On the concept of psychological risk factor

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The idea that certain mental phenomena (e.g. emotions, depression, anxiety) can represent risk factors for certain somatic diseases runs through common thinking on the subject and through a large part of biomedical science. This idea still lies at the focus of the research tradition in psychosomatic medicine and in certain interdisciplinary approaches that followed it, such as psychoneuroimmunology. Nevertheless, the inclusion in the scientific literature of specifically mental phenomena in the list of risk factors pertaining to a specific pathological condition would seem, to say the least, problematic when not completely absent, unlike what happens for certain behavioural factors, such as smoking, sedentary life, and alcohol abuse. It is also significant that insurance companies and health and welfare services do not pay for interventions and treatment for states of anxiety, disorders of mood and of the personality, alexithymia and stress reduction, as means of prevention or treatment of somatic diseases, as instead they do for the treatment of tobacco addiction.

However, as I shall endeavour to argue here, there are numerous and well grounded reasons why this different consideration of psychic conditions compared with behaviours is valid and must be maintained in the evaluation of pathogenetic risk factors.

Behavioural risk factors and psychic risk factors

Several different methods are now available which establish on a firm basis that some behavioural aspects play a significant role in the etiology and progression of a disease. To return to the case of smoking, for example, the following types of study have provided evidence that this kind of behaviour contributes to the development of lung cancer: A) the epidemiological studies carried out to demonstrate whether smoke represents a risk factor for cancer of the respiratory system, comparisons between smokers and non smokers, the demonstration of the existence of a dose-effect relation; control of confusing factors. B) laboratory studies related to the possible development of lung cancer. C) Short term and follow-up studies on the effects of the reduction of smoking on the etiology of cancer and its progression. D) Analysis of the components of cigarettes and of the smoke inhaled and the isolation of the active ingredients having pathological effects on tissues, experiments on animals carried out using these components. E) *in vitro* studies aimed at determining the molecular path from the active ingredients to pathophysiological changes of lung cancer development.

None of the mental processes postulated as causes or risk factors for psychosomatic disorders has ever been examined using such methods. This is due in the first instance to the very identity of the psychological and psychiatric constructs. Emotion, stress, anxiety and depression have a complex and multidimensional nature, both as concepts and as actual nosological entities, and are therefore constitutionally non quantifiable and hard to investigate using epidemiological studies.

This set of problem elements nevertheless represents a basis for another series of difficulties of a methodological nature in the psychosomatic approach. One of the main characteristics of the controlled studies is the capacity to indicate the mechanisms and transitions that link diseases to the risk factor.

The typical model of psychosomatic conceptualization involves a structuring and a causal direction by psychological factors of the somatic factors through one or more physiological mediators. Therefore, in order to acceptably document the hypotheses of psychosomatic etiology, it would be necessary accurately to identify the psychological factor involved or to characterize it univocally and then to evaluate its physiological effects and the way the latter promote the pathogenetic process.

The uncertain identity of psychological constructs

We have seen how the univocal identification or accurate characterization of a psychological element or process actually proves impossible. Then, despite the efforts made to detail the various components of mental disorders undertaken by diagnostic handbooks and international classifications, today embodied in DSM-IV-TR and ICD-10, psychosomatic

tradition tends to use the terms referring to pathological emotions in a rough and ready fashion. For example, studies based on a psychosomatic approach point to anxiety as a risk factor in cardiovascular disorders (CVD), and depression in cancer and again for CVDs.

In the case of anxiety, these studies seem completely to neglect the fact that they are using a multiform and controversial psychological and psychiatric concept. As a clinical category, the term anxiety disorder comprises several different subtypes characterized by widely differing symptoms ranging from various phobic manifestations to generalized anxiety, posttraumatic stress disorders and obsessive-compulsive disorders. According to some researchers, however, the breakdown into subtypes is still highly ambiguous and controversial (e.g. Barlow, 1988). The widespread, multidimensional and approximate appearance of the psychological constructs that, like anxiety or depression, are adopted as risk factors, makes it impossible to isolate them and to manipulate them experimentally, as is generally done when active ingredients are being identified.

