INTERACTION OF GENOTYPE AND ENVIRONNMENT IN EXPRESSION OF PHENOTYPE: DO UNIVERSITY STUDENTS INTEGRATE KNOWLEDGE ABOUT EPIGENETICS

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ABSTRACT: In recent decades, genetic issues play a large role in health and public policy and new knowledge in this field continues to have significant implications for individuals and society. In spite of this increased exposure to genetics, recent studies of the general public's genetics knowledge show a relatively low understanding of genetics concepts. Epigenetics is a new paradigm in biology. Nevertheless, the notion of genetic determinism is still present in syllabuses and textbooks. The present research explores the university students' conceptions related to the genetic determinism of behaviors and human performances and if they integrate recent knowledge in Epigenetics. The research method is a questionnaire elaborated by the Biohead-Citizen consortium. The findings revealed that these students were still reducing the biological identity to a genetic program. The set can also enhance the danger of hereditarian ideology that justifies the fatalism and racism. We concluded that the teaching of epigenetics becomes a scientific and citizen challenge.

Key words: Genetic determinism, students, conceptions

INTRODUCTION

In the twentieth century, the nature-versus-nurture debate was one of the most important themes of genetics (Castera et al, 2008). Now, most scientists accept that both factors have a crucial role and that phenotypes result from the actions and interactions of both, which often change over time (Petronis, 2010). Most phenotypes show some degree of heritability, a finding that formed the basis for a series of molecular studies of genes and their DNA sequences (Nicol-Benoit et al, 2013). In parallel to such genetic strategies, thousands of studies have been carried out to identify environmental factors that contribute to phenotypes (Georgel, 2015). The new paradigm is not one of nature versus nurture, but of a complex and dynamic interaction between DNA sequence, epigenetic DNA modifications, environment, gene expression, and environmental factors that all combine to influence phenotype (Gibson, 2008; Kilpinen et Dermitzakis, 2012).

Over the last years, several university programs introduced bit by bit epigenetics as part of the genetics (regulation of the expression of multiple genes, cell differentiation…). However, in most countries, university programs of Biology do not include the wealth of information gathered over the last 30 years of investigation of epigenetics. This article aims to explore if the students integrate the recent scientific knowledge about Epigenetics when they are asked about relationship between Genotype and environment in expression of phenotype. The article also tends to identify their conceptions related to the genetic determinism of behaviors and human performances.

THEORETICAL BACKGROUND

The Genotype-Phenotype Relationship

The Genotype, carried by all living organisms, holds the critical instructions that are used and interpreted by the cellular machinery of the cells to produce the "outward, physical manifestation", or Phenotype of the organism. Thus, all the physical parts, the molecules, macromolecules, cells and other structures, are built and maintained by cells following the instructions given by the genotype. As these physical structures begin to act and interact with one another, they can produce larger and more complex phenomena such as metabolism, energy utilization, tissues,

organs, reflexes and behavior; anything that is part of the observable structure, function or behavior of a living organism (Braun, 2015).

The genotype of a cell is its genetic makeup while the phenotype encompasses its traits, such as morphology and function. Genotype and phenotype represent two separate cellular entities; while the former is the structure of the genome-the DNA sequence, the latter is the determination of the form, growth and interactions with the external world of the cell. It can be any observable property of the living organism.

The establishment of a phenotype, given a certain genotype, depends on the protein makeup of the cell. The set of expressed proteins, a subset of the entire genome potential, and their concentrations, are determined by regulatory systems at many levels. Thus, the emerging phenotype depends on the spectrum of regulatory modes-temporal profiles of expressed genes. However, a snapshot of the molecular content of a cell and the structure of its underlying interactions do not capture the spectrum of regulatory profiles that define the relevant observables that determine the phenotype (Braun, 2015).

