PATHOLOGY, COMPLEX SYSTEMS, AND RESONANCE

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A new vision of matter and life is emerging on the frontiers of science, particularly from the fields of quantum physics and mathematical theories and research, which have yet to be systematized. Organisms are seen as highly regulated, complex, dynamic systems which display a characteristic meta-stability around certain homeostatic levels. This meta-stability is the net result of continual oscillations, rhythms, networks, amplifications and feedback cycles. Living systems are "suspended" between order and chaos [Cramer, 1993; Mainzer, 1994; Bellavite *et al.*, 1995; Kauffman, 1995; Goldberger, 1996], they partake of these two fundamental characteristics of matter and exploit them in a manner designed to promote survival.

Linkage phenomena between oscillators, which generate synchronism and cooperativity, are of paramount importance in many physiological functions, particularly in the nervous system, but also in the cells regulating cardiac rhythm, in the cells secreting insulin in the pancreas, in the ciliated epithelia, and in the involuntary contractions of smooth muscle [Breithaupt, 1989; Engel *et al.*, 1992; Strogatz and Stewart, 1994]. The various rhythms in sleep, body temperature, antibody concentrations, potassium excretion, cortisol, growth hormone, etc., co-vary and interact. The subsystems of the organism that generate the fluctuating signals are in constant communication with each other; together they compose the organism. Because the organism is also in continuous communication with the variable environment, the subsystems appropriately respond when conditions change. It has been clearly shown that the interactive nature of signals operating in a rhythmic manner makes their perturbation likely [Weiner, 1992]. Transformed rhythms characterize many states of ill health and disease.

Order and chaos are to be found at all levels of homeostasis, from the molecule to the human mind. Living creatures are "open systems" far from equilibrium, subject to regulatory apparati which cannot necessarily be represented by linear equations, and thus are capable of perceiving minimal perturbations, particularly when they are predisposed to such sensitivity, possibly by the very pathological process itself. New evidence from electromagnetism studies lends support to the possibility that living systems respond to extremely weak magnetic fields, and particularly to specific frequencies and specific intensity ranges. At the same time, studies regarding the physics of water suggest, or at least do not rule out, the possibility that water itself may act as a store and vehicle for electromagnetic oscillations.

We cannot see how these new perspectives can fail to have an impact on the new orientations and trends in medicine. Medical theory, methodology and technology have always proceeded hand in hand with the general scientific theory and socio-economic situations of the times. In this context, also the physiopathological changes leading to disease can be considered under a wider perspective and this new integrated concept of disease can not fail to have an impact on the therapeutic approaches.

An integrated concept of disease

The behavior of any complex system, from single molecules to cells and to the whole body is dictated both by rigid structural or functional constraints and by other events or phenomena, which are endowed with a higher degree of variability and freedom. These latter are represented by all the

instances where the choice between two opposite or diverging states of the system is linked to minor and subtle variation of the conditions of the system itself or of its interactions with the environment. Far from equilibrium systems and "*bifurcation points*" are found at each level of organization of living organisms, from molecules to cells, to spatiotemporal oscillations of physiological variables [Nicolis and Prigogine, 1987]. Here we consider specifically these bifurcation points occurring in the dynamic progression of diseases.

The story and intimate nature of a pathological process present various phases or aspects which integrate one another in sequences in time and space. If we are referring to the majority of diseases, which are not exclusively of genetic origin, what usually appears as the "disease" according to the traditional diagnostic criterion is the *last phase*, consisting in precise biochemical and anatomical abnormalities.

Before this, however, there are at least three other phases: we have the very *first stage* in which an initial disorder, mostly nonapparent apart from a number of very indistinct symptoms or variations in very subtle parameters, makes the body susceptible to perturbations induced external agents. The subject cannot be defined as a sick person, but is more predisposed to falling sick than normal and has a tendency to fall sick. In this stage we could, for instance, include those who are subject to overwork (stress) or to an unbalanced diet, those who smoke, who are exposed to low doses of ionizing radiation, or who present particular genetic characteristics making them statistically "at risk" (heterozygous carriers of autosomal recessive diseases, a number of HLA groups, race, etc.). To what extent this disorder is "normal", in the sense that it is a simple reversible oscillation of a state of equilibrium, and to what extent it is "pathological", in the sense that it generates disease in the presence of other perturbing factors, is an extremely subtle and hazy issue. Some people support indeed the same situations, which may even be quite severe, as a normal burden of life, whereas they are regarded as serious diseases by others (often defined as imaginary or psychosomatic illnesses). Clearly, at this level the balance between normal and pathological is extremely precarious, and the subsequent course of the disease can come down on side or the other according to shifts in minor factors.