Research in neuroscience, for instance, is showing how the various subtypes of anxiety are linked to different biological correlates (Kandel, 1983; LeDoux, 1998; Grillon, 2002). The latter would conceivably have a pathogenetic basis in apparatuses having different mechanisms and with consequently different morbid outcomes.

The same may be said for depression. It is actually impossible to determine the biology of "depression" as this condition consists of a complex set of different subjective elements – anxiety, detachment, loss, despair, etc., of behavioural and relational processes associated with an extensive array of physiological and pharmacological alterations (Schatzberg et al, 2002, Musselman et al., 1998).

In the case of both anxiety and depression, moreover, there is a high incidence of reciprocal co-morbidity or the onset of other psychiatric manifestations (Nesse, 1999), which further complicates the characterization of factors having an etiological role and their possible interaction.

What has been said above points to the absence of any fundamental assumptions to characterized anxiety or depression as risk factors for CVDs or more in general for somatic diseases.

Furthermore, like all other affective states, anxiety is a complex process related to several domains, from subjective experience to the various physiological equivalents, as far as behavioural manifestations which in their turn refer in a circular fashion to environmental and social variables are concerned. The correlation with somatic disorders should therefore be investigated for each of these domains, also taking account of the fact that, during the possible pathogenetic process thus triggered, these different aspects of anxiety interact, reciprocally modifying each other, modifying the biological substrate and being transformed by the latter.

Imprecision, the overlapping of these psychiatric concepts, the circular relationship between domains and different processes thus precludes the possibility of making an adequate assessment of the extent, specificity, biological coherence and even the temporal relationship of the postulated causal association, qualities that instead represent important criteria for ascertaining causality in medicine.

The case of stress

Also when confronted with a more neutral concept such as stress, research into psychosomatic mediators and mechanisms betrays its imprecise nature. Although apparently better characterized than depression at the biological level, if for no other reason than the wide use made of animal models, which have been late to appear for depressive states, stress places a series of exceptional obstacles in the way of studies aimed at isolating psychological risk factors and the characterization of pathogenetic mechanisms and processes leading from the psychological to disease in the clinical sense. Above all, stress is another multidimensional concept used to refer to different psychological and physiological processes and in this sense ultimately becomes a secondary risk factor. It is potentially linked to all the affective dynamics and each affective reaction above a given threshold may be stressful. Furthermore, stress represents a complex variety of psychological processes ranging from the cognitive dimension to behavioural reaction and passing through a multitude of intermingled subjective dimensions of affectivity. For instance, emotional response and stress response are known to be strongly modulated by experience and by the cognitive dimension. In this sense, the same event or stressor can produce different effects in different persons, as well as at different stages in the life of the same individual. It is consequently

impossible to generalize with reference to the exposure to stress as a possible etiological factor as stress itself actually reproduces a two-fold and mutually related plurality of effects referring to individuals and to different periods in the life of the same individual: those dependent on predisposition and on the current biological terrain, and those mediated by experience and the cognitive dimension. This implies in turn that it is impossible to identify a consistent biological gradient of responses to exposure to stress or to negative emotions: on the other hand, this is a fundamental element in the formulation of suitable hypotheses regarding the causal relationship between risk factors and disease.

At the same time the fact that the emotional reaction and response to stress both depend on circular relationship with the cognitive level and learning does not allow us to determine satisfactorily whether a dose response relation exists between emotions and disease, and what form this takes, as in this case the dose is also a function of the response.

This complexity is related to a large number of mutually interacting physiological equivalents.

This complexity makes it extremely difficult to isolate the various pathways through which stress affects the biological terrain and thus to provide an adequate description of any etiopathogenetic role played by psychological events.

