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EC NEUROLOGY
Review Article

Pathological Expression and Circuits in Addiction and Mood Disorders: Informational Relation with the Brain and Info-Therapy

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Received: June 07, 2021; **Published:** July 22, 2021

Abstract

Introduction: The relation between mind and body, particularly between pathological expression and brain supporting processes in addiction and mood disorders is not yet well understood, either in neurosciences and nor in neurology.

Aim: The aim of this paper is to contribute to a better understanding of the addiction and mood disorders in terms of informational processes in the brain and to propose supporting palliative/helping/preventive info-therapy for relapse avoidance.

Analysis of the pathological expression and circuits in addiction and mood disorders: It is shown that the pathological expression of addiction to alcohol/drugs/nicotine and mood - anxiety, depression, bipolar and schizophrenia disorders are related mainly to the excessive/insufficient stimulatory/inhibitory neurotransmission and to the impairment of some fundamental balancing YES/NO circuits including the limbic system, specifically amygdala, caudate-putamen, nucleus accumbens and hippocampus connected to prefrontal cortex, the area of judgment. The potential involvement of mitochondria in the energy imbalance and of the growth factor in mood disorders are also highlighted, and the importance of a fine-tuned/precise diagnostic revealed by the blood biomarker analysis is also pointed out. The main risk factor is associated with the genetic inheritance, but the influence of the external factors is also important.

Informational relation with the brain and info-therapy: The analysis allows to discuss the addiction and mood disorder from informational perspective, in correlation with the informational structure of the brain, consisting in seven main distinct functions supported by various zones, defined as: CASI (the centre of acquisition and storing of information), CDC (the centre of decision and command), IES (info-emotional system), MIS (the maintenance informational system), GTS (the genetic transmission system), IGG (info-genetic generator), IC (info-connection). In terms of information, the relation of addiction and mood disorders with the brain can be synthetized as following: (A) the dysfunctionality of the brain is mainly due to the imbalance of IES (stimulatory) vs. CASI/CDC (inhibitory) YES/NO role and of the stimulant/inhibitive neurotransmitters; (B) the susceptibility/vulnerability of addiction/mood disorders are mainly related with IGG; (C) the external stress and life conditions as informational stimuli/factors are related by epigenetic mechanisms, which determine the integration of information in genetic system of the brain.

Conclusion: The control of information in a selective way is a basis for a prevention/palliative info-therapy process, activating the involvement of the epigenetic mechanism to substitute the obsolete older stereotype patterned/"engraved" habits and the associated pathological expression.

Keywords: *Pathological Expression; Mind Operability; Addiction; Mood Disorders; Susceptibility/Vulnerability; Prefrontal Cortex; Amygdala/Limbic System; Informational System; Epigenetic Info-Integration; Info-Therapy*

Introduction

The study of the mental disorders are strongly correlated with the understanding of the mind-body relation, specifically of the functions of the nervous system and brain management of such functions. However, this issue still remained a not clarified problem, both from philosophic point of view and from that of the neuroscience, because the body and mind are regarded traditionally as two distinct entities since many centuries ago [1]. One of the reason of such a situation is a consequence of the still limitative possibilities of investigation, which should be able to focus on the low-level scale of interaction, to observe the molecular and sub-molecular processes and their effect on the macro-level scale. Moreover, the scarce application of new concepts like that of information in the neuroscience sciences is still a brake for the understanding of the relation between the material substrate and the mind properties.

Within such a panoramic scene, the approach of understanding, diagnosis and treatment of addiction and mood diseases (anxiety, depression, bipolar personality (0.5 - 1.5% of population)), which affect 1 from 4 persons during the life, co-morbid with other psychiatric disorders like schizophrenia [2,3], became already a social problem in the advanced societies, where the life stressing tasks overpasses the natural resilience capacity of the human organism [4-6], so contributing solutions are urgently required. The frequency of such disorders in the population is moreover enlarged owed to stigma and lack of objective tests, so some potential patients are not registered or are underdiagnosed and/or sub-optimally treated, and they may culminate in some cases with violence or aggressive behaviour [3]. Therefore, the society should respond to each case of frequent abnormal symptoms with obligatory examination, diagnostic and treatment of the mental health to prevent the adverse antisocial behaviour [4,7].

In our informational era, based on informational large-scale communication, driven by the high tech development of microelectronic circuits and systems, the advances in the non-invasive and non-destructive analysis of the living tissues and systems, specifically the frequency magnetic resonance imaging (fMRI) and its variants, have been allowed significant results, especially in the investigation of the brain dynamic processes and correlation with the behaviour. High tech analyses methods and techniques like convergent functional genomics (CFG) [8] and the expanded variant including a Bayesian analysis of data [9] allowed also to correlate some mental diseases and their effects with the micro-scale activity in the brain, on the basis of the detection of specific biomarkers in blood [2,3].