A second bifurcation is to be found in the *reactive phase* of homeostatic biological systems. These systems - particularly the inflammatory and immune systems, but also the liver detoxification systems, the hemostatic system, the production of a variety of hormones and cytokines, and so on are "two-faced", i.e. they bring about healing, but they may also cause damage because they can either attack or disorder the host itself. To what extent, in each individual case, the damage prevails over the restoration of the state of health or vice versa, depends on subtle variations in the behavior of the homeostatic system itself. In particular, the fate of the reaction depends on the "choice" that the system has to make between the "price to pay", in terms of toxicity and suffering, and the guarantee of success of the operation in terms of survival of the body. For instance, in the presence of a lesion of the surface of a blood vessel, the hemostatic system comes into action to block the risk of hemorrhage and to initiate repair (clotting, platelet aggregation, and increase in connective tissue and vascular musculature). Yet, through the same mechanisms a pathological event can occur: the hemostatic system entirely blocks the circulation of the blood in the vessel (thrombosis, atherosclerosis). What is it that "tips the scale" in favor of the positively directed action rather than the unnecessary and frankly pathological one? It is the complexity of the multiplicity of mechanisms involved. A "choice" of this type depends, in fact, both on the individual elements involved (receptors, concentration of mediators, presence of exogenous chemical substances) and on the type of coordination available, on a "centralized" control system that assesses the information coming in from the various regions and elements involved and regulates accordingly the various responses. Thus, at the level of such a bifurcation, the outcome of the reaction may

depend on an item of information that is *significant in terms of the coordination* of the reaction system or systems.

A third phase of the disease process, in which another very critical moment of decision presents itself, is when the reactive systems fail to cope with the situation and fail to rapidly restore the original state. At this point *adaptation* may set in, which is a semipermanent modification which, on the one hand, reduces the symptoms, but, on the other, may lead to various consequences, including deposition of toxins, hyperplasia, shifting of the receptor sensitivity threshold and biochemical and anatomical changes. These modifications "defer the problem" for lengthy periods or shift the pathological consequences from one organ to another. Adaptation makes it possible to *live with* the disease, but also constitutes, in a certain sense, a renunciation of complete healing. Also the choice between reaction and adaptation is very complex, being determined by a number of factors.

From a biophysical standpoint, disease may be regarded not only as a functional or molecularstructural abnormality, as in the classic view, but also (and not by way of contrast) as a disturbance of an entire network of electromagnetic communications. This network is based on long-range interactions between elements (molecules, nerve centers, organs, to mention but a few) which oscillate at frequencies which are coherent and specific and thus capable of resonance. This would be a *disturbance of internal oscillators and their communications*. Our knowledge is still too scanty to say whether or not these oscillators can be identified with certain nerve centers in particular (the ability to oscillate at characteristic frequencies is typical, though not exclusively so, of nerve centers) or with the collective behavior of nerve centers and/or other tissues or cells. With regard to cell to cell and intracellular communication, biophoton research suggests the existence of extensive coherent fields interaction in the visible range [Ho and Popp, 1993; Ho and Popp, 1994].

Chaos and fractals

In dynamic system that are far from thermal equilibrium, minimal variations in the conditions of the system (such as those induced even by a very small oscillatory resonance) may play a decisive role in the subsequent evolution of the system itself. The new concepts emerging from chaos and fractal studies can help to interpret and possibly dominate these complex events. In a variety of systems, the "butterfly effect" may be used to control chaos, on condition that the parameters to be controlled and changed are well known [see Firth, 1991; Shinbrot et al., 1993; Schiff et al., 1994; Moss, 1994]. The relationship between these new mathematical theories (and experiences) and homeopathy can hardly fail to be extremely close. In fact, the communication of information from the solute to the solvent and from highly diluted compounds to the disordered (ill) organism is nothing other than the transition from chaos to order, and the dilution/dynamization processes has been suggested to follow fractal dynamics observations [Garner and Hock, 1991; Shepperd, 1994]. The term "fractal" was coined in 1975 by B.B. Mandelbrot and gained extensive notoriety in scientific circles in the early '80s [Mandelbrot, 1982]. What is meant by this term are those mathematical or geometrical entities, which are endowed with a fractional dimension (from the Latin *fractus*, meaning "broken"). Many fractal figures have a repetitive configuration on changing scale, a sort of self-similarity between details and the general pattern.