The primacy of the mind

It should be noted how the idea that the mental contents and dynamics can represent risk factors is based on the assumption that the mental element, for instance in depression or anxiety, takes priority over the somatic symptom and is thus the cause of the disease. This assumption seems to depend solely on the priority given in our culture to the mental, as opposed to the physical, dimension of the person. Also with reference to neurobiological evidence it now seems reasonable to investigate the relations between emotions and disease by examining somatic symptoms as one of the two dimensions making up affective disorders. It would not thus be totally unreasonable to reverse the causal order and investigate these morbid conditions as the manifestation of a process of 'psychologization' of somatic phenomena.

On the identity of emotions

Two other problematic aspects of the idea that the psychological content of the emotion can be taken as representing risk factors must be mentioned. The first of these is dependent on the substantial continuity and overlapping of the spectrum of the shared affective life, the customary emotional response to common stimuli and on which, in the approach we are now analyzing, the onset and progression of certain forms of chronic pathology are believed to depend. The somatic symptoms would therefore be difficult to relate to specific emotion and all forms of causal argument would thus be precluded.

Emotional experience also displays aspects of strong relativity and indeterminacy in all the various theories that have attempted to explain it and that may be related to three main conceptualizations: peripheral theory, central theory and cognitive theory.

The peripheral theory of emotions

Introduced by William James in 1884 in his famous article in *Mind*, the peripheral theory of emotions claims that emotional experience consists in physical sensations, of feedback from vegetative and behavioural responses. We do not run away because we are afraid, but we are afraid because we are running away, we tremble, and our pulse and breathing rate shoot up. But, as Walter Bradford Cannon (1927) had already pointed out, the most intense emotions generally are accompanied by very similar vegetative modification patterns. Furthermore, Cannon pointed out that although we are generally conscious of the type of emotion experienced, visceral activities are not perceived very accurately as these somatic regions are not highly innervated. These objects reflect the type of difficulty encountered when it is endeavoured to relate the various emotional states to specific physical symptoms.

The central theory of emotions

The central theory, first proposed in the mental content psychology of Wilhelm Wundt and Edward Bradford Titchener and then systematized and related to nervous processes by Cannon (1927), identifies the specificity of emotions as characteristic subject experiences. The peculiar psychological content of the emotions is thus believed to be the effect of corresponding brain processes that can nevertheless give them meaning and distinction. In

this conception the emotional response is subsequent to the activity giving rise to the emotional experience. The subjective experience, with its variability, its irreducibility, it purely qualitative nature, becomes the causal agent of the emotional response. Also this conception of emotional experience is hard to frame within quantitative studies and in causal explanation models specific to research on risk factors.

The cognitive theory of emotions

In order to explain the differences between emotional experiences also cognitive representations have been used. In this sense the experience of fear, for example, consists above all of awareness of having to face a dangerous event or thing. The cognitive theory of emotions was proposed for the first time in a radical version by Stanley Schachter and Jerome Singer in 1962. They claimed that emotional experience was above all a process of attributing significance or of the verbal labeling of processes of physiological activation. In this case, the emotions become relative to experience, learning and individual culture.

Self-report of emotions and epidemiological investigations

Many of the epidemiological studies on emotions and disease are based on self-reports of specific affective states and involve the use of a vast array of measurement scales. Despite some interesting convergence of results, there are obvious methodological gaps and the absence of studies and procedures to compare the evidence.

Data collection through self-reports is problematic, to say the least. It has long since been recognized that the perception of emotions is strongly influenced by experience, by cognitive elements, by the personality, by the capacity to distinguish among the constantly overlapping emotional states (e.g. Lazarus, 1977; Lazarus et al., 1970). Furthermore, the perception of possible negative and pathogenic emotions may be falsified by psychological defence and adaptations mechanisms capable of deceiving the subject as to his/her mental health (Shedler et al., 1993).

