Evolutionary Psychopharmacology, mental disorders, and ethical behaviour

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INTRODUCTION

The concept of *pathology* has a built-in normative character. An individual (or a state) is pathological if and only if it is not normal, i.e., if it fails to be as an individual (or a state) of that sort *ought to be*. In other words, a pathological individual (or state) is an individual (or state) which does not conform to the standards to which all the individuals (or states) falling under its very sortal concept *must* conform.

When applied to mental disorders, this view entails that the concept of psychopathology has a normative character. A human being is psychopathic if and only if he fails to have the mental capacities which are normal for humans, i.e., the mental capacities that humans *ought to have* to correctly respond to the environment, and to correctly perform certain perceptual and cognitive task. Let us call this the *received view of psychopathology*.

The received view has two main implications, concerning psychiatry. The *first implication* is that psychiatry is ethically relevant, in two respects. First, the results of psychopathology may help to define what is normal for humans, and thus, psychiatry may help to grasp the determination of ethical norms. Second, the psychiatric treatment of mental disorders rests on various assumption concerning what is normal for humans, and, thus, psychiatry has profound ethical bearings.

The *second implication* of the received view of psychopathology is what we could call the *universal treatment thesis*. This is the idea that each mental disorder must have one perfectly appropriate cure, which scientists have to work out and clinical psychiatrists have to apply to individual patients. Naturally, the universal treatment thesis does not rest on the received view alone, but it is also grounded on at least two other complementary assumptions. First, humans (which, in this case, constitute the set of normal individuals setting the normative standards) are sufficiently similar to each other for it to be the case that two individuals which have equally non-normal mental capacities must be equally and similarly different from normal individuals from a neurological point of view. Second, psychiatrists have to cure mental disorders by acting on the nervous systems of mentally ill people so that mentally ill people may turn out to have mental capacities falling within ranges of variation which can be considered normal. The universal treatment thesis, it seems to us, follows from the conjunction of these two assumptions with the received view.

In this essay, we want to argue that the received view may be accepted and that the first implication mentioned above follows from it, but we will

also claim that the second implication does not follow, since the first complementary assumption can be rejected on evolutionary grounds. In section two, we will briefly discuss the received view and its relevance for the links between psychopathology and ethics; we will suggest that the notion of *function* plays a central role in this respect. In section three, we will try to show that the *universal treatment thesis* is a widespread view, but we will also suggest that it is unacceptable, since it purports that the notion of function can be defined in reference the a whole species. From an evolutionary perspective, though, it seems that the notion of function must be defined in reference to both an individual and the species to which it belongs. In section four, we will consider some data taken from pharmacogenetics and from psychopharmacology, and we will try to explain why psychiatric treatments have to be moulded for individuals, not for the entire species, contrary to the universal treatment thesis. We will conclude with some remarks concerning the ethical bearings of our claims.

It is worth noting that this paper is intended as a contribution to the evolutionary approach to pathology. Although a contender in medical debates since Darwin's times (cf. Corbellini 1998), the evolutionary approach to pathology became an autonomous field of study and research during the early '90s, especially through the work of the psychiatrist Randolph Nesse and the biologist George Williams (Nesse, Williams 1991 and 1995). Several collections of essays have subsequently been published on the topic (cf. Donghi 1998; Stearns 1999; Trevathan, Smith, McKenna 1999), and mental disorders have also been at the centre of the attention, from this perspective (cf. Stevens, Price 1996; McGuire, Troisi 1998; Canali 2001).

The main contention of the evolutionary approach in medicine, which we want to support, is that each individual is, at least partially, the expression of a particular genetic programme and that this programme is a historical and unique product of evolution, that was moulded by the mechanisms of phylogenesis (i.e., genetic variation and natural selection). Therefore, according to evolutionary medicine, epidemiological phenomena, specific individual vulnerability to particular diseases, the ways and timing in which each individual reacts to a pathogen, falls ill or regains its health, depend also on historical, phylogenetic processes. In this view, an exhaustive explanation of pathology cannot be limited to the immediate causes triggering a pathological process, but it must also take into account the remote causes, that is, it must make use of evolutionary explanatory categories.

More recently, the evolutionary approach was also applied to the analysis of drugs consumption, with the hope of helping the prediction of therapeutic effectiveness - particularly in the case of antibiotics, antivirals and the treatment of cancer through chemotherapy (cf. Davies 1996; Levin, Anderson 1999; Normak, Normak 2002). Surprisingly, very little work has so far been done on psychopharmacology, despite the fact that the practice of psychiatry seems to look at the Darwinian paradigm with much more sympathy than any other medical specialty does. Therefore, this paper should be considered as a contribution both to philosophical reflection, and to evolutionary psychopharmacology.

PSYCHIATRY, ETHICS, AND FUNCTIONS

Let us now give a closer look at the received view and at its relations with ethics. As seen, the received view claims that, in psychiatry, an individual (or a state) is pathological if and only if it fails to be as an individual (or a state) of that sort *ought to be*. This means that sortal concepts allow us to group together individuals (or states) in virtue of some of their characteristics; those characteristics must belong to all the thus grouped individuals. A pathological individual (or state), will then be one which falls under a certain sortal concepts, but fails to have one or more of the properties which individuals (or states) falling under that concept must have. It might be objected that sortal concepts must be clear cuts, and that it makes no sense to claim that an individual falls under one of them, while failing to have one or more of the properties which individuals falling under that concept must have. Let us think about the case of humans and mental capacities. Either an individual has all the relevant mental capacities and thus falls under the concept *human*, or that individual lacks one of those capacities, and cannot then be called a human.