However, no systematic approach of the mental processes both at the global and low-level scale from informational perspective were reported. In order to cover this gap, sustained endeavours were addressed to this issue recently, leading to remarkable results in the understanding of the nature of consciousness [10] and of associated phenomena like near-death experiences (NDEs) [11], extrasensorial detection [12], religious and mystic experiences (RMEs) [13], cognitive properties of mind, attitude and its evaluation [14,15], equilibrium and healthy life mechanisms [4], mental aggressive behaviour [7], multi-task music-based optimization therapy for neurorehabilitation [16], to name only a few of them.

As a continuation of the informational line in the approach of the mental processes, the aim of this paper is to investigate the addiction and mood diseases from informational perspective, on the basis of the successful results mentioned above in the understanding of the brain and mind operability.

Analysis of addiction and mood disorders from pathological perspective

According to statistical data in USA, 10 - 13% of population is affected by alcohol addiction [2], and the genetic factors contribute with (40 - 70)% of the risk to possible addiction, the studies revealing about 600 genes involved in such a possible risk [17]. It was deduced that gene expression in the brain cells are changed under three main forms: (i) the alteration of gene function; (ii) the variation of the inherited patterns of gene expression; (iii) the alteration responses in gene expression to alcohol exposure [17]. Such studies mainly concluded that the cellular receptors and neurotransmitters, specially GABAergic, and glutamatergic neurotransmitter systems [18], serotonin and do-

pamine and their corresponding machinery are deeply implicated. The addiction has a deep organic origin at the cell level: by adaptation reasons, the cells produce specific receptors on their surface to receive the drug, if this habit is repeated sufficiently. Therefore, in the lack of the drug, the cells will signal the necessity of this specific drug, which will be actually detected as a addicted necessity.

In a recent study there are reported 26 top gene expression candidates as blood biomarker of mood diseases in blood, referring to circadian abnormalities, neurotrophic, and cell differentiation function, along with serotonergic and glutamatergic signalling, supporting a view of mood as be reflected in reactivity (via serotonin and stress response), activity (by energy and growth processes) and connectivity (by calcium intracellular signalling) [3]. These findings resulted from the identification of changes in the peripheral gene expression induced by the brain activities, probably due to the fact that the brain and immune system have developmental commonalities [3]. Indeed, the main parts of the immune system include the bone marrow and thymus [19], which are actually managed by hypophysis and hypothalamus, as immunologic axis in the brain.

The key specific brain regions related with the gene expression in alcoholism are the frontal cortex, amygdala, caudate-putamen, nucleus accumbens and hippocampus, marked in red colour in the right upper side of figure 1. Studies carried out permitted the identification of high probability candidate genes, pathways and mechanisms for alcoholism, showing that the alcohol has multiple effects on various systems, which may explain the diversity of neuropsychiatric/medical pathology in alcoholism [2]. The main findings of such studies on biomarkers in blood for alcoholism and cocaine addiction show that these are related with myocardial fibrosis, cardiomyopathy, hypertension, coronary artery disease and stroke, increased risk for cancers by intervention in iron-heme metabolism, many correlated with the change of the cell adhesion signalling (cell communication). Some of them overlap on bipolar disorder and schizophrenia, because alcoholism can lead to psychotic, mood and anxiety symptoms, and have permanent deleterious effects on the brain infrastructure.

The anxiety is correlated especially with the overreaction of amygdala, which memorizes the alarm signals/frightening events and associated/induced emotional experiences, together with hippocampus. Amygdala appears therefore as a central zone of the mood type expressions, including fear and aggression, whereas hippocampus is an inhibitor over the hypothalamus by means of a negative feedback reaction including hypophysis (hormone-controlling) gland. In opposition with amygdala, the prefrontal cortex, which is the headquarter of short-term memory but also of the judgment, planning and decision making (predicting consequences, moderating social behaviour), suppresses the emotional impulses, controls and extinguishes the stress, fear response and mood states in general. As fear is one of the ancestral impulse of the animals, so of human, a zone in the brain stem called locus coeruleus seems to be involved in fear symptoms [20]. Therefore, the mood and anxiety disorders seems to be rather a result of the disruption of the centres/circuits of the emotional system than one due to the judgement/cognitive system. In relation also with above commented on the hormonal and neurotransmitter activities, it is to be noted an Increased activity of the excitatory glutamate-type signalling and an inhibitory GABA-type transmission signalling in the involved emotional brain regions. Genetic inherited and epigenetic acquired participation are also contributing risk and vulnerability factors of mood disorders, particularly of anxiety and depression, with individual clinical expression as a combined result. Panic and post-traumatic disorders are variants of the anxiety, each of them manifested with different degrees of intensity and individual specific behaviour.