It thus appears odd, to say the least, to indicate as a cause or risk factor of a somatic disease a fact determined by interpolating constitutionally subjective values. Moreover, if the emotions depend on other psychological elements rather than on affective states it is more likely that the primary risk factors will be cognitive type constructs, an individual's culture, his/her personality. In this case, it would thus actually be impossible to identify the active ingredient, the causal agent, the specific correlate, as the cognitive type constructs, individual culture, the personality, are all elements that are difficult to break down as they are specified by value systems and meanings.

Expression of emotions and biological coherence of symptoms

Another singular aspect of psychosomatic conceptualization and the identification of emotions as risk factors in certain diseases is the fact that the various explanatory hypotheses have indicated as potential etiopathogenetic factors all the different and conflicting dimensions of emotional experience. Risk factors for identical psychosomatic phenomena, for instance, affecting the cardiovascular system, have been observed to some extent in alexithymia, that is, in the incapacity to verbalize affective processes, in the unconscious repression of emotions (e.g. Davison and Petrie, 1997, Marshall, 1972), in the conscious inhibition of emotions in the face of emotional arousal (e.g. Weinberger et al., 1979), in the excessive outpouring of emotions (e.g. Gross and Levenson, 1993, Pennebaker and Beall, 1986). This radical uncertainty conflicts with all criteria of coherence and biological logic which should instead be observed in postulating a causal link between emotion and disease.

State or traits? From emotions to personality

Another significant question in the analysis of emotions as risk factors in somatic diseases is the problematic nature of the distinction between emotional states and traits. The distinction between the two is considered a function of their duration: the former are thought to refer to transient emotional phenomena, while the latter are constituent elements of the personality, permanent characteristics. Although appreciable at the extremes of the temporal

continuum, in normal everyday conditions the distinction between states and traits is seen to be arbitrary (e.g. Allen and Potkay, 1981).

This has important logical consequences with regard to the hypotheses concerning the links between emotions and somatic diseases. Investigation of the relations between emotions and disease could sometimes measure traits and on other occasions more or less transient emotional states. The impossibility of distinguishing the object of the observation would therefore lead to the impossibility of ensuring the comparability of studies.

Personality and disease

The idea that personality type is causally linked to specific somatic disorders is an old one, and was to some extent already formulated in the Hippocratic doctrine of the relations between humours, or vulnerability and character traits. It was Helen Flanders Dunbar who gave this belief systematic form prior to World War II through an extensive use of psychological tests, statistics and the comparison of character traits with clinical signs (Dunbar, 1935 and 1943). According to Dunbar a kind of character *cliché* existed for each disease. The patient with coronary problems, for example, was a person who worked and struggled tenaciously, possessed strong self-control and tended to be successful and to fully attain his/her goals. The peptic ulcer patient, on the other hand, was a hyperactive and over-enterprising type. Dunbar's ideas were given wide circulation in the subsequent literature. The public at large was quite familiar with Friedman and Rosenman's (1959) theories on the associations between CVD and personality type, which had been in the limelight of the medical debate ever since the 1980s. Claus Bahnson (1969, 1980, 1981), on the other hand, attempted to find a correlation between personality type and cancer.

However, let us examine the meaning and the implications of the idea of personality types as risk factors in the relative somatic diseases. The idea that a certain type of personality is prone to a particular disease generally leads to the conviction that a causal link may be hypothesized between an inclination towards certain emotions and somatic symptoms. In the final analysis this idea may lead to two distinct meanings: 1) It may mean that a person tends to experiment certain emotions and to be predisposed towards certain events and experiences. In this case, it is therefore evident that the causal agent that is supposed somehow to link the psychological side to the symptom is not the personality type but perhaps the emotion. 2) It may mean that both proneness to certain emotions and emotional responses and the symptoms depend on a certain type of individual constitution that reacts to certain experiences in specific ways that are psychologically and somatically coordinated. Also in this case, therefore, there is no true causal relation between personality and symptom, while the link between psychological dimension and somatic disease ought to be related to the general framework of proneness, the individual constitution.