The protein content of each isolated gene is by itself not such a relevant observable. Therefore, inquiring into the genotype-to-phenotype associations requires a shift in focus from structure to dynamics, from the molecular stuff of the cell to its temporal organization. The genotype-to-phenotype mapping is largely assumed to be deterministic in nature, accompanied by 'noise' by environmental influences and intracellular stochastic processes due to the small volume of the cell and the small number of molecules involved (Braun, 2015).

Epigenetics

Epigenetics has become a topic with implications across a diversity of biological disciplines, inspiring exciting theoretical and empirical work. The term dates back to the work of Waddington in the 1940s who was one of the earliest researchers to disavow a simple relationship between genotype and phenotype. Since that time, interpretations of the term have evolved, particularly as molecular-level mechanisms that modulate gene expression have been revealed. Still, even since Waddington, the term has been used to refer to the interactions of the genome with the internal and external environment in the production of phenotypes (Richards, 2012).

Prior to the middle of the twentieth century, before DNA was given a special status in biology, the developmental biologist and evolutionist Waddington (1905-1975) emphasized that genetics and developmental biology were related, hypothesizing that patterns of gene expression, turning genes on and off, and not the genes themselves, define each cell type, thus linking genes and gene action to development. To denote the dynamic actions leading from the genotype to the phenotype, Waddington coined the term 'epigenetics' from the Greek word epigenesist, referring to embryology and genetics as "a gradual coming into being of newly formed organs and tissues out of an initially undifferentiated mass". In this way, Waddington indicated that an epigenetic landscape underlies each developing organism, referring to the existence of a complex network in which genetic interactions, the feedback and "feedforward" relationships among DNA, proteins, and other internal and external biochemical compounds are highly intermingled. Riggs (1975) proposes a molecular model for the switching of gene activities, and also the heritability of gene activity or inactivity. This model was based on the enzymatic methylation of cytosine in DNA. The suggestion was that DNA methylation could have strong effects on gene expression, and changes in DNA methylation may therefore explain the switching on and off of genes during development, and that the pattern of methylation could be heritable, persisting through cell divisions (Barros & Offenbacher, 2009).

Epigenetics, as the term suggests, can be seen as a major turn away from molecular biology's Central Dogma, recognizing that there are epigenetic inheritance systems through which no sequence-dependent DNA variations can be transmitted in cell, tissue, and organismal lineages (Barros et Offenbacher, 2009).

Models of Genotype-Phenotype Relationship

The concept of phenotype, which corresponds to the observable attributes of an individual, was coined in opposition to the genotype, the inherited material transmitted by gametes. Since the early proposal that genotypes and phenotypes form two fundamentally different levels of biological abstraction, the challenge has been to understand how they articulate with each other, how genotypes map onto phenotypes.

Linear Causal Model

From a genetic change causing a variation in phenotype, it is often convenient to assimilate the corresponding gene as a causal determinant of a trait (Figure 1a). It is common to find headlines expressing these simplifications,

trumpeting to wide audiences the discovery of the "aggressiveness" or "intelligence" gene. According to this model a variation at a given gene causes variation in a given phenotype (Waters, 2007).

The genetic reductionist approach, which only explores a few genetic parameters among the variety of causal factors, is vain to fully address the broad question of what brings forth a particular biological structure or process in its entirety. Nevertheless, genetic reductionism can be perfectly appropriate for identifying genetic loci where a change causes a phenotypic difference (Orgogozo et al 2015).

