral genes have in sum the larger influence although each peripheral gene may have a much smaller impact than a core gene. When Boyle et al. (2017) test their hypotheses in respect of human height - using one of the recent GWAS+ approaches - they come up with the estimate that more than 100,000 gene variants exert independent causal effects on this trait. They generally conclude that "the heritability of complex traits ... is spread broadly across the genome, implying that a substantial fraction of all genes contribute to variation in [these traits]".[8] There has been substantial resonance of the model in the literature, having been cited (Scholar Google, July 2022) more than 2,000 times since its publication, i.e. on average about 400 times per year.

The omnigenic model makes strong statements about the flow of causality. By construction it postulates that causality runs from the (regulatory) genes to the traits and actually, if one extends the model, from the environment to the traits. This is illustrated by Figure 2, a simplified as well as amended adaptation from figure 6A on p. 29 of Liu et al. (2019), one of its authors' subsequent publications on the topic. On top we see environmental influences (the amended part) causing variations in the expression of DNA (variants) that mostly affect peripheral genes but also some core genes, where then the peripheral genes influence core genes, before all of this together gets expressed in the phenotype.

Figure 2: Adaption from figure 2B of Liu et al. (2019), entitled: Regulatory variation impacts [phenotypic] traits by affecting peripheral and core gens*



* Not part of figure 2B in Liu et al (2019).

What are the conclusions from empirical studies that have taken up the model and tested its implications? First, we note again that the original paper by Boyle et al. (2017) presented evidence according to which human height was influenced by more than 100,000 genes. Further, of the five studies cited, four present supportive evidence while one is critical. Chen et al. (2018), after becoming aware of the omnigenic model, checked their data and found that over 20,000 genes were detected to be involved in the transcription of the neural tube. Zhang et al. (2021), after identifying in an animal study the impact of candidate (core) genes on two

[8] The authors' discussion is with respect to physical aspects like height or disease, but it is obvious that their results apply generally to all complex traits.

particular traits, picked at random 45 genes that had in the preceding GWAS not passed the significant threshold for an effect on the traits and manipulated them such that they became mute. It showed that this manipulation had an impact on the traits comparable to those of the candidate genes. The authors interpreted this result as evidence supporting the omnigenic model. It would also support the hypothesis, if there is causality from the environment to the phenotype, that this becomes effective through many genes, i.e. omnigenically through core as well as peripheral genes. In another animals study, DeRaad et al. (2020) state "(b)ecause signals of environmental adaptation are so diffuse and confounded throughout the genome, we argue that genomic adaptation to ecological niche is likely best understood under an omnigenic model wherein highly interconnected, genome-wide gene regulatory networks shape genomic adaptation to key environmental conditions". In their turn, Chateigner et al. (2020, 2019) express strong support for the omnigenic model, stating in the shorter 2020 version that their "work is globally in accordance with the recent work on the omnigenic model", while in the longer 2019 preprint version even claiming that it "is the first empirical proof that omnigenic holds in trees, providing one step further towards the universalization of this model". Visscher et al. (2021), in a study primarily concerned with the human genome, while not agreeing with the biological categories introduced by the omnigenic model (e.g. core and peripheral genes), neverthless state that it would be statistically consistent with their own approach which they call the 'additive liability threshold model of common disease'.

The articles referred to above, introducing and validating the omnigenic model, tended not to invoke epigenetic processes, although these, especially when environmental influences are at play, would obviously be instrumental in bringing omnigenic effects about. There have actually by now been research reports from applied areas of biology the results of which are based on both conceptions (Kitazumi, 2019, for plant and earth sciences; Noble and Noble, 2022, for human physiology; H. Wang et al., 2021, for forestry and statistical genetics). As already the original contributions on the model did, this type of work sees all these processes embedded in networks, the ones of interest here being 'gene regulatory networks'. We cannot assess here all the insights following from the network perspective except to note that it implies interactions among hundreds or thousands of genes, all taking place within a complex network (Schlitt and Brazma, 2007; Sonawane et al. 2021). This in turn also implies that there will be bidirectional causation and therefore some degree of what in other contexts is referred to as 'reverse causation', but which here only raises the question as to what the net impact of an environmental influence would be.