But does personalityactually exist?

Intuitively we believe that our actions are coherent, that is, that they depend on some profound element in our individual nature: our personality. On closer examination, however, the idea of personality is seen to be fraught with controversial aspects. It has been incorporated in a large number of conflicting theories: to cite but a few – from behaviouralism to the theory of individuality, from psychoanalysis to the biosocial theory, and even in radical approaches in which the personality is a mere psychological concept. A cognitive construct, an intellectual product, as Boethius wrote as early as the 6th century: "Persona est substantia individua rationalis naturae"

This multiplicity of conceptions developed parallel with the emergence of an astonishing array of instruments for measuring the personality. Unlike for other psychological concepts, however, research has failed to identify any satisfactory definition of a simple operational nature, which is only further evidence of the elusive nature of the reference of this category.

It is problematic, to say the least, to consider personality as a risk factor for psychosomatic symptoms, as the cause or correlate of a somatic disease.

Psychological research itself has begun to question the concept of personality. In the late 1960s, Walter Mischel suggested that personality possibly accounted for less than 10% of the variations in the behaviour of individuals and among individuals (Mischel, 1969). Mischel also considered that the perception of continuity and coherence of behaviour was a cognitive construction and that therefore personality practically did not exist.

Measuring of personality traits and representation of the temporal dimension

Let us however assume that personality exists and that psychometric instruments are capable of measuring the traits properly. Epidemiological studies on the relations among the various personality types and somatic diseases are based on psychometric measures. In this case we would have a snapshot of the person fixed on a single time frame. The exclusion of the temporal dimension leads however to two serious epistemological inconsistencies. In the first instance the time dimension appears to be fundamentally specific to the doctrines aimed at investigating personality, as it represents the only quantity within which it would be possible to understand and explain the fact that it apparently remains constant even in changing circumstances. In the second place, this synchronic description of the personality is found to be inconsistent with the theoretical framework surrounding it when it is used as a risk factor in epidemiological type investigations and to seek explanations of a psychosomatic type. Indeed, as a causal element in this case, personality is considered an active element precisely because it is spread over the whole period of the individual's existence. The single snapshot portraying the personality thus becomes relatively unimportant in understanding or identifying any physiological mediation mechanisms, in order to explain how personality traits act at the etiological level and contribute to determining the pathogenetic progression of morbid conditions of a chronic nature, such as the disorders for which today we seek a correlation with factors of the psychosocial type probably linked to very lengthy time scales.

Emotions and disease: from problems of time frame to the indefinite complexity of the web of causation

Reference to the temporal dimension introduces a gap between the limited time frame surrounding emotional phenomena and the larger one in which chronic diseases develop and in which emotions are viewed as risk factors. Also in the case of negative emotions associated with long-term psychiatric conditions, such as untreated depression which may last from 6 months to more than one year, we are dealing with periods of time that are certainly shorter than those needed to bring about and maintain the lengthy process of a disease such as CVD, cancer or diabetes, which are instead often associated with depressive syndromes.

It is therefore impossible in the narrow sense to attribute an etiological role to certain psychological conditions. It is therefore necessary to speak of relations, of the action of psychological elements inside a multi-stage process made up of successive exposures to pathogenic elements. And this is ultimately what the psychosomatic approach has actually started to do, reformulating its basic epistemological elements and shifting from a search for the causes to the identification of the relations (Mizrachi, 2001).

Nevertheless, also in this new approach investigations of the relations between emotions and disease continue to perpetuate a mentalistic model and tend to assign a predominant role to the psychological dimension of the emotions. However, considering mental phenomena and emotional experience, as a risk factor leads to an inadequate thematization of the role of behaviours associated with emotional disorders, mood and in general all the psychiatric conditions involved in the causation of a somatic type of pathological condition. And it stands in the way of reflecting on another causal circularity, that between psychological experiences, behaviour and nervous processes. In this way, the persistence of a mentalistic approach on the one hand hinders the development of research strategies focused on the objectivizable plane of behavioural risk factors and, on the other, limits the perspectives and variables with which to investigate as required the individual portions and the different planes of the close network of relations between emotions and somatic symptoms.