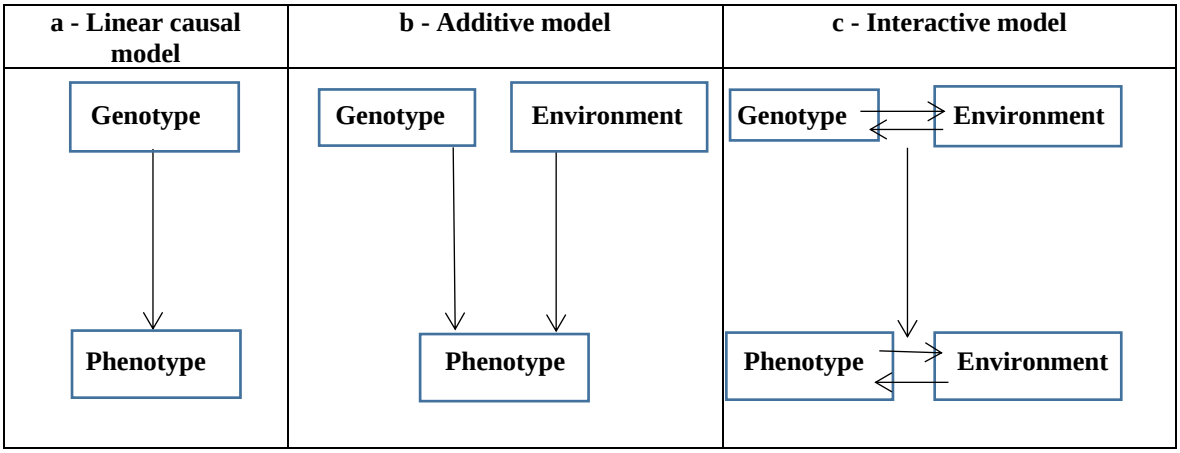

Figure 1. Different models of genotype-phenotype relationship

Additive Model

In fact, a gene alone can neither cause an observable phenotypic trait, nor can it be necessary and sufficient to the emergence of observable characteristics. Genes need a cellular environment, the combined action of multiple other genes, as well as certain physico-chemical conditions to have an observable effect on organisms. The expression of the phenotype results from the additive action of effects of genotype and environment (Figure b).

Interactive Model

Gene-by-Environment (GxE) interaction occurs when the phenotypic effect of a given genetic change depends on environmental parameters. Similarly, epistasis, or GxG interaction, occurs when the phenotypic effect of a given genetic change depends on the allelic state of at least one other locus (Hansen, 2013). There is increasing evidence that GxG and GxE interactions are of fundamental importance to understand evolution and inheritance of complex traits (Hansen, 2013). Both phenomena can be integrated into the basic GP differential framework, where both GxG and GxE interactions inject a layer of context-dependence, and result in differences embedded within differences (Orgogozo et al 2015).

In summary, in presence of epistasis or GxE interactions, a genetic change is not associated with a single phenotypic difference but with multiple possible phenotypic differences, among which one will be achieved, depending on the environment and the genetic background. The context-dependence can be represented schematically as GP differences embedded into other genotype and environment differences (Orgogozo et al 2015).

As underlined by multiple authors (most notably Waddington, 1957; Keller, 2010), genes and environment act jointly on the phenotype, and in most cases, it is impossible to disentangle the effect of one from the other. Here we show that reasoning in terms of differences helps to clarify the comparison between genetic and environmental effects on phenotypes. However, we identify certain cases where the comparison remains difficult (Orgogozo et al 2015).

Understanding of an organism's ability to respond to its environment has advanced dramatically during the last few decades, in large part through studies controlling for genotypic variation and manipulating environmental factors. These studies typically confirm not only that genotype and environment contribute to phenotypic variation but also that these two factors interact; that is, different genotypes often respond differently to environmental variation (Richards 2010). (Figure c).

Nature Versus Nurture: Genetic Determinism

The 'nature versus nurture' debate is an old, traditional but outdated discussion. All biologists consider today that any phenotype emerges from the interaction between the genome (nature) and its environment (nurture). Working on this interaction is a new trend of biology, called 'epigenetics'. Consequently, the traditional debate of genes 'or' environment, or '% of genes and % of environment' (which is possible only for an additive model 'genes + environment'), is outdated because there is an interaction between genes and environment. Genetic determinism is not sufficient to explain the complexity of human phenotypes. Only the multiple interactions between genome, environment and organism can give an overview of the biological complexity. Genetic determinism explanations can be used as a justification for social fatalism, with political or religious issues (Castera & Clement, 2014).