It can be replied, though, that sortal concepts need not be such clear cuts. The reasons why we claim that different individuals fall under a certain concept may vary, and our criteria for grouping together individuals may differ from individual to individual even within the same group. We can claim that both *a* and *b* are humans, but on different grounds. E.g., we may talk to and discuss with *a*, and this is a good enough reason to call it a human, but we might not be able to do the same with *b*, who's in a coma. However, we can still claim that *b* is a human, if we know his parents, and we know that they are both humans. Conversely, we might not be able to apply this latter criterion to a_s if we do not know its parents and, had we not possessed other good grounds to trust its humanity, we could have reasonably wondered whether they were aliens. Thus, it seems that different things can be claimed to fall under the same sortal concept on different grounds, but, still, sortal concepts tell us what properties should ideally have things falling under them (cf. Strawson 1959; Wiggins 2001). Sortal concepts, then, are linked to the stereotype that we associate with the things falling under them.

It is worth stressing the identification of the properties linked to a certain concepts and claims of sortal identity about individuals do not constitute a circle. It could be objected, indeed, that one needs to know what the necessary properties required by a sortal are, before claiming what individuals fall under it; yet, at the same time, one needs to know what individuals fall under a certain concept, before understanding what the necessary properties required by that sortal are. The reply offered in the previous paragraph can be readjusted for this objection: sortal attribution is not a clear-cut process, but it is a process which involves grouping together individuals on different grounds, and subsequently realizing that they can be grouped together because they all conform to some standards, at different degrees. When we start reflecting on this standards, we come up with the idealized set of properties, which an ideal individual falling under that sortal concept should have. This is not to say, however, that the idealized set of

properties cannot be changed: the more individuals falling under that concept we encounter, the clearer can we be about what properties are necessary for individuals of that sort.

This account does not attempt to say *how we should think* about the world, but it describes *how we do think*. In Strawson's terms, it is descriptive, rather than revisionist. It is in virtue of the fact that we do think "sortally" that we can make sense of the idea that something is pathological, i.e., that it is not as it should be.

We can now turn to the second point which needs to be discussed in this section: the reason why the received view entails the fact that psychiatry is related to ethics. The point is that, as noted, the concept of *pathology* is normative, and normative concepts may be the ground for ethical norms. Why should this be so? One way of explaining the link between normative concepts and ethics could the following. In the case of living organisms, the standards which set what an ideal member of a species is like, set also what the correct what the correct functioning of such an individual is. This is a clear consequence of the normative character of sortal concepts: different living beings may be grouped together under a certain sortal concept, i.e., may be considered a species, because they can live the same sort of life, that is, they have functional parts which enable them to perform specific operations. Naturally, the species sets the standards for the correct functioning of its individuals, but different individuals may conform to those standards at different degrees. However, performing their function at their best is what they all ought to do.

At this point the reader may worry that this approach is naïvely open to an objection, which is commonly advanced against attempts to explain normativity through the notion of function. It may seem, indeed, that the view which we are suggesting rests on an equivocation between two senses of 'function': the unquestionable claim that living organisms have functionally organised parts does not entail, let it alone is identical to, the claim each of those organisms as a whole has a function. Parts are functional because they contribute to the life of the organisms to which they belong, the objection goes, and thus their contribution may be what they ought to do; but entire organisms cannot be said to have functions because they are not parts of bigger wholes. Recently, however, several philosophers have persuasively attempted to respond to this objection and to contend that entire organisms have functions. It is not necessary to get into the details of these debates here, but it is worth mentioning at lest few attempts. Murphy (2001), for example, has argued in favour of the principle of function-compositionality, according to which the parts of a whole may have a function only under the condition that the whole has also a function. Murphy's point is that we cannot make sense of the idea that a part has a function, unless we consider it as contributing to an activity of the whole to which it belongs. That activity, though, is the correct functioning of that individual, and, thus, is its function. Foot (2001, 25-37) has also suggested that the natural function of an organism is the organized activity which all the organisms of that species perform when they live:

> All the truths about what this or that character does, what his purpose or point is, and in suitable cases its function, must be related to [its] life cycle. The way an individual *should*

be is determined by what is needed for development, self-maintenance, and reproduction: in most species involving defense, and in some the rearing of the young. (Foot 2001, 32-3).

Ricciardi (2003) took a similar line and contended that the very possibility that we identify humans (or other animals) as individuals of a certain species rests on the condition that we can recognize that they do the sort of things, i.e., they have the sort of life, which individuals of that species do. That sort of life is the function of individuals of that species.

One could worry that the appeal to functions makes attempts to explain normativity of this sort intrinsically incompatible with an evolutionary approach to these matters. The reference to functions, in fact, seems to suggest that things having functions have purposes, e.g., are made for some end or other. But, according to neo-Darwinism, there is no purpose in nature: the existing forms of life are not designed to be how they are, and their functioning is the mere result of casual systemic variations and fitness to the environment (cf. Ayala 1972). It must be recognized, though, that the notion of function referred to by the above mentioned theories does not require any purpose, nor any design. In order to explain how this may be so, let us consider Bedau's (1992) distinction among three grades of teleology.

Grade 1 is the sort of teleology in which an end benefiting an individual (e.g. favoring its survival or reproductive chances) is arrived to by chance, in the sense that it was not the intended aim of an agent, nor the result of a normal etiological chain characterizing the functioning of that individual. In *grade 2*, though, the end of a teleological process is good for the individual and is arrived to through an etiological process characterizing the functioning of that individual, but its goodness did not play no causal role in that process. In *grade 3* teleology, the end is good, is arrived to through a proper etiological chain, and the goodness involved does play a causal role in the process. This is the case of intentional action: the content of a representation in the agent's mind, the realizations of which is the end of the process, is part of the causal conditions which give rise to the process.