Fractal shapes can be generated by the computer using algorithms (lists of instructions which specify the operations to be performed to solve a given problem) using mathematical functions which are suitably iterated (i.e. repeated for the desired number of times, each time using the result of the previous calculation as the basis for the following). By means of these operations, two- or three-dimensional figures with the following characteristics appear: a) an enormous variety of details of different shapes, b) the presence of subtle ramifications that can be pursued in the finest

detail, c) self-similarity, whereby, on magnifying part of the structure, details can be detected which repeat themselves on different scales of magnification.

In very complex mathematical structures such as the sets of Julia and Mandelbrot, extremely varied and fanciful details can be observed (circles, spirals, helixes, stars, various ramifications), within which other, different details can be discerned on magnifying the image. Within some of these particular images one finds, surprisingly, "mini-sets" very similar to the macroscopic ones from which they originated. In the close-up detail we rediscover an image which appeared to have been lost in the variety of details and ramifications. By increasing the number of iterations, a better definition of the fractal image is obtained.

Fractal patterns are easily found in chaotic systems, representing elements of regularity. In several chaotic functions, on continuing the iterations and further increasing the coefficient value, after the periods of chaos periods of order may reappear, followed by new zones of chaos and then order. There is thus a "recurrent regularity" [Hofstadter, 1991] in successive generations of transitions from chaos to order, with the reappearance of single solutions or regular oscillations which undergo cascade duplication on increasing the coefficient value. This recurrent regularity creates figures with regularity and irregularity "bands" which are repeated and resemble one another, with a fractal type pattern.

Mandelbrot and, more recently, other investigators have observed that many apparently disorderly natural objects possess this fractal property. This is having a very considerable impact in the scientific world. Despite the fact that these forms were discovered by a mathematician and are still studied mainly by mathematicians and computer scientists, fractals are useful instruments for describing a whole variety of physical phenomena and natural forms. One example of a fractal form is a tree, whose trunk is divided into branches; the branches themselves then divide into smaller branches, twigs, and so on until you get to the leaves, which in turn present veins with multiple subdivisions. Other examples of natural fractals are clearly illustrated by certain flowers and snowflakes, as well as by noncrystalline molecular aggregates, viscous ramifications in unmiscible fluids, corals, electrical discharges such as lightning, the ramifications of the airways and blood vessels, the dendrites of the neurons, the Purkinje system conducting electrical signals in the heart, and the folds of the intestinal mucosa [Nonnemacher et al., 1994; Elbert et al., 1994; Goldberger, 1996]. It has also been demonstrated that, in many different physical situations, particles floating on the surface of an irregularly moving fluid display a fractal arrangement [Sommerer and Ott, 1993]. Fractal geometry thus refers to some form of conditioned randomness, so much so, indeed, that some people talk about a determinism of chaos (deterministic chaos).

Various experiments have suggested that the biological activity of homeopathic dilutions does not diminish or increase regularly with increasing dilutions, but follows a "pseudosinusoidal" trend, with peaks of activity and troughs of inactivity. The most evident example is in the famous experiment performed by Benveniste's research team [Davenas *et al.*, 1988], but similar trends have also been reported by others [Poitevin *et al.*, 1988; Boiron and Belon, 1990; Sainte-Laudy *et al.*, 1993; Sainte-Laudy and Belon 1996; Carmine *et al.*, 1996]. I the Davenas's paper, it can be seen that the activity causing basophil degranulation is present at the 9 log dilution (corresponding by and large to the homeopathic 9x dilution), and then drops to a minimum level at the 11 log dilution, only to pick up again and rise to a peak at the 15 log dilution, thereafter descending again, and so on. The recurrence pattern of the peaks is not regular, but chaotic and unpredictable, but at the same time it must be admitted that this recurrence exists, i.e. that the effective information re-presents itself after a number of log dilutions. According to the logic of current chemical reasoning, such a trend appears thoroughly and quite definitely absurd, but in the light of new knowledge of chaotic

phenomena and the nonlinearity of many biological mechanisms perhaps some kind of underlying logic can be traced.