On another hand, several authors have developed critical analyses of innatism (Atlan 1999, Jacquard & Kahn 2001). They proposed a synthesis by distinguishing four forms of innatism: The first one claims that there would be inherited biological differences in mental abilities between individuals within each human group. The second postulates such differences between racial groups. The third claims that social structures and behaviors would reflect the weight of genetic factors. The fourth form of innatism considers the belief that mental gender differences would be genetically determined. Beliefs in strong genetic determinism engender intolerant attitudes. (Castera & Clement, 2014).

METHODS

This study is mainly qualitative, our methodology was mixed. We used a questionnaire and interview. These qualitative analytical methods were supplemented with statistical analysis to identify students' misunderstanding in Epigenetics.

Students Sample

All the students surveyed in the study were enrolled in a graduate science program at the University, the sample is composed of 86 Graduate Students (baccalaureate plus 3 years of study) and 20 Master' students (baccalaureate plus 4 or 5 years). Females comprised 46 percent of the sample.

The Questionnaire

We composed a questionnaire to acquire information on several key issues: (a) the students' understanding of Epigenetics and interaction between Genotype and Environment in expression of the phenotype (b) the students' conceptions of the genetic determinism of human performances (Table 1). Some of the questions were inspired by previous studies especially those relating to the genetic determinism of behavior and intellectual performance (Clement et al, 2006). However, we developed many new questions appropriate for students at the graduate level.

The responses to all the questions about genetics are based on a Likert scale on which each teacher was asked to tick one of four boxes, ranging between 'I agree' and 'I don't agree'. The majority of the questions concern genetic/biological determinism of human behavior. These questions can be grouped into four different categories: (1) Genetic determinism of personal or individual features: questions about clones and twins (A3, A6, A19, A24, A43 and A53). (2) Genetic/biological differences related to gender (A9, A14, A21, A25, A36, A38 and A46). (3) Genetic determinism of human behavior (B8, B10, B14 and B20).

Table 1. The 16 questions related to biological (mainly genetic) determinism (their ranking throughout the whole questionnaire is stochastic).

	Question	I agree					I don't agree

A3.	If clones of Einstein could be obtained, they all would be very intelligent.						
A6.	Due to identical genes, identical twins have identical immune responses to transplants from another person.						
A9.	Women are less intelligent than men because their brains are smaller than men's brains.						
A14.	Thanks to their physical features, men perform better in athletics than women.						
A19.	Due to identical genes, identical twins have identical brains and, therefore, identical behavior and ways of thinking.						
A21.	women can be as intelligent as men Biologically						
A24.	If clones of Mozart could be obtained, they all would be excellent musicians.						
A25.	It is for biological reasons that women cannot hold positions of high responsibility as men can.						
A27.	The human genome contains more genes than the genome of any other living being.						
A31.	When a couple has already had two girls, the chances that their third child will be a boy are higher.						
A35.	Ethnic groups are genetically different and that is why some are superior to others.						
A36.	Men might be more able to think logically than women, because men might have different brain bilateral symmetry.						
A38.	It is for biological reasons that women more often than men take care of housekeeping. I						
A43.	In identical twins, one can be right-handed and the other left-handed.						
A46.	Biologically, men cannot be as sensitive and emotional as women						
A53.	Due to identical genes, identical twins have identical immune responses to microorganisms.						

The Interview

Interview was conducted on six students. The interviews lasted approximately 30 minutes. Thematic interview questions are used to explore in greater detail the most commonly held misconceptions identified by the questionnaire analysis.

RESULTS AND DISCUSSIONS

More than six students out of ten states that the phenotype is determined solely by the genotype (62%) and that the action of the environment on the phenotype requires a change in the DNA sequence (60 %). This reflects that a majority of students don't know epigenetic mechanisms. This is confirmed by the fact that more than the half of them state that chromatin is a DNA carrier and is not involved in the expression of the phenotype (58%) (Table 2).