The notion of function involved in the above mentioned theories of normativity requires only grade 2 teleology. If a living thing has a function, there is something which is good for it, i.e., the correct performance of its proper action. Thus, the condition for grade 1 teleology is satisfied. However, the above views also claim that living organisms have functions because they are included in a certain species, that is, in virtue of the fact that they have a structure which makes them fall under a certain sortal concepts. The performance of the function proper of their species, thus, etiologically depends on their organic structure, and the further condition for grade 2 teleology is also satisfied. However, the normative views mentioned above do not claim that the organic structure of the individual which belongs to a certain species is the result of intended action, nor that it is an end chosen by a designer. In fact, they do not need to affirm that the function has any causal role in determining the organic structure typical of the individuals belonging to that species. That structure may well be the result of evolution. As a consequence, those normative views do not need grade 3 teleology and are compatible with evolutionism. These views, indeed, attempt to ground normativity on nature.

A last remark about the notion of function involved here. A living thing *i* falling under the sortal concept *C* has the function *F* in virtue of the fact that things falling under *C* ought to have a certain set of properties *P* (which include both mental and physical properties, and constitute the stereotype which we associate with things falling under *C*). The individuals having the properties contained in *P*, in fact, in virtues of those properties, are suitably structured to live a certain kind of life, which is their function *F*. Thus, the function *F* of *i* is a function of the properties included in *P*, which make it a *C*.

So far, we have seen that living things have functions, and that what functions they ought to have depends on the sort of things they happen to be (i.e., on some properties they must have in virtue of the fact that they fall under a certain sortal concept). This means that the notion of a function is a value-notion, i.e., it is good for an individual to function well. But this value-notion does not need to involve a *moral* value. Why should we do what is good for us? Or for some other living thing? The above mentioned theories give different, but probably entrenched and compatible, explanations of the relation between morality and the existence of functions of living being. Murphy claims that the attainment of its own function is what a human being ought to do, since the same state of affairs, which is its well-functioning, can be both the content of its theoretical reason (which grasps it as her well-being) and the content of her practical reasons (which considers it as a reason for action). Foot, instead, takes over Davidson's famous distinction between two kinds of reasons for action, i.e., those which are reasons relatively to a certain consideration, and those which are reasons all things considered. Only the latter are moral reasons. And considerations on what a human should do, on what it is to behave well for her, gives us precisely reasons *all things considered*.

We can now finally turn to psychiatry. Within a conception of normativity which grounds norms on nature in one of the manners considered above, psychiatry is relevant for ethics since it can help to understand what the correct functioning of a human being is. One of the things that psychiatrists do is to define normal mental behavior and to distinguish it from pathological mental behavior. The correct functioning of a human being, which constitutes a reason for an action and grounds ethical behavior, includes also different sorts of mental activities. Thus, psychiatry can contribute to determine how a human being ought to be.

It must be noted that this does not entail that psychiatry is the only or preferred foundation for ethics. As we have seen, sortal concepts have fuzzy borders and their application may involve the deployment of several criteria. To decide what a human ought to do in a moral sense, i.e., what its *all things considered* reasons for action are, one needs to take into account all these criteria, and to balance together different opposing reasons to claim that a living things falls under a certain sortal or that things falling under a certain sortal must have certain characteristics. Psychiatry delivers some of these reasons, which need to be weighed against those coming from other fields of experience. Psychiatry is an autonomous discipline, which rests on its own grounds and does not need to consider other points of view. But its results can be used to try to determine how a human being should be – *all things*

considered –, and it is at this point that its results have to be weighed against the conclusions of other fields. At that stage, though, we have already abandoned psychiatry to get into ethics.

There is at least another way in which psychiatry and ethics interact. As we have seen, psychiatrists try to understand what is a normal human mental behaviour, and, in order to do that, they must try to figure out what mental properties and capacities an individual must have in order to fall under the concept *human*. Given the above mentioned autonomy of psychiatry as a scientific field, they will try to do that on purely empirical grounds, in particular in virtue of evidences coming from neurobiology, genetics, cognitive psychology, etc. Once a provisional understating of what normal human mental behavior is (namely, what set $M = <m_1, m_2, \ldots, m_n>$ of mental properties an individual *i* must have in order to fall under the sortal concept *H*, which is the concept *human*), abnormal cases can be identified, and means of treatment looked for. The rational beyond the behavior of psychiatrists includes at least the five following preconditions: i) psychiatrists realize that there is a sortal concept *H*, which allows us to group together humans; ii) they believe that a standard individual falling under *H* must have the set of mental properties $<m_1, m_2, \ldots, m_n>$; iii) they encounter an individual which they take to fall under the concept *human*, although fails to have at least some of the properties $<m_1, m_2, \ldots, m_n>$; iv) they take it that, as an *H*, *i* should have all the mental properties $<m_1, m_2, \ldots, m_n>$, and thus they qualify *i* as abnormal, ill, or deviant *H*; v) they look for a "cure" for *i*, that is for a means to render *i* as "normal" as possible; they attempt to grant him as many as possible of the properties included in the set $<m_1, m_2, \ldots, m_n>$.