Depression, with the deep grave form, which is the major depression disorder (MDD) is characterized by persistent low mood accompanied by cognitive dysfunction, physical symptoms, and impaired social function, leading sometimes to suicide [21]. An improved diagnostic is now available, by identification of 12 genes expression biomarkers related to MDD in blood [3].

Magnetic resonance imaging (MRI) has been able to reveal pathological changes in brain anatomy, showing that the grey and white matter are altered in MDD in frontal lobe, hippocampus, temporal lobe, thalamus, striatum, and amygdala, including frontal-subcortical circuit and the reward circuit. This circuit consist fundamentally in cortical-basal ganglia network, which leads adaptive behaviours and good decision making, and in the prefrontal cortex which exploits the basal ganglia for additional processing of rewards to effectively

modulate learning and action plans. This circuit includes also anterior cingulate cortex and midbrain dopamine neurons, with neuromodulatory role: executive functions, motor control, motivation, arousal, reinforcement and reward, including lactation, sexual gratification and nausea [21-23]. The thalamus is considered a sensory information node that controls emotion, memory, and arousal [22] Together, the connections among these areas form a complex neural network that underlies incentive-based learning [21].

The bipolar disorder (BD) changes the operability of the brain, much frequently as the age advances [24], having a direct and evident impact on the cognitive functions. The pathological expression of BD consists in extreme opposite manifestations of mood and energy, alternating from exciting manic highs to depressive mood minima, expressed by rapid talks/racing thoughts and non-controlled reckless, restless, paranoid, hyperactive, and impulsive behaviour [25]. The clinical criteria include distractibility, inappropriate speech and increased goal-directed behaviour, with potential painful consequences (in mania episodes) and lack of concentration, difficulty making decisions, motor slowing and changes in memory (during the depression stage) [26].

Alcohol consumption aggravates the symptoms, triggers the crises and diminishes the chance of a healing process. During a manic episode, extremely high energy and irritability is manifested. Taking into account that two-thirds of people with bipolar disorder originate from family with a relative with either bipolar or major depression, it is considered that the heritability factor is one of the most important cause of a major risk, between 4-6 higher than a non-risky person. The bipolar disorder is related mainly with hippocampus (long-term memory/emotional response), determining racing thoughts and paranoia, frontal lobe (judgement and self-control), which can suffer structural modifications, showing a smaller volume that the normal brain. The decrease of the grey matter observed in the bipolar disorder [27,28] determines an abnormal processing of information, thoughts and feelings, of impulses and senses control, motor skills (reaction time), balance, speech, drawing and writing, leading to impulsive, careless and thoughtless actions, to feelings of sluggishness and frustration, as well to trouble in doing simple tasks.

The amygdala is the central area with dysfunctions in BD [26], involved in animals in "fight-or-flight" responses. In humans (Figure 1), amygdala acts as emotional modulator, which sets an emotional expression marking the rest of the brain functionality and determines also the modulation of other circuits like that of cerebellum (found in the immediate right side of amygdala), involved in motor functioning/error-detection, in the motor control and social-emotional responses. The hypothalamus, as a part of the limbic system, is located beneath the cerebellum and is connected to the autonomic nervous system with role in the generation of internal feelings of happiness or sadness. Amygdala is also connected to the anterior cingulate cortex, which links the emotional brain with the cognitive brain, determining the emotional/cognitive brain activity as a YES/NO type balance [4], so that when one is increased, the other is decreased.

Neurotransmitters imbalance in the brain contributes/determines also the bipolar symptoms and dysregulation of mood as follows [25,29]: (i) noradrenaline increases alertness, arousal, and speeds up of the reaction time, with a role in the ability to concentrate; (ii) high norepinephrine levels can trigger manic episodes of false sense of superiority and invincibility, impulsivity, racing thoughts, touchy sensations, whereas low levels of norepinephrine can determine depressive episodes of lethargy, non-ability to focus/concentrate, anxiety/depression, no interest to connect with reality; (iii) serotonin regulates happiness, anxiety and mood, sleep patterns and sociability depending on its level, i.e. the high level determines restless, anxiety, irritability, hyperactivity, whereas the low level determines low-self-esteem and feeling worthless, insomnia, poor appetite, depression. Hormones play also a major role in bipolar disorder, related with the thyroid gland, associated with hypothyroidism or an underactive thyroid. As it was recently shown, the bipolar disease could be diagnosed by blood biomarkers, a method which permits a differential prognosis of this type of disease compared with mania or depression in MD [3].