Depression as a risk factor in CVD. Critical observations

Let us take for instance the idea that depressive conditions represent a risk factor in CVD. This now represents a rather widespread conception in the modern approach to psychosomatic research as it is supported by a large body of epidemiological studies (e.g. Anda et al., 1993; Barefoot and Schroll, 1996; Carney et al., 2002; Glassman and Shapiro, 1998; Frasure-Smith, Lespérance, 1998; Hippisley-Cox et al., 1998; Ford et al., 1998, Wulsin et al. 1999), to the point that François Lespérance and Nancy Frasure-Smith, two of the most distinguished workers in the field, have written: It is time that depression replaced type A behavior as the number one psychological concern for cardiologists (Lespérance, Frasure-Smith, 2000).

A vast literature has now been produced by research on the possible biological mechanisms underlying the relationship between depressive symptomatology and CVD. It suggests a wide range of potential mechanisms and also present numerous contradictory aspects. One of the explanations considered more plausible suggests that depression can cause CVD through neurohumoral dysregulation. Alteration of the functionality and of the parameters of the autonomous nervous system and the endocrine system is actually found both in depression and in CVD. Neurohumoral dysfunctions lead to the alteration of blood supply to the heart and to the lowering of the variability of the heart rate, thus contributing to the progression of a CVD. However, in this case it cannot be demonstrated that depression is the cause of these neurohumoral alterations or that the latter represent the origin of the neurohumoral dysfunctions observed in CVDs. Depression and CVDs could therefore be two different manifestations, with different clinical expression times, of these alterations.

Another widely supported explanation points to a possible causal mechanism in inflammatory processes. One of the ways in which CVDs can be understood is in fact to consider them as chronic inflammations caused by damage to the vascular endothelium. In this hypothesis, depression could facilitate and thus increase the inflammatory response by altering the secretion and lowering the anti-inflammatory action of cortisol. In depressed patients a hypersecretion of cortisol is found together with the down-regulation of expression of gluco-corticoid receptors, a phenomenon which thus reduces the anti-inflammatory action of corticosteroids. Further evidence in support of this explanation is that in depression an increased level of cytokines, C-reactive protein and tumoral necrosis factors are observed, which are all risk markers for cardiovascular morbidity and mortality. The objection raised in connection with hypotheses regarding the causal relationship between depression, neurohumoral alterations and CVD is valid also in this type of explanation: depression and CVDs might just represent two different ways of clinical entities manifesting themselves in time. This observation is reinforced for example by the large body of research pointing to the presence of depressive symptoms as the side effects of cortisone and interferon therapy.

Emotions and CVDs: a web of causation model

At the current state of affairs a less problematic explanation would thus have to place the main focus on behavioural variables as the causal nexus between depressive conditions and CVDs and possibly pursue the analysis of possible relations among individual biological aspects of depression and CVD.

Depression brings with it alterations in varying degrees to eating and grooming habits, exercise, smoking and the use of substances with psychotropic effects and so on. These behavioural changes represent risk factors for CVD. At the same time, however, these behaviours contribute, on the one hand, to certain mental experiences and, on the other, to certain alterations of biological processes. Moreover, the psychological experience of depressive disorders is related to a series of transformations in the functioning of the nervous system, which then have an effect on all the control and organic regulation processes governed by the nervous system and ultimately on behaviour itself.