The following consideration may explain why this must be the rationale beyond psychiatric practice. We all normally believe that a psychiatrist trying to heal a dog for failing to read would be insane, whereas a psychiatrist trying to heal a dyslectic human for the same reason would be absolutely rational. This difference among our judgments can be best explained if we accept the truth of i)-v). Both the dog and the human fail to have a certain mental capacity, but we think that the human should have it, whereas the dog is just not the kind of being which should be expected to have it. Thus, it make no sense to try to make a dog read, whereas it seems to us absolutely mandatory to try to help the human.

The link between psychiatry and ethics lies in the fact that the set *M* is a subset of the set *P*, which includes all the properties (mental and non-mental) that an *H* should have. For the autonomy of psychiatry, *M* should be determined by psychiatry, on its own grounds. But when it comes to deciding weather and how to cure and individual *i*, that is, to enforce on *i* as many as possible of the properties contained in *M*, a problem arises. The psychiatrist must consider weather each of the properties in *M* is consistent with all the properties in *P*, overall considered. If there are inconsistencies, the conflicting properties must be weighed against each other and the prevailing one will deliver a reason for action. This means that psychiatry can give reasons for action which are relative to psychiatric considerations, but these have to be weighted against reasons coming from other sources, in order to find out reasons which hold *all things considered*. This implies that

when deciding how to treat a certain individual, psychiatric considerations have to be balanced with considerations having to do with what the function of a human being is. With this step, the psychiatrist abandons her own field, and enters the realm of ethics.

As a consequence of these remarks, we can claim that notions like *normality* and *pathology* are not dispensable. They lie as a rationale beyond the sorts of (the psychiatrist's) behavior, which we consider normal and rational. However, they need to be flexible, since *sortal concepts*, which are their preconditions, have fuzzy and unclear borders. Our evidences for determining the set *P* and its subset *M* may vary, and this might eventually push us to revise our conceptions of normality and pathology. This can be called *epistemic flexibility*, since it depends on our epistemic standpoint. There may also be, however, a kind of *ontological flexibility*: evolutionism teaches us that species may change across history, and thus we may need to revise our conceptions of normality and pathology due to changes in the very structural and organic organization of the standard individuals of a species. In the former case, the flexibility depends on our limits in determining what properties an individual ought to have in order to fall under a certain sortal concept. In the latter case, there are real changes of the properties which are necessary in order for an individual to fall under a certain sortal.

The upshot is that the received view of psychopathology entails this requirement: an adequate psychiatric practice needs to consider ethical questions while deciding what mental properties are required for a normally functioning human being. In order to do this, psychiatry has to be both epistemically and ontologically flexible. Epistemic flexibility requires that psychiatrists recursively remould their notion of mental normality, through wider considerations about what the function human beings is (i.e., what the required properties of a standard *H* are), by considering fields of experience other than psychiatry, and by observing new cases of *H*s. In this case, the set *M* can be changed on the ground of reasons coming from other subsets of *S*, or on the ground of previously unconsidered traits of *H*s, which can be highlighted by a newly encountered *H*. Ontological flexibility requires that psychiatrists recursively remould their notion of mental normality, by considering weather cases of non-standard individuals should be taken as deviant cases, or as the marks of a shift in the history of the species.

The universal treatment thesis (i.e., the idea that each mental disorder must have one perfectly appropriate cure, which scientists have to work out and clinical psychiatrists have to apply to individual patients) does not seem to be neither epistemically nor ontologically flexible. It is not epistemically flexible since it rests on the false idea that sortal concepts can be at least in principle be clear cuts, and thus that an universal characterisation of normality and pathology can be defined. It is not ontologically flexible since it overlooks the contribution of evolutionism and does not consider the possibility that species may change; indeed, it does not consider that treatments may be made inadequate by the evolution of the species, even if they were perfectly efficient when they were first shaped.

It is our persuasion that an evolutionary approach may render psychiatry suitable to meet the ethical requirements set by the received view.

THE UNIVERSAL TREATMENT THESIS AND ITS PROBLEMS: THE FUNCTIONS OF INDIVIDUALS

The evolution of psychotropic drug consumption

The wide acceptance of the universal treatment thesis is witnessed by data concerning the drug consumption relative to the treatment of certain mental diseases. These data are telling about what the ordinary attitudes toward those disease are. After considering this example, we will discuss how an evolutionary approach could lead to very different attitudes towards those diseases.

Recent evidence indicates that the way psychotropic drugs are prescribed in the United States (Pinkus *et* al.1998) and in Italy (Pani 2000) is changing. In the United States, in the ten years period 1985-1994, the number of GP checks in which a psychotropic drug was prescribed rose from 33 to 46 million. In the last few years, tranquillizers/hypnotics, which had previously been the most frequently prescribed drugs, have been overtaken by antidepressants, which have doubled in quantity, reaching over 20 million prescriptions in the past five years; the use of stimulants and "tonics" increased by 500% over the same period. Similar trends were observed in Italy (Table I), where prescriptions were grouped into three broad categories: tranquillizers, antidepressants and antipsychotics. The data show a large increase in antidepressants prescriptions, a smaller increase in antipsychotics prescriptions, and an even smaller one in tranquillizers prescriptions.

Table I – Source: WHO
The Psychotropic Drug Market in Italy
(Million pieces sold per year)

	1995	1996	1997	1998	1999	2000	2001
Antipsychotics	11,675	12,432	12,468	12,940	13,428	13,114	13,267
Antidepressants	16,750	18,275	19,413	20,524	22,493	24,435	28,380
Tranquillizers	61,107	64,051	63,464	63,292	63,497	63,267	63,608

These data seem to suggest a possible generalization concerning industrialized countries. These countries are characterized by several areas in which a rapidly changed environment presents traits of evolutionary "novelty", which may be deemed significant. The effects on individuals of these new conditions seem to be the emergence of psychic unfitness, as the constantly rising numbers of people requesting psychiatric treatment seems to testify. The efficiency of these treatments, though, seems quite dubious, since the situation of mental diseases in industrialized countries seems to be far worse than in developing countries (Brown *et al.* 1998).

