Genetics of behaviour and psychiatric disorders: from the laboratory to society and back*

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Behavioural genetics aims to explain in genetic and molecular units mental dysfunctions that carry heavy societal burdens, and behavioural patterns that are pertinent to a vast array of an individual's social competences. The purpose of this paper is twofold: to briefly assess the current conceptual and technological framework of this branch of experimentation, and to remind of its contextualization in contemporary society. Medicalizing forces in our society increasingly bring non-pathological conditions under the scrutiny of medicine and genetics. Reflexivity is required among practitioners of behavioural genetics, who need to be aware of how social norms and context can influence the selection of traits and behaviours as objects of their investigations.

Keywords: Genetics, gene–environment interactions, genetic variation, psychiatric disorders.

Background

BEHAVIOURAL genetics, and in particular the genetic investigation of psychiatric disorders, are scientific practices with enormous societal relevance. Ongoing advances in these fields aim to explain in genetic and molecular units mental dysfunctions with heavy societal burdens and behavioural patterns that are pertinent to a vast array of an individual's social competences and strategies to respond to the environment as well as to social norms and procedures. Searching for genetic factors that influence behaviours has the potential to develop new diagnostic and therapeutic avenues to treat mental illness.

Experimentation in these fields cannot afford, therefore, to move on unaware of its contextualization in contemporary society and without an assessment of its impact on many aspects of our lives, especially the understanding of disease, normality, subjectivity and equality.

The aim of this article is twofold. First, I briefly assess the current approaches in behavioural genetics experimentation and their validity and limitations in elucidating the origins and mechanisms of behavioural patterns and psychiatric disorders. I will draw a brief outline of the main shifts in addressing the genetic origins of behaviour and of some of the fundamental difficulties around this enterprise. In this respect, I will also partly draw from my own experience as a practitioner of behavioural genetics and will focus on the meaning and goals of gene–environment (G × E) interaction studies.

Secondly, I emphasize how the adherence of the behavioural phenomena under study to the social context and various levels of individual and interpersonal social life, makes their study transcend the boundaries of behavioural genetics to penetrate a multitude of knowledge domains and embrace several levels of complexity. I will describe how in our society, medicalizing forces increasingly bring non-pathological conditions under the scrutiny of medicine and genetics, with special attention to anxiety-related behaviour, and how this process may influence the enterprise of behavioural genetics.

I will finally advocate for reflexivity and awareness among practitioners of behavioural and psychiatric genetics about this intricate relationship.

Ongoing conceptual shifts

The conceptual and technological frameworks in which behavioural genetics are premised have undergone important changes in the past 50 years or so. Theory and experimentation in the field have changed through a succession of shifting paradigms, each with its logic, potential and limitations[1].

Genetic epidemiology and quantitative behavioural genetics, such as family, twin or adoption studies, tried to dissect the genetic and environmental contributions to individual liabilities for the manifestation of behaviours or mental disturbances. In other words, they tried to establish the 'heritability' of the behaviours in question. In this case, the genetic factors are not directly measured, but they are inferred from patterns of behavioural and conduct resemblance among family and relatives groups.

When molecular biology techniques became available in the 1980s and 1990s, researchers sought to confirm

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genetic risk factors inferred with epidemiologic strategies by determining the location on genomes of genes that display variants (or polymorphisms), with different impacts on behaviour. This is done by either association studies, in which a known genetic variant (often a single nucleotide polymorphism, or SNP) is statistically linked to a phenotype in a heterogenous population sample, or with linkage studies, in which chromosome markers spaced along the genome are associated with a phenotype.

Enthusiasm about these approaches inspired a long list of association studies linking genetic variations to various features of human conduct or mental states. The origins of attitudes and traits as complex as sexual orientation were therefore reduced to variation in nucleotide sequences[2,3]. With the completion of the Human Genome Project in 2000, this reductive approach reached its peak moment and the genome was easily and often mistaken for the identity or essence of an individual[4,5]. However, some of the genetics claims made using this approach ended up having limited predictive power as their empirical solidity was challenged by lack of reproducibility, as in the discovery of the gay gene, for instance see Le Vay[6].

Finally, one approach that has potential to go beyond the relatively low predictive power of traditional association studies and that is currently gaining momentum is to include measurements of environmental influences and search for G × E interactions[7–9].