The relation between clinical expression of CVD and the depressive event is however the expression of an individual history of successive exposures to factors and elements able to cause alterations in the functioning of the cardiovascular system. However, this historical process is extremely complex in nature. It represents the effect of the two-fold, peculiar sequence of instances of exposure to pathogenic elements undergone by the individual, at both the somatic and the psychological level. The relation between clinical expression of the CVD and the depressive event is an expression both of the peculiar relationship between events and activating behaviours and the individual biological terrain – vulnerability -, the latter being determined at the genetic level and thus linked to a further historical level of the philogenetic path. On the other hand, in the course of life and thus during possible CVD progression, this given relation gradually becomes more and more modulated by the cognitive and behavioural levels, since the response to the events and stimuli having psychopathogenetic potential is modified through experience and its cognitive elaboration in both the somatic sphere and that of psychological experience. Furthermore, even before an acute event or an appreciable clinical sign is produced, the pathogenetic trajectories followed by the cardiovascular system may trigger or mediate some of the depressive symptoms, thus modifying emotional reactivity and therefore, in a circular fashion, all that is reproduced on the cardiovascular system as an activating element.

The idea of depression as a risk factor in CVD is thus linked to a series of processes laid out on different causal and temporal planes, which are characterized individually and in their mutual relations both by linear mechanisms and circular dynamics. Such complexity can only be penetrated through particular sections or individual perspectives, from a certain point of view, or for particular purposes, for the purpose of identifying a significant criterion and thus isolating a portion, a limited plan of the processes under way.

In this sense, the unshakeable complexity of this idea, in its generically accepted version, is such as to make it impossible to come up with any effective causal explanation or concrete clinical application. It rather represents a suggestive image, an appeal for research without being a scheme that can be translated into an investigation.

The idea of depression as a risk factor in CVDs is therefore an exemplification of the epistemological difficulties that arise when it is attempted to considered the “web of causation” notion of McMahon, Pugh and Ipsen (1960) as something more than a heuristic tool, a metaphor for expressing the idea that the causal processes of etiopathogenetic pathways are complex and interrelated (Krieger, 1994).

An emerging model

To some extent paradoxically, in recent years, investigations carried out at a high level of analysis and reduction have been clarifying the issues at stake more fully in the characterization of our understanding of the etiopathogenesis of diseases in the psychosocial approaches, holistic perspectives implicit in the idea of web of causation and of multifactoriality. By focusing on gene transcription processes, molecular biology and functional genomics these investigations have been identifying the fundamental mechanisms underlying the integration of the various physiological systems involved in emotional and individual adaptation processes, the causal network by which experience and individual history moulds the shape and functions of organisms, the circular nature and continuity of the interactions between mental events and somatic phenomena, the overlapping and concatenation of metabolic and plastic events by means of which the psychological dimension produces or contributes to the triggering or development of a morbid process.

On the other hand, the very acquisitions of molecular genetics are revealing the need to reflect on the cascade of biological phenomena related to emotions and to psychosocial dynamics that also converge on the regulation of gene expression in order to more fully understand and cope more effectively with all morbid conditions.

Internal and external stimuli such as stages of development, hormone and chemical mediator concentrations, stress, learning and social interaction affect the formation and behaviour of gene transcription factors, which is referred to by the term epigenetic regulation. In other words, just as a combination of genes shapes behaviour, including social behaviour, so behaviour and social factors – through their action on the organism and on the central nervous system – modify gene expression and thus the functions of the nerve cells, then modulating, again in a circular fashion, the behaviour and projection of the individual in the psychosocial dimension (Andreasen, 1997; Kandel, 1998; Gabbard, 2000).

The regulation of gene expression in nerve cells literally incorporates the various environmental and psychosocial factors. In the processes of gene transcription culture can thus become nature, without any mysterious leaps from the mental to the somatic. Thus, in effect, the evidence that has accumulated in recent years has actually done away with the very need to seek out the socalled “psycho/somatic transducer”. Psychosomatic transduction actually does not exist insofar as all the stimuli, whether environmental, physiological or psychosocial, have one and the same final target – gene regulation. At the same time, gene regulation represents the initial element in a cascade of behavioural and biological processes aimed at adapting the organism or which conversely are moving towards a possible gradual detachment from homeostasis and thus towards disease.

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