The issue of reverse causation has haunted and continues to haunt the social sciences when it is the question of what the direction of causation is in the relation between social conditions and human traits. We can use the complex network perspective to look at this vexing question from a new angle. Given an observed statistical association between a social condition and some trait, a typical argument has been that this trait may have been caused by some so far unidentified

confounding mechanism and that the observation in fact reflects effects running from that trait to the social condition. Paraphrasing a statement in this vein by Deary et al. (2009), it says that "... follow-up studies ... have shown that intelligence test scores from childhood are associated with health variables and health risk factors in middle and old age. Therefore, the cross-sectional 'variable X [social condition] versus cognitive ability scores' finding in old age might - in part or whole - be the result of reverse causation: [traits of cognitive ability] from early life affect later health" (insertions added). The implication of that statement would be that low cognitive ability in early life led to poor health decisions causing both the social conditions and mental health problems in later life, or the reverse in case of high cognitive ability. Now, under the network+omnigenic+epigenetic perspective espoused here, it is that many environmental influences, occurring continually, over generations, each time at the level of genes, becoming effective through a large regulatory network, shaped the genes responsible for cognitive ability the way they are (Aguilar-Hidalgo, 2015; Sinha et al., 2020). What it indeed needs is to think out of the box and to widen one's view beyond what may be the currently defined research question.[9] In the context of the following last section we will attempt to deal with the issue raised here in a constructive way.

4. Implications for economic analysis

In this section we will explore how the insights generated so far may contribute to opening up perspectives for economic analysis and policy. For this we first summarize the relevant insights as follows:

(1) Levels of intelligence and of other personality traits are the joint product of genes and environment, where the interaction between genes and environment are regulated by epigenetic mechanisms. "Epigenetic processes act as a link between environment and individual development" (Jones-Mason et al., 2016).

(2) Specifically, according to the so-called genetic nursing effect (Kong et al., 2018; Bates et al., 2018; B. Wang et al., 2021), it is the immediate familial environment, which besides their own genetic endowment is the source of children's educational attainment - as well as of levels of intelligence and the other personality traits that form human capital.

(3) The epigenetic processes involved take place in a highly interconnected, complex and genome-wide gene regulatory network, as represented by the omnigenic model (Boyle et al., 2017).

(4) Changes in intelligence at the level of society are a collective phenomenon (Dickens & Flynn, 2001).

[9] A very relevant contribution in this context is the article by Grosz et al. (2020) who complain about the complacency of psychological researchers working with non-experimental data who are satisfied with simply reporting statistical association instead of putting effort into establishing what the underlying causal relationship would be. They claim, a claim supported here, that there are methodologies that would allow doing this.

As suggested already by (2), at this point there is a shift in terminology insofar as the human traits referred to until now, i.e. intelligence, personality traits in general and educational attainment, will be subsumed under the term of human capital, which in economic analysis, especially in the context of economic growth, is widely used. Arguing with the help of this wider concept also has the advantage of including non-cognitive skills and health (Kautz et al., 2014), levels of which, the same as cognitive skills, would be subject to genetic nurture.

The concept of human capital has a long pedigree in economics whereby the focus has primarily been on its relationship with economic growth. This relationship has consistently been found to be positive where, however, the question of reverse causation has usually also been in the background. Recent studies find that there is indeed a bidirectional relationship but that on balance there is a net contribution from human capital to economic growth (Hanushek and Woessmann, 2020; Osiobe, 2019; Christainsen, 2013, for intelligence as a part of human capital; Hanushek and Woessmann, 2008, focusing on economic development). Given this conclusion, we should consider how the above insights could be used to design policies that would help to strengthen the positive relationship - in a self-reinforcing collective process - between human capital and economic and societal growth.[10] While the following ideas concern all strata of society, they are developed with primarily those at the lower ends of socio-economic status in mind, tending to be most in need of building up human capital,