Gene–environment interactions

G × E interactions take place when the effect of exposure to a particular environment on behaviour or health is dependent on an individual's genotype. According to this principle, individual differences in genetic endowment, which are the raw material for natural selection, equip individuals differently to respond and adapt to environmental conditions. When studying G × E interactions, one measures how genes alter an organism's *susceptibility* to environmental features or how these latter control genetic effects[10]. This framework underlines that the link between genotype and phenotype involves a constellation of variables synergistically interacting across the developmental trajectory of an organism.

Although the rationale behind G × E interactions has a long scientific history[11–13], they were thought to be rare and, therefore, negligible. A rapidly growing body of evidence, coming also from other branches of somatic medicine, is now supporting their existence and validity. For instance, G × E interactions have been measured that underlie complex diseases such as coronary heart disease and those that link genetic variation with dietary conditions and tobacco consumption[14,15]. Similarly, recent descriptions of several gene-by-environment risk factors for mental traits[7,8,16–18] have underscored the need for considering both genetic and environmental factors when studying the aetiology of mental illness. Currently, initiatives are ongoing to implement global national epidemiological cohorts to facilitate the discovery of G × E interactions[19].

Testing for hypotheses of G × E interactions in psychiatric genetics requires the specification of plausible triads of behavioural phenotype, a gene, and an environmental influence[7]. I will examine each component of such a triad in turn.

The definition of phenotype and interspecies trait genetics

A long-standing challenge in the elucidation of genetic origins of psychiatric disorders, compared to other types of common disorders, has been the difficulty in defining the phenotype to be investigated. Because of its estrangement during a large part of the 20th century from medical science, psychiatry was seen as dealing with not as real phenotypes as other domains of medicine. In addition, the definition of psychiatric phenotypes has hinged upon subjective clinical evaluation and diagnostic criteria, in the absence of distinct biological markers.

The most recent developments have pushed towards a re-evaluation of the boundaries between different psychiatric categories and the utilization of animal models, more amenable to the dissection of the molecular mechanisms, for the observation of phenotypic features related to human disease.

The current classification of psychiatric disorders, according to diagnostic manuals such as the *Diagnostic and Statistics Manual* (DSM)[20], separates each disorder into non-overlapping diagnostic categories, based on symptoms of the condition and not on the underlying aetiology. Diagnostic categories are valuable for clinical management and treatment of psychiatric conditions. However, often they do not reflect the heterogeneity of the disorders they purport to encompass, nor do they reflect the neurobiological premises underlying the disorders they define. Also, there is more aetiological overlap among psychiatric conditions than previously thought. Accumulating evidence from linkage or association studies that places a gene polymorphism at the basis of a variety of diagnostic categories highlights this problem. It has, therefore, been proposed that diagnostic categories be regarded as continuous domains of disorder-related traits rather than dichotomous categories[21] and that phenotypes be assessed by measures of observed (or self-reported) behaviour that transcend traditional diagnostic classification.

Efforts are also increasingly being made for the application of *interspecies* trait genetics, that is the complementary study of phenotypes and their genetic origins across animal and human models, more specifically rodents[21].

Evolutionarily, interspecies genetics makes sense as common survival mechanisms that allow adaptation to a

changing environment, and the genes that orchestrate these mechanisms, are predominantly conserved across species. Mice, like other mammals, are physiological and biochemical models of humans, with nearly identical biological pathways for the regulation of basic processes. A very crucial requisite in this approach, however, is to identify traits that are complementary between animals and humans and that are relevant to the behavioural spectrum in question – in other words, the identification in the mouse of a phenotype that can be considered as an equivalent of a human psychiatric phenotype[21].

Certainly, there are differences between the premises of psychiatric disorders in humans and assumptions of behavioural observations in mice that challenge the credibility of this parallelism. Mice do not (probably will never) get schizophrenia and we will not have anxious or depressed mice, or at least not in the same way as we talk about anxious or depressed people. The problem of credibility is inherent in any study of subjective states via externally observable behaviour[22].

However, this type of translational research, based on interspecies trait genetics rather than complex syndrome disorders, may be useful in improving our understanding of the genotype–phenotype relationship in psychiatric disorders and paradigms of G × E interactions in the mouse that faithfully model human psychiatric results are being developed[23,24].