If we are prepared to give credence to such paradoxical results (note that most of the above-reported experimental data are still awaiting unequivocal confirmation by independent laboratories), one question inevitably springs to mind: how can information disappear and then reappear? Where did the information go in the mean time, while the inactive dilutions were being done, between one peak and another? To answer this question the fractal "line of reasoning" may come in handy. In fact, if we are to take the results of the experiments seriously, we have to admit that the information of the compound dissolved is not completely "dissipated" in the course of the successive dilutions, even when the dilutions are inactive. Evidently there should exists some mechanism of transmission and storage of the information in the course of the dilutions such that the next dilution following an active dilution may give rise to a form (or vibrational frequency) differing from the previous one (and for this reason inactive), but capable, after a few steps of further diversification, of causing the original (active) information to "reappear". The dilutions, then, would not produce a loss of information (increased entropy), but only a change and variety of forms, which in turn may regenerate the starting form. Such behavior is reminiscent of what we one can see apropos of the mathematical iterations that generate fractals [Cramer, 1993; Bellavite et al., 1995; Bellavite and Signorini, 1995]. This, then, would be a phenomenon similar to the "recurrent regularity", typical of chaotic systems.

The hypothesis has been advanced [Garner and Hock, 1991] that the successive dilutions and dynamizations performed in the preparation of a homeopathic remedy introduce an element of *information gain*, as is observed in the Mandelbrot sets with successive iterations. It is suggested that low dilutions (few iterations) produce poor definition of details and carry rough and imprecise information, whereas high dilutions (many iterations) are characterized by better definition of details, as can be seen in the profiles of the Mandelbrot sets. If the dilutions/iterations are few, the image is "blurred", whereas, if they are repeated many times, the image is precise and, surprisingly, "reappears", i.e. it is reproduced in detail in subsets and in subsets of subsets. The image of a certain structure (in the case of homeopathy, the mother tincture) reappears in a "similar" form in successive dilutions, practically to infinity.

Such a phenomenon may basically be responsible for the fact that in classic homeopathy the high dilutions are regarded as more specific and profound in their therapeutic effect if there is perfect matching of the symptoms of the patient and the remedy, i.e. if the "*details*" of the analogy have emerged clearly from the homeopathic history-taking. In practice, the fewer the symptoms shared by the patient and the remedy, the lower will be the dilutions used; the more symptoms they have in common, the higher will be the dilutions prescribed.

We must acknowledge that this discussion is highly speculative and hypothetical. Our aim in referring to these aspects is to stress how a scientific approach to homeopathy in future will require the joint contribution of several disciplines, including mathematics, geometry and computer sciences. In general terms, the suggestions we are making here emphasize the fact that those researchers who are prepared to engage in the study of the unsolved, complex problems of biology and physics (including the study of homeopathic high dilutions) must begin to include the dimensions of chaos and the fractals in their conceptual, and possibly also in their experimental armamentarium.

Resonance and the homeopathic approach

We shall attempt here to summarize a few points with the aim to present a frame of reference for putting homeopathy into rational and experimentally viable perspective. Of course, the following points should be underlined: a) hypotheses are essential to the evolution of knowledge, but one has to guard against presenting them as certainties, b) the following discussion is based on the assumption that highly diluted remedies prepared according to the homeopathic methods are endowed with specific information of biophysical nature (superradiance, water clusters, isotopic lattices, and so on), a highly controversial issue that is discussed in other sections of this book, c) here we restrict our consideration to the possible mechanism of interaction between high-dilution homeopathic approach and d) a biophysical perspective does not exclude that many effects of low-and ultra-low doses of drugs are due to "conventional" molecular interactions. The hypotheses set forth here also refer to theories proposed by other authors [Vithoulkas, 1980; Callinan, 1986; Rubik, 1990; Popp, 1990; Ullman, 1991; Bernal, 1993; Schulte and Endler, 1994; Poitevin, 1995; Schiff, 1995; Jonas and Jacobs, 1996].

If the disease process involves a disturbance of oscillation frequencies - and of the communications associated with them - it should be brought back to a state of equilibrium by means of *syntonization or tuning, i.e. by means of a change in frequency imposed by interaction with another oscillator.* According to this notion, the homeopathic remedy might act in the patient as an external guide frequency.