When economists talk about the creation of human capital they mostly mean investment in the education of children, to which more recently has been added the empowerment of women (Duflo, 2012; Hornset and de Soysa, 2022). On the other hand the four points above make it clear that a very large part of the creation of human capital must take place within the family which implies that, as far as direct interventions are concerned, this lies largely beyond the reach of society (or the state as society's representative). There are two reasons for this. One is that in democratic societies the spheres of family, childbearing and child-raising are constitutionally protected as spheres of privacy which is none of the business of society (Gusy, 1986, for Germany). Another is that the corresponding relationships involve categories like nearness, affection and warmth between family members, regarding the 'technology' of which public policy - rightly so - has no means of direct intervention, and economics has no language and tools of analysis. The latter point is now alleviated a bit by the emerging knowledge - summarized by insights (1) through (3) above - about how the consequences of the relationships within the family are mediated at the sub-personal level through processes controlled by epigenetic mechanisms.

[10]When growth is advocated in this type of paper, this may need some elaboration. Growth would explicitly be expected to be societal growth with improved attitudes towards democracy and public institutions (Schoon et al., 2010; Menés and Donato, 2015), and, more topical, involve heightened awareness of climate issue. As regards economic growth the vision is that as argued by Nayyar et al. (2021) it would take place primarily in services and less in resource using manufacturing.

Having this knowledge but taking into account the restrictions mentioned, the question then is what can be done to enhance the creation of human capital within the family. The motivation for this would be twofold, to enhance human wellbeing through the value of greater abilities to the individuals themselves and through the value of their greater ability for society at large. We mean here its contribution to societal growth, not only economic growth, from which then all would benefit individually in terms of benefits such as enhanced social support and cohesion. When asked the question, economists would point out that for what is at stake the family should be considered a black box, but would argue that the framework within which families live and raise children be as favorable as possible. Such a framework should involve support in terms of finances as well in terms of dissemination of information regarding what it needs to allow children to develop to the best of their future.

Turning to the dissemination of information aspect first, a public awareness must be created that besides the items of PISA, human capital in terms of many personality traits are important. Success in building these up is one of the guarantors for success in the classical goals of education and for later life outcomes (Bergold and Steinmayr, 2018; Zhang and Ziegler, 2018; Bleidorn et al., 2019; Mammadov, 2021; Haider and von Stumm, 2022). To have an idea what particular kinds of information would be needed, we consider 'neuroticism' (the technical term for the opposite of psychological stability), perhaps one of the most relevant traits from the Big Five. Given that this trait may be responsible for many significantly harmful life outcomes (Widiger and Oltmanns, 2017), the information would have to cover what is required to prevent that the preconditions for it develop already during pregnancy and what type of parental care would foster the development of psychological stability from the first moments of the child's life (Provençal and Binder, 2015; Short & Baram, 2019). Regarding the type of intervention to bring this awareness about, no attempt is made here to suggest any particular approach, except to submit a few general points. The approach will have to be very sophisticated and involve many aspects, in particular take into account people's sensitivities - and preconceptions - regarding interventions in personal affairs. It should be made clear that - other than bring home to people the relevant information - there would be no interference with people's freedom to make choices whatever they are. Many institutions of the civil society should be involved; and the insights from the literature on parenting styles and child conduct should be taken into account (Burton et al., 2002). As regards management of the scheme perhaps an independent agency should be created (possibly modelled on a cross of such German agencies as the Sachverständigenrat and the Bundesagentur für Arbeit[11]).

Before turning to appropriate financial incentives, it is instructive to consider for a moment the experience with the efforts of reducing the consumption of tobacco. Over the past 50 years, it took a many-thronged approach (antismoking information,

[11]Translated as: Advisory Council for the Assessment of Overall Economic Development, Federal Labor Office.

banning of advertising, banning of smoking in public places, high consumption taxes) to get a reduction of the average per capita consumption of cigarette equivalents of about 50% in Germany, in the US a reduction of the proportion of cigarette smokers from about 50% to now less than 20% (John and Hanke, 2019; U.S. Department of Health and Human Services, 2020). Taking further into account (Kahneman and Tversky, 1979; Barberis, 2013) that people are usually more sensitive to losses (in the case of smoking, one's health) than to gains (here enhanced personality traits of one's kids), one would tend to be skeptical as to whether even the most sophisticated information campaigns would be sufficient to boost a corresponding understanding and bring about the hoped for adjustments. In order to overcome the reluctance to properly value future gains, a reluctance furthered by the presumably on average greater lack of understanding the more people with lower levels of human capital (and therefore on average lower levels of income) are involved, it would be necessary to provide for positive incentives accruing presently and in the immediate future. It is suggested that these incentives consist of financial means made available to those who it is wished that they respond to the call but might otherwise be less likely to do so.