Relaxing the constraints imposed by diagnostic hierarchy may facilitate the investigation of overlap in genetic risk factors. If extensively adopted, it has the potential to provide novel and powerful disease models that, in addition to the discovery of genetic modulators, will most importantly help identify the biological substrates, their developmental role and the environmental factors that are critical components underlying these disorders.

Measuring genetic variation

What elects a gene to be a putative candidate factor behind a phenotypic outcome and how is genetic variation measured?

Evidence linking the role of the candidate gene to physiological mechanisms in the brain related to the behaviour or disorder in question is highly desirable to support the choice of a gene. Even more so, if the evidence links the gene to an organism's reactivity to an environmental factor. In this respect, one strategy to resolve the link between genes and complex psychiatric phenotypes has been to concentrate on 'endophenotypes'. These are subcategories of phenotypes – usually physiological, anatomical or biochemical measures, such as heart rate, neural activity, hormonal changes or markers of synaptic structures – bearing a closer relationship to the biological processes underlying the symptoms of the disease than do phenotypes[25]. The deconstruction of psychiatric disorders into these components makes them more easily amenable to a successful genetic analysis, by facilitating the search for genetic bio-markers. This is valuable in the investigation of developmental aspects and G × E interactions underlying complex psychiatric disorders.

The function of the gene under analysis should also be conserved across species. If a gene polymorphism exists in humans, its function should be analogous to the role of the same gene in a rodent model, which is more amenable to sophisticated technologies of genetic manipulation that are impossible to carry out in humans. The genome of a mouse can be manipulated in a conditional manner by removing, inserting or mutating a gene in a specific tissue of the animal and at a specific time and observe the phenotypic outcome. (Similarly, it is more feasible to manipulate and control the environment in which the behaviour of a mouse is observed in the laboratory.)

In general, it remains disputable, however, how we can lastingly anchor diagnostic concepts and disease classification on distinctive identifiable genes, especially since the basic definition of the nature of a gene is shifting in light of advancing knowledge and ways to measure individual genetic variation[26,27]. Today, it is possible to sequence elevated numbers of SNPs in thousands of individuals. However, genetic variation is not only measured by the number or nature of SNPs. To differentiate an individual from another, researchers have also reverted to the organization along chromosomes of consecutive sequence variants in structures that have been called 'haplotypes'[28,29] whose identification has already reached its second generation[30]. Another recently discovered form of individual genetic variation is the number of copy number of genes. These are entire segments of chromosomes containing genes that are either multiplied or deleted differently across individuals, resulting in changes in the copy number of genes[31].

Additional levels of individual variation are found at several steps in the gene expression machinery, including epigenetic control of DNA sequences[32], variations affecting RNA metabolism[33] or that are induced by somatic mutations such as transposons or other mobile DNA elements[34]. For instance, data are being produced that confer micro-RNAs a role in the development of brain structures and disorders[35–37]. The tools available for cataloguing genetic variation seem to have reached a certain degree of sophistication. However, it is clear that our abilities to link genetic variation with phenotypic outcomes have not developed at the same speed.

Environmental components and the importance of biographical information

Of crucial importance is the appreciation and measurement of environmental risk factors on behavioural outcomes. Ideally, environmental risks of choice are those

that affect a neurobiological pathway to the behaviour under study[7].

A thorough assessment of environmental contributions is in and of itself much more difficult to conduct than the assessment of genetic variation. While the genome of an individual is encoded in a bounded set of information, is basically stable over time and is amenable to multiple analytical approaches, the range of potentially adverse environmental exposures is diverse and more difficult to grasp.

In the majority of studies, the occurrence of adverse environmental exposures is measured post-occurrence of the disease, thereby imposing a recall bias due to the retrospective nature of the risk-factor annotation[19]. In contrast, longitudinal surveys collect information over many years. Longitudinal studies have large sample size and long duration requirements, but they most importantly allow researchers to look back in time and record the antecedents of current events and their transition. When examining the environmental causes of a psychiatric disorder, longitudinal data help to determine the 'directionality' of the causal effects by sorting out time relationships with respect to environmental hazards preceding onset of the disorder[38–41].