These treatments, furthermore, seem to follow the "universal treatment thesis", since they suggest that cases of psychic dysfunctions are increasingly coped with standard pharmacological remedies. Since these remedies prove to be inadequate, though, the universal treatment thesis should be reconsidered. Our contention is that the problem with the

universal treatment view is that it does not take in account the evolutionary meaning of some mental diseases. Were the evolutionary meaning considered, the universal treatment thesis would be abandoned, and the resulting view would be more flexible in the senses required by the ethical demand considered above, and, probably, more effective with the psychiatric consequence of the evolutionary mishmash created by contemporary industrialized societies.

We will soon considers some examples showing that the universal treatment view is insensitive to the demands of evolutionism. Before doing that, though, we should consider some argumentative patterns that evolutionary theory could provide to medical and, in particular, psychiatric thinking.

Evolutionary explanations in psychiatry

According to a recent analysis of explanation in pathology (cf. Nesse, Williams 1991 and 1995), evolutionary models to account for psychiatric disorders may be grouped into seven categories:

1) *Adaptation and defence*. Several pathologies or organic weaknesses actually act as sensitive defences and adaptation mechanisms. In the psychiatric field, they consist of the reactions of alarm and fear. These conditions are linked in the first instance to adaptation aimed at preparing the individual to cope with stimuli relevant to his survival and to that of the species. Depression may also be considered a defence mechanism, aimed at inducing the implementation of a detachment or a break with the past, and the reconstruction of novel forms of adaptation (cf. McGuire *et al.* 1997; Nesse 2000).
2) *Conflict with other evolving elements*, for instance, co-specific or pathogenic organisms. One specific case is that of the conflict between parents and children starting with the pathogenic potential exerted by the foetus on the mother's body and neurochemical equilibria and extending to the load of elements with possible pathogenic valence implicit in the caring for children and in relations with them. Also the social environment through which the competition among individuals and the evolution of the various systems comprising it engender a series of potentially pathogenic conflicts.
3) *Evolutionary mismatch*. Our bodies and our behavioural reaction patterns, which evolved slowly during our ancestral life in the savannah, are no longer adapted to the environmental and social contexts of the modern age (Eaton *et al.* 1988). One striking case is that of substance abuse. The epidemic of drug addiction related to the modern age can be interpreted as the result of exposing human beings to pure psychoactive principles towards which the human nervous system is currently unable to come up with any adaptive response (Nesse, Berridge 1997). Moreover, although the emotions are adaptive tools that can be used to cope with situations relevant for survival, it is also possible that they are elicited by erroneous evaluations of stimuli and that their expression threshold, defined by means of slow selective processes, can no longer cope with the transformations produced by man in his environment, by the

practically infinite number of cognitive stimuli or the rules governing social behaviour. This is true, for example, of the fight reaction, which in contemporary society is produced by a large number of stressful or frustrating situations, but cannot be expressed at the behavioural level, sociocultural reasons (Marks, Nesse 1994; Nesse, Young 2000). Eating disorders can also be accounted for with patterns explanation which can be included in this category (Neel *et al.* 1998).

4) *Evolutionary trade-offs at the genetic level*. A number of pathological conditions are the result of specific genetic adaptations to a given environment. A gene may afford several advantages in specific environmental contexts, but, at the same time, it may increase the likelihood of developing certain diseases. The most striking example in psychiatry seems to be the bipolar or manic-depressive disorder. This disorder seems to have a highly hereditary component, actually believed to be as high as 50%. The conservation of a gene that causes a disorder that can sometimes be highly incapacitating may be explained in virtue of the fact that its presence may bring about advantages, which offset any negative effects. Several studies suggest that people suffering from manic-depressive disorders are more creative, more enterprising and better in achieving social success than ordinary people; that is, they are bearers of behavioural traits which can ensure a reproductive advantage. Consequently, the gene or gene combination responsible for this psychiatric disorder thus maintains a high frequency (Goodwin, Jamison 1990).
5) *Evolutionary trade-offs at the level of the complex phenotypic traits*. Each somatic or behavioural trait in an individual is the expression of a complex genetic and epigenetic equilibrium between somatic structures and psychological functions. Some genes are simultaneously part of the biochemical systems governing different processes; for example, organ development, hormone synthesis, or a specific enzymatic reaction. In this way, a genetic mutation that increases the efficiency of one function may jeopardize the effectiveness of another biological activity of a behavioural programme and, thus, expose the organism to the onset of specific diseases. For example, the strong reactivity of the cardiovascular system to emotional stimuli may increase vulnerability to disorders in this organ. On the other hand, were the cardiovascular apparatus less sensitive to the stimuli which can trigger affective reactions important for the survival of the individual and the species, the organism could turn out to be inadequate to cope with risk situations or even to reproduce.
6) *Historical constraints and dependence on evolutionary pathways*. Evolution proceeds by recycling and coadapting the "old" biological and psychological material of the species. The best trade-off between materials and pre-existing biological functions can hardly coincide with the best and most effective solutions which could theoretically elaborated for a functional structure. An example

could be the conditioning determined by the affective responses on cognitive faculties. This interference can sometimes be quite pathogenic. This mishmash depends on the fact that the development of cognitive faculties was superimposed on a consolidated inheritance of emotive patterns.