The phenomenon of resonance is well known in physics, where it occurs in many fields: acoustics, mechanics, and electromagnetism, as well as nuclear physics. By virtue of this phenomenon, a system which is characterized by its own oscillation frequency can enter into vibration if stimulated (subjected to sound waves, electromagnetic waves, or mechanical vibrations according to the nature of the system) by frequencies close to those peculiar to the system itself. If the system is already oscillating, the resonance may greatly increase the amplitude of the oscillation, whenever the waves overlap, while the opposite may also occur, namely an arrest of oscillation, if the interaction is between two waves of the same frequency but opposite in phase. Of course, biological systems are characterized by very complex oscillatory frequencies, in keeping with the complexity of their components. For resonance phenomena to occur, the frequencies do not need to overlap exactly; it is enough for there to be matching of one or more harmonics (harmonics are the simplest components into which periodic functions produced by their overlap can be broken down). The harmonics of a given periodic system all have frequencies, which are multiples of the fundamental frequency, called the first harmonic.

Resonance, then, is a way whereby information is transmitted between two *similar* systems (as regards vibrational or harmonic frequencies) without structural modifications and without the passage of matter. Interestingly, it has been suggested [Tsong, 1992] that resonance may transduce information between an oscillating, low-level, electromagnetic field and molecular sub-domains of cell enzymes. This type of interaction should lower the activation barrier of the rate-limiting step of enzymatic reactions, thus increasing the overall catalytic activity.

On this basis, a hypothetical model of the possible action mechanism of homeopathic drugs can be advanced. A potentized homeopathic drug might be regarded as a small amount of matter containing elements oscillating in phase (coherently), capable of transmitting these oscillatory frequencies, via a process of resonance, to biological fluids (in turn mostly made up of water), but also to complex "metastable" structures. These structures (macromolecules, a-helixes, membranes, filamentous structures, receptors) are subject to nonlinear behavior patterns and capable in turn of oscillating. There would thus be the possibility of a resonance link between drug frequencies and oscillators present in the living organism perturbed by the disease.

Even signals which are extremely small, but which are endowed with highly specific information and are capable of resounding in unison with the recipient system, could act as regulators, if it is admitted that the dys-regulated system or systems are in a state of precarious equilibrium, near to the bifurcation point, where the choice whether to move in one direction or the other is related to minimal fluctuations on the border between order and chaos. It has been suggested [Torres and Guadalupe, 1996] that *stochastic resonance* is an important mechanism by which very small signals can be amplified and emerge from random noise of physiological oscillations, thus accounting for homeopathic phenomena.

Homeopathy should therefore act on the initial "decision-taking" levels of the body's repair and defense systems. When a disease reaches the stage where gross biochemical and anatomical consequences of the disease process are present, we are entering a field in which there would appear to be a much greater indication for the use of strong therapies such as surgery, replacement therapy, or the use of drugs at high doses. However, even here a possible contribution of homeopathy should not be ruled out (provided at least some of the homeostatic control systems can intervene).

Even as referring to the diagnostic sphere, it is clear that the more a disease claims attention in terms of biochemical and anatomical abnormalities, logically the greater will be the tendency to resort to laboratory investigations and diagnostic imaging techniques, whereas a homeopathic "diagnostic work-up" aimed at capturing the subtle differences in personality and symptoms between one patient and another would make very little sense. Conversely, however, conventional diagnostic means can achieve very little within the framework of the initial subtle changes in complex homeostatic equilibria, or, even if they manage to pinpoint individual variations in biochemical or functional parameters, yield no criteria for "reconstructing" the picture as a whole and thus for implementing a complete therapy. Depending upon the level at which they operate, different methodologies of both diagnostic and therapeutic type are adopted. Homeopathy is a "probe" into complex systems. Despite all the limitations related to difficulties in rendering the homeopathic approach objective, it is clear that it entails an attempt to "explore" the patient's medical history at the level of the neuroendocrine system and thus to calibrate some form of therapeutic intervention at this level, too. Homeopathy and homotoxicology regard inflammation as a "symptom" (i.e. as a signal or message) and not as a "disease", and they regard this symptom as the expression of an alteration of the relationship between subject and environment and/or between systems in the same subject. In the light of what we have said about the complexity of living systems, these concepts appear to be of great topical interest, quite apart from the difficulties encountered in rationalizing and perhaps even in demonstrating everything that homeopathy claims.