This 'to whom' question is an important and at the same time sensitive one. The intention of the scheme should be to create a society that is explicitly child-friendly, an attitude to be as widely espoused as possible (neighbors, employers, bureaucrats) and therefore not only by families with children. This implies that a basic income would be appropriate. This argument for basic income, in order to give families and their environments the incentives to (still) better support the development of children's human capital, differs from the reasons for it proposed elsewhere (Van Parijs & Vanderborght, 2017; Standing, 2020), although they might broadly be compatible. It differs however sharply from most other proposals insofar as it abstains from the universality aspect through incorporating an idea akin to the Friedman negative income proposal, i.e. that the level of the basic income should depend on the level of the market derived income of the family. While support for people at the lowest levels of income should be 100%, this support should taper off and reach zero somewhere in the middle of the income ranks. There are two reasons for this. First, in the hierarchy of concerns of lower income people, existential concerns, like making ends meet, place a relatively high demand on their physical and emotional resources so that less of these resources tend to be left for their parenting style; this would necessarily affect the readiness to heed provided information, so that financial bolstering would help to overcome this obstacle. Second, as regards the economically well-to-do, their attitude towards the scheme is expected not to depend so much on what they might gain from it directly but rather on what they believe it will accomplish in general and what they would have to contribute to finance it, which would be less if the scope of the scheme were so restricted. As concerns the relevance of the scheme for this latter group of people, regarding parenting styles it appears to exist as much as for people at all levels of socio-economic status (Hou, 2001; Ritchie and Buchanan, 2010). For the well-to-do, however, openness to attempts at persuasion would, as indicated, not be expected to depend on receiving financial support.

One aspect needs still to be taken up. Insight (3) reminded us that the sub-personal (epigenetic) processes by which environmental conditions influence the forming of personality are diffuse, extremely complex, and - most important - interactive. On the one hand, this intricate complexity was the reason to argue that economists should abstain from any attempt to define direct interventions. On the other hand, it leads to the recognition that these processes involve somewhere in the whole chain of events reverse causality. From the literature cited earlier (Kong et al., 2018; Bates et al., 2018, B. Wang et al., 2021), we know however that on balance there is a positive causative relationship between environment and the development of human capital. But there is more to it than this. When stimuli in the right direction take place, their effects set in motion processes that feed back positively onto the initial effects. At both activity levels addressed in the presemt analysis, that of inputs - i.e. more supportive families and investment in personality traits - and that of outcomes - more human capital and greater societal and economic growth - a bi-directional causality would support a virtuous cycle reinforcing the one effect and the other. Much will depend for this on the proper design of the scheme, how the information campaign and financial assistance are interlinked, which to be effective and efficient would need input from all the human sciences, from economists in particular regarding what the cost and benefits would be.

This paper's aim has been to establish that in addition to the genome there is an epigenome which is the link between environment and the development, individually and collectively, of people. The aim has further been to show that people, being aware of what epigenetic processes do, have an opportunity to influence such processes positively provided the right steps are taken. Economics' role in this consists in developing a decision framework within which the prospect of advantages may actually be realized. One particular approach is suggested on grounds of expected effectivity and efficiency, involving dissemination of information and the provision of basic income. No doubt, both parts of the proposal would be criticized, the one for its interventionism and the other for its costs. But the intervention should be judged in comparison with what happens elsewhere in society, in the world of publicity where the influencing of decisions in whatever direction is endemic, in the social media, in which adolescents are largely allowed to roam unchecked with effects on their developing personality that on balance are not favorable (Cataldo et al., 2021). The costs in turn should be set against the substantial long-term gains brought about by the expected increases in the general level of human capital, i.e. in terms of growth in the economy (Rindermann, 2018; Hanushek and Woessmann, 2020) and, overall, of growth in society at large (Schoon et al., 2010; Menés and Donato, 2015).

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