7) *Random factors*. The evolutionary process does not follow any prearranged pattern of development aiming at maximum efficiency. It uses, adapts and remodels existing functional apparata and anatomical parts (a form of biological tinkering) and is largely the result of the action of random factors (genetic variations, environmental modifications, changes in ethological relationships, and so on). Evolutionary randomness alone would be sufficient to account for many human diseases. In this sense "randomness of drugs prescriptions" adds a further contextual variable of considerable interest. In the case of psychotropic drugs, randomness may depend on the therapeutic options of different therapists or on a single therapist changing his mind in a short period of time. Frequent and rapid changes from one molecule to another may be the result, which leads to predictable but unpleasant consequences, such as withdrawal symptoms, and sudden change and necessary adaptation in receptor interactions, signal transduction and even in gene transcription. Random variations entails the reading of non random genetic programmes, which were selected for other purposes, and had evolved in response to different stimuli. A non unitary (dimension- or category-based) nosography amplifies the impact of non univocal therapeutic decisions, i.e., decisions which are not dictated by homogeneous working hypotheses and models of the health/disease continuum. Indeed, there are several therapeutic approaches available (dynamic, behavioural, familial or biological), which have resisted numerous attempts of unification or integration.

With these evolutionary explanatory patterns in mind, we can now turn to consider some examples, in order to underline the faults of the universal treatment thesis and the respects under which an evolutionary approach in preferable.

Psychotropic drugs and the adaptive significance of psychiatric symptoms

The evolutionary approach suggests that drug therapy should take into account the adaptive significance of certain psychiatric symptoms (McGuire, Troisi 1998). Historical constraints and the dependence on evolutionary trajectories have actually led to the cognitive processing of external stimuli and the assessment of the personal condition vis-à-vis the surrounding context to be largely based on emotional processes, which are largely influenced by the affective dimension (Damasio 1994; LeDoux 1996). From this perspective, the use of tranquillizers and antidepressants to treat subclinical conditions, for sub-threshold action, or to act on the penumbra of mood disorders may jeopardize the adaptive function of certain emotional responses. Let us consider two cases: first, the relation between the emotive

information and the motivational drive; second, Medicalization of character and generalization of temperament.

1. *Emotional information and motivational drive*. A certain degree of anxiety is quite physiological insofar as it can signal a danger or threat, when it has not yet been processed and perceived at the conscious level; alternatively, it may reinforce the motivation to act functionally once the state of awareness has been reached (Nesse 1999).

Several depressive symptoms have a similar adaptive function, both informative and motivational. They can signal an existing gap between expectations or investments and results, or a profound clash between one's personality and the condition in which one lives. They can lead the subject to break off the investment and to abandon the situation and make a halt in order to recover and to work out a fresh strategy.

Sub-threshold intervention may consequently interrupt the information flow from the deepest levels of the brain to the cortical areas and thus hinder or prevent the cognitive processing of the problem, or the search for a suitable solution. Likewise, an incorrect use of drugs may inhibit functional responses and motivational drives aimed at eliciting more appropriate behaviour. Paradoxically, drugs may contribute to maintain the pathogenic situation.

This problem has important psychological and social bearings. Therapeutic abuse can in fact force individuals to adapt to existential situations and contexts, which are objectively painful or in any case display a discrepancy in respect to character profiles. This acceptance or acquiescence can have severe repercussions on individuals and on society. Chronic pathogenic factors will continue to affect the former, while other unacceptable conditions will probably continue to be maintained and reproduced in society.

Certain drugs used to treat mood disorders change the expression of emotions by the patient and thus may suppress an important way of ensuring interaction with and modification of the external environment. Consequence, this could affect the behaviour of the individuals who surround the patient, and possibly modify their understanding and willingness to help (Lewis 1934). In this sense, the treatment could modify and sap the effectiveness of some of the relational and social factors, which would normally help the recovery and the reconstruction of meaningful affective and social relations.

2. *Medicalization of character and generalization of temperament.* Similar remarks may be spelled out about the increasingly widespread use of antidepressants to modulate mood, and to correct "character flaws." This trend seems a real attempt to medicalize character, in order to conform it to socially prised models. The social phenomenon is analogous to the boom of aesthetic surgery to conform to socially accepted standards of physical beauty (Kramer 1997; Knutson *et al.* 1998).

This trend may increase interventions in cases of sub-threshold symptoms, in the face of sub-clinical disorders, and this may eventually lead to the generalization of temperament and the levelling down of individual differences. This scenario would have various hidden risks. Temperament, as the genetic expression of personality, is strongly

predetermined and its alteration by means of drugs may cause a strong conflict between genetic inheritance and a chemically modified phenotype. (Of course, we are referring to cases in which there is no ongoing disease). The following problem then arises, since certain character traits are hereditary.

Let us imagine an individual who transmits to his descendants a genetic endowment with a proneness to fear (a phobic vulnerability). Let us also imagine that the same individual, under antipanic drug treatment, displays a non phobic phenotype to his children. Even if this may be desirable in a sense, we cannot to predict the effects of this apparently irremediable clash between a (genotypic) Darwinian inheritance and a (phenotypic) Lamarckian one. Will the children too be obliged to be medicalized or will the example be sufficient to prevent the phobic potential of their genome from being expressed? And if this were the case, would this not paradoxically show that non biological variables are able to influence the expression of the genetic endowment and that, therefore, behavioural desensitization therapies, in such cases, would be preferable to the use of psychotropic drugs? Around this issue, there is currently a very heated debate.