However, an outstanding limitation in environmental data collection has been the impossibility of grasping in detail biographical information of the individuals involved in a study. One of the reasons underlying this limitation is that the influence of the environment on brain substrates via the genetic make-up of a person is permanently ongoing, taking place over hours, days, months and years. All life events therefore make sense only if viewed as part of a life-course trajectory[42].

Current estimates of environmental exposure are cross-sectional and cumulative in nature and are based on between-person differences among large cohorts. This approach overlooks the individual nature of the life stressors taken into account; stressors that are, in turn, contingent on the prior experiences of a person. Thus, current studies fail to capture the necessary level of detail for encapsulating the meaning of social experiences for the individual.

Perhaps, such social experiences will always remain inaccessible to investigation owing to the lack of either appropriate tools or empirical measuring capacity. Or perhaps new technologies will allow more nuanced monitoring of environmental reactions. One such effort is the proposal to develop real time biosensors capable of detecting changes in the environment as they take place in the everyday life of an individual[40]. The development of such technology would be an attempt to go beyond traditional measurements of frequency, duration and severity of adverse environmental exposure and would allow to capture the ongoing individual and dynamic extent of exposure as well as its impact on fundamental biological processes. In a futuristic approach, proponents of the biosensors imagine the realization of specialized wristbands or 'smart' shirts that could alert you to the fact that your positional environment has become unfavourable and could measure the consequential changes in gene or protein expressions.

An integrative operational framework

Each of the theoretical and experimental paradigms that have been employed to dissect the genetic basis of behaviour are not exclusive of one another. On the contrary, they serve as complementary units of a unified complex approach[1]. Genetic epidemiology can be a useful source of information for gene identification approaches, which in turn can be the starting point for measuring $G \times E$ interactions.

What emerges, however, is that the development of the conceptual and technological frameworks of behavioural genetics has led to a general rebuttal of the notion of simple causes and to a growing tendency towards the embrace of complex and multi-factorial origins of most disorders.

It is clear that the one gene–one phenotype relationship valid for conditions such as Huntington's disease simply cannot apply to more complex mental dysfunctions without univocal symptoms or neuro-physiological defects. The simplistic presumption of a causative link between a gene and a behavioural phenotype that originated in the enthusiastic decades of molecular genetics and that gave rise to claims of genetic essentialism and determinism[41,42] has been replaced by notions of 'susceptibility'. Subtle measurable changes in genetic material equip individuals differently to cope with environmental stimuli and manifest a phenotypic outcome.

As Cornelius Gross and I have underlined elsewhere, understanding behavioural differences in terms of susceptibility is also too simplistic. What is required instead is an aetiological description that goes beyond susceptibility and refers to a complex framework of interacting genetic, environmental, stochastic and emergent phenomena[43]. Measurements of $G \times E$ interactions underlying a behavioural disorder must synergize with molecular neuroscience measurements of individual differences, including reactivity measures such as heart rate or hormonal changes and, if possible, brain functional imaging[8].

The re-evaluation of the boundaries between different psychiatric categories suggests that psychiatric disorders ought not be regarded as 'things-in-themselves', but as outcomes arising from a complex mix of direct and indirect effects at different points in a causal chain. Similarly, genetic factors included in the causal chain should also not be regarded as fixed determinants of psychological characteristics, but as restricting factors channelling behavioural outcomes by producing the structural building blocks of the underlying mental apparatus, and at the

same time moderating the impact of past and present environmental and biographical experiences on fundamental behaviour.

Integration with the social context

The plurality of the causal chain underlying the actualization of behaviour needs to take into account an integration with the socio-cultural context.

The conceptual shift, or new 'style of thought'[44,45], that ascribes psychiatric conditions as reducible to the operations of the brain[46] has accentuated their abstraction from society. Because the brain is a physical entity, and therefore subject to the laws of cause and effect of nature, mental functions and psychiatric disorders, too, are being considered as such. Perhaps, a modest degree of independence from context is applicable to overt physical dysfunctions, when there is a direct connection between manifestation of symptoms and a univocal underlying biological defect. However, this is not entirely pertinent to complex behavioural phenotypes and to psychiatric disorders, which, I think, tightly adhere to, and cannot be separated from, the social context in which they arise.