Table 2. Students' responses related to genotype-phenotype relationship (in %)

Responses in %	I strongly agree	I rather agree	I rather disagree	I strongly disagree	I don't know
The phenotype is determined solely by the genotype	35	27	13	11	14
The action of the environment on the phenotype requires a change in the DNA sequence	42	18	14	17	9
Chromatin is a DNA carrier and is not involved in the expression of the phenotype	35	23	9	12	21
DNA methylation / demethylation is a signal for activation or deactivation of a gene	27	25	16	9	23

One student out of two state that DNA methylation / demethylation is a signal for activation or deactivation of a gene (52%).

In the interview, we identified a common perception held by the students which stipulates that genes, as units of information controlling various traits, are distinct and totally separate from the environment (Figure 2). This perception is certainly true of the physical-structural- chromosomal entity called gene, but it does not apply to genes as units of information or function. The notion that information resides in the genes and that the environment simply provides the medium through which information is displayed is incorrect. The only sure evidence of epigenetic inheritance involves methylation of genes through which identical genes coming through the two parents can behave differently in their expression (Singh, 2015; Agorram, 2010).

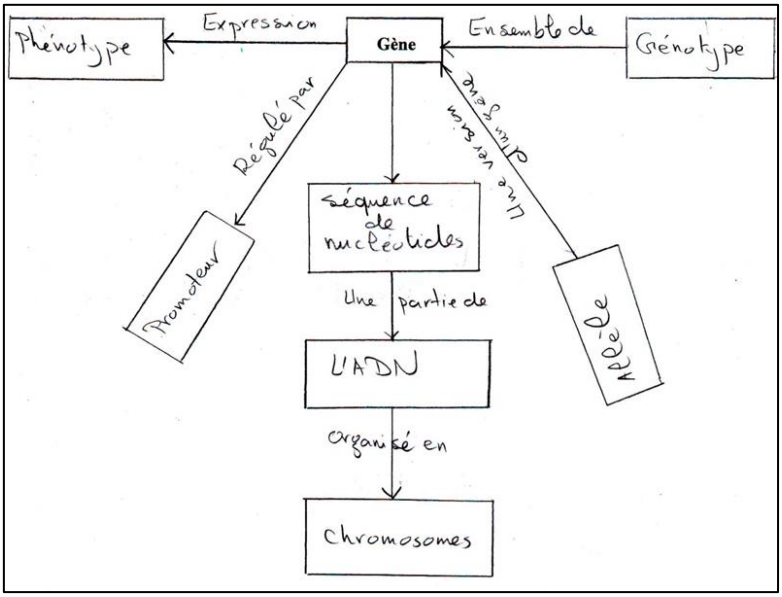

Figure 2. An example of students' responses about gene-phenotype

About half of the students surveyed say that similarity of the reactions to different factors (immune response to micro-organisms and to transplantation) or similarity of behaviors of identical twins is due to the identity of their genes (Figure 3).