In these two examples, the application of the above considered evolutionary explanatory patterns (which are here entrenched in ways which we leave to the reader to work out), leads to the conclusion that medicalization ought to be avoided. Were the evolutionary considerations overlooked, the output would have be the opposite. The point is that the evolutionary approach is more flexible, in the both the sense considered above, than the alternatives. The above considered patterns of explanation, indeed, allow us to consider the evolutionary significance of certain mental traits: they show us some of the possible processes which make us remould the set *M* of mental properties which we stereotypically associate with humans, through the consideration of other intuitions of ours about what humans have be from a non-psychological standpoint (i.e., through the consideration of all the properties contained in the set *S*). As we have seen, the set *M* cannot be determined purely on the grounds of psychiatric evidences, but must be shaped according to considerations concerning other reason-giving characteristics of humans, which cannot be accounted for by psychiatry itself. The evolutionary explanatory patterns considered above offer a substantial amount of these considerations.

These patterns of explanation, as we noted, are flexible in both sense, epistemic and ontological. They may bring in considerations relevant for the remoulding of *M*, and these considerations may depend either on the focus on previously unconsidered data, or on the realization that evolution caused a species change. However, one could claim that all this is compatible with the universal treatment thesis: cannot the evolutionary considerations be conjoined with the universal treatment approach? The answer is the negative, and this is why, while considering the notion of flexibility, we noted that the remoulding of *M* requires both considerations concerning other non-psychical stereotypical characteristics of humans, and questions concerning the stereotype associated with the concept *H*, which may originate from the encounter with deviant *H*s. It seems to us that evolutionary thought offers a

characterization of the relations between an individual and the species to which it belongs which offers the desired sort of flexibility, but which is incompatible with the universal treatment thesis. As we note in the introduction, evolutionism makes the individual central, more than alternative approaches. In next section we will see why.

WHY FUNCTIONS ARE ALSO MATTERS OF INDIVIDUALS

Evolutionism, pharmacogenetics and pharmacogenomics

In order to explain the role of individual in sortal identification, we can focus on the case of response to drugs. This is both a suitable example ad the case which we want to discuss. Genetic variability, the raw material of phylogenesis, is obviously expressed also in the specificity with which each individual responds to drugs. One aspect of genetic variability at the population level is represented by genetic polymorphism. As a source of variability, polymorphism is filtered through natural selection and is thus functional to adaptation to environmental and ethological changes, that is, it is neutral but in any case essential to phylogenetic transformation.

At the pharmacogenetic level, polymorphism is important for genetic flexibility, which has made it possible for organisms to cope in the encounter with new substances and probably represents one of the most complex expressions of the co-evolution of the animal and plant kingdoms. A large number of genetic polymorphisms of pyschopharmacological interest are known today which are thus of clinical relevance to psychiatry (Kalow 2001). One of the better known is that linked to the polymorphism of an element in the Cytochrome P450 hepatic enzymatic system, CYP2D6, identified for the first time as responsible for the variation in the metabolism of debrisoquine (an antihypertensive). Dozens of genetic mutations are now known to be associated with this polymorphism. CYP2D6 is one of the most important enzymes involved in the oxidative metabolism of the drugs, and catalyses the oxidation of several dozen drugs, about 20% of all commonly prescribed substances. The list of CYP2D6 substrates is a long one and includes all the tricyclic antidepressants, several serotonin reuptake inhibitors, such as fluoxetine and paroxetine, as well as many antipsychotics such as haloperidol, perphenazine and risperidone (Kalow 1991; Bertilsson 1995; Ingelman-Sundberg *et al.* 1999). In individuals with weak metabolization all these drugs reach concentrations from 2 to 5 times greater than in normal metabolizers, which implies that in more serious phenotypes the recommended dosages can lead to toxic concentrations.

Very relevance for clinical psychiatry and psychopharmacology is also the polymorphism of another element in the hepatic Cytochrome P450, CYP2C19, which affects about 3% of white Caucasian individuals. CYP2C19 metabolizes several drugs in psychiatric use such as imipramine, diazepam, citalopram and amitryptiline, which are consequently affected by this polymorphism.

Other important pharmacogenetic polymorphisms in psychopharmacology are those of the receptors with which the psychotropic drugs interact (Masellis *et al.* 2000).

These facts indicate that pharmacogenetic provides molecular evidence to corroborate the idea that an individualized approach to therapy is required (Brockmoller 1999; Ozdemir *et al.* 2000). The evolutionary conception of medicine calls for such and individualized approach, since evolutionism takes each organism to have an irreducibly individual nature, in virtue of the idea of population on which Darwin founded his doctrine.

Specificity of drug action
and integrative aspects of biological and adaptive functions

Research on psychotropic drugs and their therapeutic use are increasingly being concentrated on substances characterized by a highly specific action. These are pharmacological principles capable of acting selectively on individual neuronal systems, or, even better, capable of modulating the functioning of specific receptors in the same neuronal system.

This approach, although innovative, might not be particularly effective, unless the molecule selected displays an excellent affinity and an extreme specificity for a single target of known physiology and with a proven role in the pathological process that is to be treated. One striking example of the difficulties encountered in this respect by modern psychopharmacology is given by current schizophrenia therapies. Molecules which may have radically different action mechanisms are today available to clinical psychiatrists. Several of these (e.g. Clozapine) have a multireceptor profile, that is, they can act on several different molecular targets. Others (e.g Amisulpride) act on a single receptor. For example, in the past 50 years, dopamine D2 was shown to play a role in the physiopathology of schizophrenia. However, a unifying theory account of how both these drugs act has still to be found.

More recent research has moved towards the identification and development of substances with a capacity for action at gene level or at that of genetic networks, which specify and modulate the functions of various functional apparatuses of the nervous system.