What is meant by social context? Broadly, social context refers to patterns of social roles, behavioural routines, institutional and interpersonal relationships that are embedded in a relatively stable social frame and that tend to endure within a given period of time[47]. It is possible to distinguish between proximal and distal social contexts. Social roles, relationships and habits are considered proximal in that they dictate rights, responsibilities, opportunities and limitations that confront the person. The distal social context refers to macro-sociological units such as various kinds of societal institutions[48]. Within the social context are embedded agreed-upon and tacitly approved rules and norms that can both elicit or limit types of behaviour.

The abstraction of behaviour and psychiatric disorders from society has, therefore, the consequence of lifting them from the cultural frameworks of motives, action, meaning and responsibility that are normally applied to social objects. However, psychiatric disorders are simply not independent from societal forces and mechanisms.

For instance, forms of social control can be placed on people to limit their behaviour and their choices. Social control mechanisms are the result of norms and other social forces that in a way 'canalize', i.e. restrict variability in the phenotype of genetically diverse people. If norms are more effective and choices are minimal, the consequences of genetic differences also diminish[48].

To further comprehend the meaning of an integration with the social context we need to go back to the definition of psychiatric disorder. As I illustrated above, the question, and the intrinsic difficulty, of defining a phenotype is crucial for the application of a sensible and accurate operational framework that incorporates the underlying neurobiological basis of the phenotype. However, it is inevitable that a valid definition of a behavioural and psychiatric disorder reconciles cultural particularism with biological universalism[49], or in other words that it reconciles the natural and the cultural aspects of the disorder in question. Wakefield has put forward a hybrid definition of disorder[50] that attempts to resolve the tension between the natural and the constructed social world. Drawing from and paraphrasing the definition of mental disorder from the DSM[20] (DSM-III-R, 1987), he suggests that a disorder exists when 'the failure of a person's internal mechanisms to perform their functions as designed by nature impinges harmfully on the person's well-being as defined by social values and meanings'.

This fundamental polarization in the current definition of mental disease readily reminds of the epistemological distinction between vital and social norms that Canguilhem made earlier[51]. According to him, vital norms exist that manifest the *normativity* of life and of the organism itself (in this case the individual), and of its adaptability to the environment. On the contrary, social norms are only the manifestation of conformity and agreement with a constructed, artificial order of society and its requirements. Vital norms represent the laws or mechanisms internal to an individual that govern natural functioning. From this perspective, pathology, too, is an expression of the normativity in which those functions are limited. However, social norms are incorporated into (or mistaken for) the vital and the impairment of normative functions clashes with what is imposed as 'normal' or deemed 'negative' by socio-cultural standards. In psychiatry, the definition of disorder or pathological behaviour is therefore often a product of the tensions between normativity and normality, between a plurality of vital norms on the one hand, and moral judgements and social notions of normality or inappropriateness on the other[52,53].

Behaviours and pathologies in a medicalizing society

One of the main social mechanisms that nurtures this tension is the process of medicalization, and by extension, of geneticization. Medicalization refers to the process by which 'nonmedical problems become defined and treated as medical problems, usually in terms of illness and disorders'[54,55]. With respect to psychiatric disorders, it refers to the increase in the number of non-pathological behavioural traits that are brought under the scrutiny of medical investigation. Geneticization is the extension of medicalization to the realm of genetics[56]. Both medicalization and geneticization are not only about the creation, promotion and application of medical and genetic categories to human problems and not only about the transformation of the normal into the pathological. They are central to

transformations in people's subjectivities and they have the potential to redefine and control borders of acceptable behaviours, concepts of the body and states of being, as well as notions of equality and policies of public health.

Several and diverse forces are responsible for the process of medicalization. First of all, societies can become less tolerant of certain behaviours or symptoms, whose manifestation thus becomes congruent with disorder 'styles' aligning with cultural, identity and professional norms of a particular period.