Homeopathy used with ultra-diluted drugs is thus a tentative approach to the bioenergetic regulation of the human body, utilizing a physical-biochemical interface due to the extreme sensitivity of biological systems to this type of regulation. The potential strength of the method consists in the fact that it attempts to achieve the maximum possible degree of *specificity* of the exogenous regulatory intervention. As stated earlier, the effective doses will be lower, the more specific the stimulus and the more sensitive the target system. If we admit that information is contained in "metamolecular" form in the homeopathic remedy, this information may also act in a metamolecular manner in the bioenergetic target system.

How can the maximum specificity of information be achieved, if we know so little about such bioenergetic systems? The answer is in the main principle of homeopathic tradition, the "*law of similars*". This fundamental principle, based, as it is, essentially on the observation of *effects* (i.e. on comparison of the effects of the drug with those of the disease), is in a certain sense independent of any knowledge of the mechanism which causes the effects and thus also applies to the metamolecular level, once we have admitted the existence of the latter. Further details regarding

this important point of homeopathic theory can be found in other works of the Authors [Bellavite and Signorini, 1995; Bellavite *et al.*, 1997a; Bellavite *et al.*, 1997b].

Homeopathic reasoning is based more on analogy than on inductive thinking. The use of analogy (i.e., identification of similarity) is justified on theoretical grounds on the basis of the fact that the various elements of reality are interlinked, because they all derive from the same evolutionary process; in nature, we find the result of a growth of items of information which are always kept "in contact" with one another. Animals have always lived in contact with vegetable substances and minerals, and it is for this reason that a molecule contained in a flower may be "similar" to molecules contained in the animal, and there may therefore be a transfer of information. Information is transferred only between similars, or between opposites, or in any event between elements that are capable of interacting as a result of affinity of structure or of vibrational frequencies (harmony, resonance, and coherence). Analogical reasoning consists in grasping this basic principle.

The "secret" of homeopathy lies in the meticulous gathering of information both in the proving phase and in the homeopathic history-taking phase. This information can come from the hidden depths of the homeostatic regulatory system under investigation, but is still information. In the homeopathic method it is used directly in the therapeutic intervention, trusting in the fact that the body will know how to receive, decode and utilize this informational input for the purposes of restoring the lost equilibrium.

Another "secret" of homeopathy is that it deals with the human being as a whole, devoting the maximum attention to symptoms of a psychological type and to those peculiar to each individual subject (individualization). In this way, it achieves a very substantial measure of specificity, inasmuch as it is now well known that the response to drugs can vary on the basis of the characteristics of the individual user.

Finally, we have to mention the fact that we are witnessing a convergence of the homeopathic and the acupuncture approaches, particularly as regards Voll's electroacupunture (EAV) and related techniques. Voll's electroacupuncture is a diagnostic and therapeutic method, based on the bioresonance phenomena, which combines the basic principles of Chinese acupuncture and the possibilities of modern electronics. With the aid of these techniques, the ability to gather information regarding the disturbances of bioelectromagnetic homeostasis of the individual is gaining in strength and depth. A series of studies appear to suggest [Kroy, 1989; Fuller-Royal, 1991; van Wijk and Wiegant, 1994; Lednyiczky *et al.*, 1997; see also Bellavite and Signorini, 1995], that the sensitivity of a given patient to a given compound (either toxic or beneficial) can be detected by measuring the disturbances of electrical currents on the acupuncture points. If this will prove true and reproducible, we would thus have another key to penetrating the "sanctuary" of biological and pathological information. Gathering information, such as knowing, for instance, whether a certain patient is allergic to or intolerant of a certain compound, or knowing whether a certain drug restores the balance or produces electrical dysequilibrium would be an undeniable step forward from the point of view of diagnosis and therapy.

An interpretation of homeopathy such as that presented here reconciles the "integrated" view, which considers the complexity of the human being in all his or her components, with the "reductionist" view, which considers the single organ, cell, or molecule. In fact, there cannot be a contrast between the whole and the fragment which this whole contains and therefore various medical approaches should be utilized according to which level of integration and which physiopathological mechanism(s) is the object of treatment.

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