Nevertheless, the final therapeutic effect on a patient depends on numerous additional factors: pharmacogenetic individuality - mentioned above - and peculiar traits of individual constitution. The latter can be related to complex genetic and metabolic factors, which may not depend only on parts of the genome directly responsible for the functions of the nervous system, but can still affect the pharmacodynamics and pharmacokinetics of drugs (Hofbauer, Huppertz 2002). The important point is that these genetic and metabolic factors are products of evolution, i.e., the result of a mutual coadaptation , which may depend on various phylogenetic compromises and may be influenced by evolutionary trajectories.

The evolutionary approach also highlights the integrated nature and the mutual adjustment of the functional apparatuses of an organism. In this sense, one important but usually underestimated factor in the determination of the long-term action profile of a drug is the reaction of the regulatory systems of the organism to the action of the substance itself. This is a compensatory response, which tends to restore the state of equilibrium, either functional or pathological (i.e., the homeostasis pre-existing the drug's action), and thus generally amounts to the reduction or suppression of

possible therapeutic effects. Occasionally, it may even induce adverse effects. From a theoretical point of view, it is impossible to predict the precise "re-adaptation" reactions to a drug on the basis of the profile of its receptor. It is quite reasonable to expect that the magnitude of the side effects will be proportional to the number of the action sites of the drug. But this does not tell much about its therapeutic effects. The intrinsic limit to pharmacogenomics lies in the possible confusion of psychotropic drug "safety" acquisitions with those of their “efficacy”, two dimensions of their action on the organism that are very different from each other.

The individual function

These examples be used to make a general point, and a point specific to psychiatric therapy.

The general point is that the stereotypical set of properties which we associate with a certain concept are largely phenotypic properties. A certain individual, though, belongs to a certain species in virtue of its genotypic inheritance. Thus, variation in the environment or polymorphisms may cause, concerning a certain individual, a divergence between its belonging to a species and its falling under a certain sortal, the former being ascribable on genotypic ground, the latter on the fitting of the phenotype in the stereotype associated with that sortal. Given the relationship between the normal function of the individuals falling under a sortal and the set of stereotypical properties associated with that sortal, the possibility of this divergence entails that a certain individual may be inapt to function as members of its species are stereotypically believed to function. A polymorphism or a change in an environmental variable may cause the expression of a phenotype which cannot function as individuals of its species are normally taken to have to function, notwithstanding the certainty of his species appurtenance. This leads to the need of a new notion, that of an *individual function*, namely the proper functioning of an individual. This is a function of the stereotypical function associated with its species, and of its individual phenotypic traits, depending on environmental and polimorphic variables. For example, in order to know what the normal functioning a certain human being may be, we need to consider what the stereotypical functioning of humans is, and how he differs from a stereotypical phenotype.
The notion of the individual function involved in the evolutionist approach shows that this approach is epistemically and ontologically flexible, and that it explains how the consideration for individuals can help individuating the set *M* of mental properties which an individual *should* have.

The more specific point is that the need for notion of the individual function shows that the universal treatment thesis is inadequate. Psychiatric treatment must consider a number of individual features, through the considerations of the evolutionary significance of several trait of the individual, even apparently pathological ones, before any therapeutic measure can be decided. There is no room for generalizations and for the application of standard model of treatment to all individual, since even what counts as pathological may vary from case to case.
The inadequacy of the universal treatment thesis, though, can be clear also for other evolutionistic considerations: evolutionism induce us to consider

both the individual and the social consequences of individual psychopharmacological actions. Indeed, we need to consider also the possible dysgenic effects of the spread of psychopharmacological therapies. From the evolutionary point of view, one of the most important consequences of the efficacy of the pharmacological treatment of psychiatric disorders is that of equating the reproductive rates of the subjects affected by behavioural disorders with those of healthy individuals. Of course, these quotients tend to be different and to differ also as a function of the type of psychiatric pathology. For example, a depressive or anxious tendency can be associated with a comparatively low reproductive rate, while, conversely, a hyperthymic temperament can be expressed also in a high fertility rate.

In any case, any action exerted on the ailing phenotype tends to spread the genotype associated with the psychiatric disorder in the population, and could thus lead to an increase of the disorder itself over time. In this connection, it would be interesting to make a study of the evolution of the incidence of certain psychiatric diseases by attempting to isolate the relationship between epidemiological trends and the number of treatments performed for these specific disorders.

CONCLUSIONS

The evolutionary approach emphasizes the individual dimension of diseases and, consequently, the need for personalized therapeutic actions. At the same time it suggests that the treatment should be geared to the achievement of the patients' objectives, and to the maximization of their functional capacities inside a given context.

The drugs are prescribed on the basis of a diagnosis, mainly according to the nosological criteria set out in DSM-IV and ICD-10. The classificatory logic on which this procedure is based does not correspond at all to the functional settings. The studies used to evaluate cohorts of normal or sick individuals, in an attempt to render the response rates and prognostic evaluation homogeneous, prevent the identification of the individual variables that actually determine the standard deviations and, in most cases, the therapeutic or side effects due to psychotropic drugs. A greater knowledge of the recent progress made in Darwinian medicine could lead to a new therapeutic paradigm in which any necessary drug treatment must necessarily be integrated into the context and the life style of the sick individual.

Doing this is a moral requirement, given the twofold link between psychiatry and ethics spelled out in section two. The flexibility of the Darwinian approach is needed, if psychiatry has to help understanding what humans ought to do, and if psychiatric therapy has to help deficient human being to be as they *can* and *ought* to be, without forcing on the individually untenable stereotypes.

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