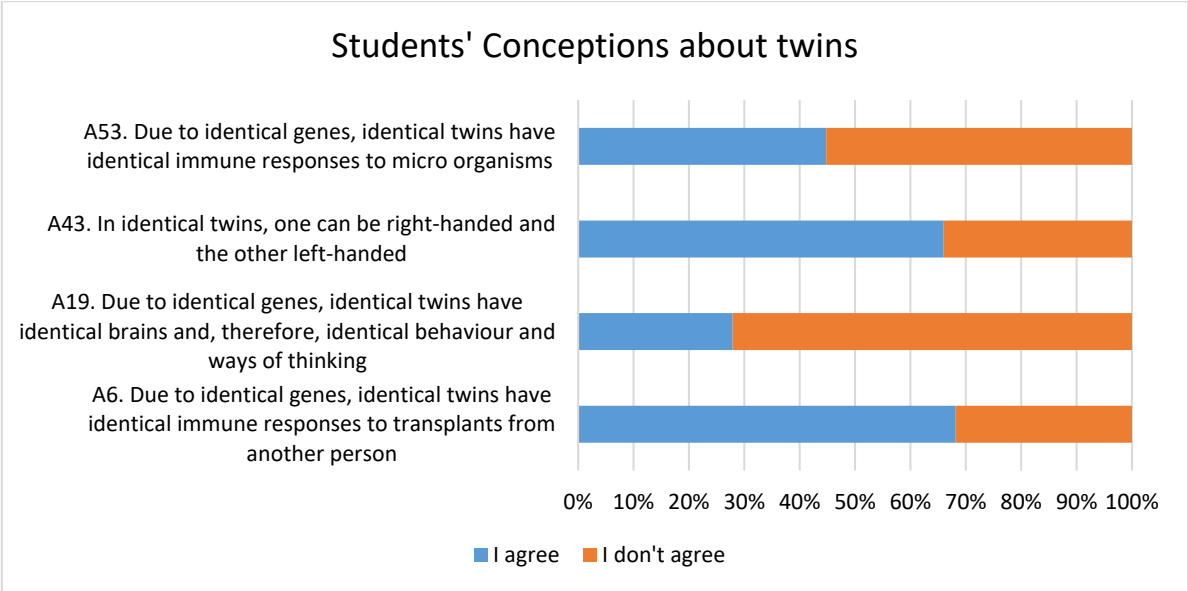

Figure 3. Students' responses about genetic determinism among twins

It is generally agreed that epigenetics provides sufficient flexibility and latitude to the developmental program of a given genotype such that even identical twins become "unidentical" as they proceed through life (Haque et al, 2009).

Numerous studies show that it is clear that identical twins have substantial differences in obvious phenotypes like disease, and in epigenetic DNA modification patterns. Earlier twin studies were based on the premise that

monozygotic twins are genetically identical, and that phenotypic differences must arise from no shared environment. However, knowledge of epigenetic mechanisms such as differential DNA methylation, skewed X-inactivation, and imprinting provides a new model to understand monozygotic twins' discordance (Gibson, 2008; Bhalla & Iyengar, 1999).

We notice that some of the students think that the differences between men and women (intelligence, sensitivity) are due to biological and genetic factors. Women are biologically different from men; these differences make them suitable for some household activities but that make them less able to do other activities. According to these students, the difference in behavior of men and women is due to the identity of their genes (Figure 4).