The medical profession and mental health communities can support the annexation of new problems to the domains of medicine and genetics. Groups of individuals, such as social movements or patient organizations, who suffer from specific disorders play an important role in the reinforcement of their medical and genetic definitions and are highly suggestible and eager to receive validation to their symptoms[57]. Furthermore, both professionals and sufferers of a condition participate in a shared culture of 'illness display' disseminated through the media, who promote the latest representations of psychiatric diagnoses[58]. Finally, the availability of pharmacological interventions, and the profitability of their markets as supported by pharmaceutical companies, further accelerates the trend toward medicalization of certain conditions[59]. The number of conditions regarded as mental illnesses and the number of affected individuals has grown considerably[60]. An emblematic example are anxiety disorders. Anxiety is an intrinsic, protective emotional reaction to dangerous, threatening situations. A high anxiety threshold would be dangerous as this condition would make us vulnerable to a variety of dangers. However, if excessive and long-lasting, anxiety could become detrimental for the individual and disrupt daily activities such as work, sleep or socializing. So the intensity and duration of anxious responses must be finely orchestrated. The number of people diagnosed with anxiety disorders has increased significantly. Recent global estimates report that the lifetime prevalence for the totality of anxiety disorders is about 16% (ref. 61).

Efforts are being made to understand the physiological mechanisms and the genetic components of this emotional state. Genetic approaches to the study of anxiety rely on estimates of heritability of patterns of anxiety behaviour and aim to find why individuals differ in their thresholds of anxiety, and in their ways to manage or respond to dangerous threats, also by revealing the neurobiological mechanisms underlying such differences[62].

However, while anxiety is a universal functionality of an organism, the contexts in which it is experienced, the interpretations of its meanings, and the responses to it are strongly influenced by historical contingencies, cultural beliefs and practices of a given time. Anxiety is not to be considered as a fixed category, but as a phenomenon undergoing secular shifts that depend both on biological programming and on societal alterations, these latter often gauging their impact and severity[63].

Next to threats that directly attempt at our lives and our survival resources – such as predators, poisonous foods, war, crime and violence – there is a cumulative load of modern threats that constantly challenges the normative adaptations of our anxiety responses. Global terrorism, climate change, environmental pollution or the spread of lethal infections are only a few examples and a list of new risks can be quickly compiled. In addition, there are more subtle and continuous threats, such as the instability of one's social status and economic income, that also have short- and long-term effects on our well-being and mental health[64].

Although many of the coping strategies that people adopt in response to the social pressures above are non-pathological in their nature, they often assume a 'medicalized', pathological form in retrospect. Global high rates of anxiety vary greatly if broken down across published single national reports. The observed heterogeneity rests upon differences in the prominence and type of specific fears in given environments as well as on culture-specific interpretations of anxiety symptomatology. Certain anxiety symptoms are considered pathologic in one context and everyday idioms of mild distress in another[65]. It is, therefore, important to incorporate into research how certain social arrangements confound people's distress and ordinary problems of the living with mental illness and how these arrangements flexibly change over time and in different contexts[66].

For instance, Western societies, with their reverence for values such as self-sufficiency, productivity and assertiveness, have become less tolerant of both disruptive and mild anxious states and have transformed our expectations of individuals in society.

A cultural praise for gregariousness and self-expression has contributed to the medicalization of 'shyness', something that has come to be considered an endophenotype of 'social phobia', one of the anxiety disorders listed in the DSM[67,68]. Shyness is a state of behavioural inhibition in the presence of unfamiliar people or situations and, according to the DSM, social phobia is a persistent and extreme 'fear of social and performance situations in which embarrassment may occur'[20]. It remains difficult to clearly define shyness or social phobia as unhealthy states of mind as it is impossible to unambiguously define the emotional states as problematic. Embarrassment, bashfulness, tightness when exposed to public scrutiny or social avoidant behaviour are symptoms that might concern us all in mild or harsh forms and that may be encouraged or judged as inappropriate forms of behaviour according to social judgements.

The diagnostic ambiguity of shyness and social phobia was a fertile ground for the creation of a large market of the drug Paxil that offered a cure for symptoms of this emergent human problem and accentuated its medicaliza-

tion. When the drug Paxil, marketed by GlaxoSmith-Kline, was approved in 1996 for the treatment of depression, it entered a saturated market for the cure of this condition. Drugs such as Prozac or Zoloft made up for most of the sales in anti-depressant drugs. The manufacturers responded to the saturation of the market by promoting a specialized use of Paxil for the treatment of anxiety, especially 'social anxiety disorder' (SAD)[67,69]. They did so by launching a well-choreographed, aggressive awareness campaign to raise public visibility of SAD by disseminating a series of advertisements which relied upon a mixture of 'expert' (clinicians, medical doctors) voices and compelling narratives of patients who lamented symptoms of the disorder. Posters were put up at bus stops with slogans such as 'Imagine being allergic to people' or 'Paxil's efficacy in helping SAD sufferers brave dinner parties and public speaking'[69]. The campaign concentrated on displaying individuals' feelings in social situations such as public speaking that are likely to evoke fear in many people. Thus, the pharmaceutical company marketed their drug by marketing (and medicalizing) a 'disease'.