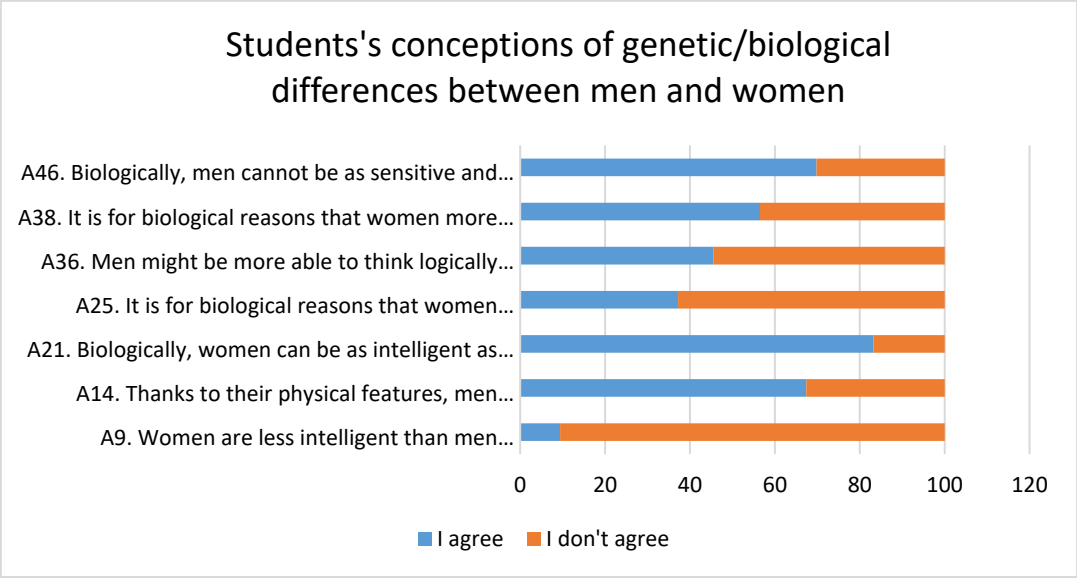

Figure 4. Students' responses about genetic/biological causes of differences related to gender

Genes determine all of characteristics, and different traits (as to be alcoholic, good in school, aggressive…) were inherited from parents. This misconception was found among more two students out of ten (Figure 5). It's sure that genes play a huge role in how an organism develops, but environmental factors also play a role and some heritable changes occur without changes in the genome. Many studies showed that gene expression in identical twin changes from environmental factors and suggested that these changes can accumulate over the life of the organism. It is possible that these behaviors have a genetic component, but they are not governed by genes alone, there is an interaction between genes, environment, and epigenetic factors.

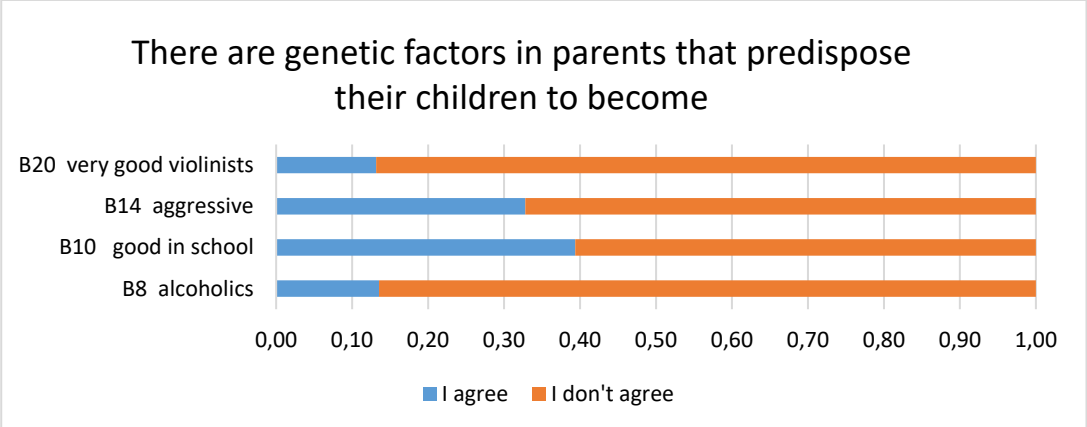

Figure 5. Students' responses about heredity of some behaviors and intellectual performances

CONCLUSION

Either cellular or macroscopic phenotype is ultimately based on the properties of synthesized proteins. Now these are the genes which code proteins responsible for the phenotypic characters. So, we would think that there is a linear relationship between a gene and a character, the first determining the second. In fact, the relationship between genotype and phenotype are often more complex.

This complexity of life cannot be reduced to a single genetic determinism. Its study needs to compete with other epigenetic, mechanisms to analyze the construction of phenotypic traits. New models (based on the concepts of self-organization, collective intelligence) contribute significantly to this change in perspective (Petronis, 2010).

The analysis of students' responses related to the genetic determinism of human features, behaviors or performances shows a clear innatism in a majority of students' answers. Moreover, this innatism is partly correlated to some sexist and even racist answers. This conclusion is illustrating interactions between the taught science (the scientific knowledge K) and implicit values (V) (Clement, 2006).

Epigenetics is still absent from university education programs reflecting an important didactic transposition delay. In the next few years, our understanding of the multiple layers of genomic information is likely to improve significantly. The school must incorporate these scientific innovations quickly enough and especially when they have an important educational dimension and which are related to socially controversial problematics.

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