Despite the difficulties in defining and recognizing shyness, research toward the elucidation of the 'genetic structure of shyness' has been carried out[70,71], but it is not entirely obvious how this could reveal something crucial or novel about the understanding of anxiety. However, it seems that low social tolerance toward this trait and the large anti-shyness campaign by the pharmaceutical industry may have contributed to it becoming an object of study of behavioural genetics.

Experimentation in behavioural and psychiatric genetics: from the lab to society and back

A dynamic feedback loop exists between behavioural genetics and a medicalizing society[43]. Social contingencies and various forces behind the process of medicalization are increasingly bringing a number of non-pathological traits under the scrutiny of medicine and expanding the repertoire of behaviours that are considered amenable to genetic study. Often, behavioural genetics investigates genetic associations with behaviours that are already defined as deviant or problematic and we are likely to continue to see more genetic explanations for human problems.

In turn, ongoing research in behavioural genetics can contribute with its proceedings to the perpetration of medicalization. A genetic discovery will contribute to the medicalization of a disorder by offering new avenues for biomedical treatments, thereby imposing a certain kind of interpretation and promotion of the condition in the medical and social world[43,72].

This complicated dynamics between behavioural genetics and society is likely to reinforce the view of behavioural and psychiatric conditions as firm categories, and to exacerbate their abstraction from the social context, by emphasizing the genetic and neurochemical components and neglecting the contextual social factors that contributed to their origin.

In this paper, I have exemplified the complexity and intricacy that characterize research in behavioural genetics and its indissoluble link with society. Objects of study in this branch of experimentation are behaviours, like anxiety, with inexorable social and personal relevance. We have entered a phase in which sophistication in the way we can describe genetic variation and crucial appreciation of the environmental components are shaping an operational framework of interacting genetic and environmental measures with the potential (despite enduring limitations) of accessing seemingly ineffable aspects of behaviour, paving the way for the development of therapeutic strategies to alleviate failures in neurobiological functioning.

However, reflexivity on their practice is expected of researchers, who need to attend more carefully to the impact of genetic research on the medicalization process, recognize its limitations and acknowledge the possible influence of social norms on the selection of traits and behaviours that become objects of their investigations.

Note

During the past recent years, 'Society in Science – The Branco Weiss Fellowship' has been invaluable for me in providing the congenial intellectual framework to think of and carry out my work innovatively and in a 'society-responsible' way.

First, it has helped me delineate and reflect on the most salient societal implications of my work. Second, and most importantly, it has allowed me to move one step further and explore how, in turn, societal awareness and considerations may resonate with me during my laboratory practice and actually have an impact on my research agenda. In other words, the experience has brought me to try and integrate 'society' and 'context' into my laboratory experimentation and to look for the strategies to accomplish this ambitious goal.

One approach that I have employed in the attempt to start this process has been to resist disciplinary specialization and to engage in a dialogue and research exchange with scholars from the social sciences to collaboratively identify the most crucial (and unresolved) questions in my field of experimentation and define possible modalities of research to address them.

Choosing between the employment of dichotomous or more continuous measures of behaviour, looking for genes underlying large diagnostic categories or quantifiable intermediate phenotypes, and the appreciation of societal and cultural interpretations of a given phenotype

in the context where a study is conducted are all methodological decisions that carry societal consequences. These are all actions that rest with the researcher and underscore and influence meanings of normality, disease and social inappropriateness. They have the potential to control and limit the number of different spurious traits that land as illnesses on the bench of behavioural genetics laboratories.

Incorporating society into science is a challenging and gradual process, but it is very intellectually stimulating and its end results are promising and, in the long term, preciously rewarding.

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