The energy imbalance can be potentially explained by the dysfunction of mitochondria, the organelles dedicated to produce energy in cells, but the relation between bipolar and mitochondria disease is still uncertain [30].

External factors plays a role in bipolar disorder, especially for the predisposed persons, more frequently in woman that in men: extreme (positive or negative) stress concerning both addicting (drugs, sex abuse) or dramatic situations in family (the loss of the loved

being), overuse or practise of too many disordered activities, disturbance of sleep, abuse of stimuli and substances (alcohol, caffeine, nicotine). However, with proper diagnosis, treatment and therapy, it is possible to moderate/eliminate bipolar crises and episodes, the relapse avoidance, and to lead a fulfilling/happy life with bipolar disorder.

Schizophrenia is related mainly with the same biochemistry (excessive release of dopamine) and area of the brain, i.e. limbic/meso-limbic system (a network of dopaminergic neurons consisting of the nucleus accumbens, amygdala, and olfactory tubercle, with input from the ventral tegmental area related to emotion, reward, and substance abuse), prefrontal cortex (connected to basal ganglia) and hippocampus like other mood disorders [31], so bipolar and schizophrenia overlap from this point of view. However, schizophrenia affects moreover the ability to perceive reality, including false beliefs and hallucinations/deliria, sight of not present objects/persons, hearing voices, disorganized thoughts and communication (thinking that creates strange narratives about reality), emotional instability, persecution mania (somebody would want to hurt the affected person at present or in the future), equally for men and woman. This abnormal mood can be manifested mainly at the persons with genetic vulnerability and/or affected by stress events and infections [32,33], especially during the childhood.

Overall, in mood diseases such as bipolar (manic-depressive) illness, there is a loosened connection between the reality and a right operability of the brain in the affected brain zones [34]. Mania (elevated mood) and depression (low mood) operate as two parts of a whole, like a YES/NO (Bit-type) bipolar system. An interesting observation shows that under the environmental stimulation, the growth fibroblast factor seems to increase from low to high level, as it is visible not only in the exercised muscles, but also in the brain volume and morphology [34]. Therefore, as the muscles shrink when they are unused, as well the parts of the brain involved in mood disorders (hippocampus, prefrontal cortex) appears to be shrined, so the same growth factors is used in both brain and muscle. This is because evolution uses the same building blocks that are already patented by nature [35]. This correlation was certified by corresponding biomarkers found in the peripheral blood [3].

Informational relations with the brain and info-therapy

From the above analysis we can conclude the following: (i) the addiction and mood disorders are mainly due to a dysfunction of the limbic system (especially amygdala and hippocampus), which can be hyper or hypo active, combined with a dysfunction/impairment of prefrontal cortex which cannot balance/moderate the signals from amygdala received via anterior cingulate cortex; (ii) an important role in such dysfunctions is played by the balance between the concentration of the stimulating and inhibitory neurotransmitters in the brain, which develop surface cellular receptors and create/stimulate the addiction requirements; (iii) a factor of risk is genetic susceptibility, but the stress type conditions and the life behaviour is also a triggering factor of stereotype expression; (iv) the brain matter reacts like the muscles to training, increasing proportionally corresponding mass by the intervention of the growth factor; (vi) the recent discovery of specific biomarkers in the peripheral blood can lead to a suitable discrimination between the mood type disorders, allowing a preventive detection, so avoidance of severe crises by a suitable intervention/treatment/therapy. In the following discussion we focus on the informational functionality of the brain to deduce the preventive and palliative measures/therapy for relapse avoidance and for a wellness life of the predisposed persons.

In figure 1 there are represented schematically the components of the informational system managed by the brain in addiction/mood disorders (right side), compared with the healthy system shown in the left side of the figure.

As per above analysis, the connection with reality in addiction/mood disorders is abnormal and the operability of the brain is dysfunctional. To better understand the functionality of the brain from informational perspective, we have to understand first of all the concept of information and distinguish various sorts of information in the brain and nervous system [35]. In a classical current view, information is regarded as a novelty within a communication process. This is somehow correct, even if we refer to the theory of information, taking as a reference an electronic communications equipment [36]. However, especially within a multicomponent system like human body,

information does exist under an intrinsic/"embodied"/integrated state. Indeed, when two or more micro-components interact to form a more complex (structured) system, a quantity of information is "embodied" inside, participating actively to the system structuration. This information can be released when this system is decomposed/deconstructed in two or more components, possibly triggering another cascade of informational subsequent reactions/processes. Such a situation is common in living systems [1,35] and this can be explicitly expressed taking into account an interaction of a simplest system composed by the components C1 and C2 as a balancing reaction of the form: (C1+C2)+I ⍰C1C2(I), where "I" is information participating/activating this reaction and (I) embodied (hidden) information in the structured form.

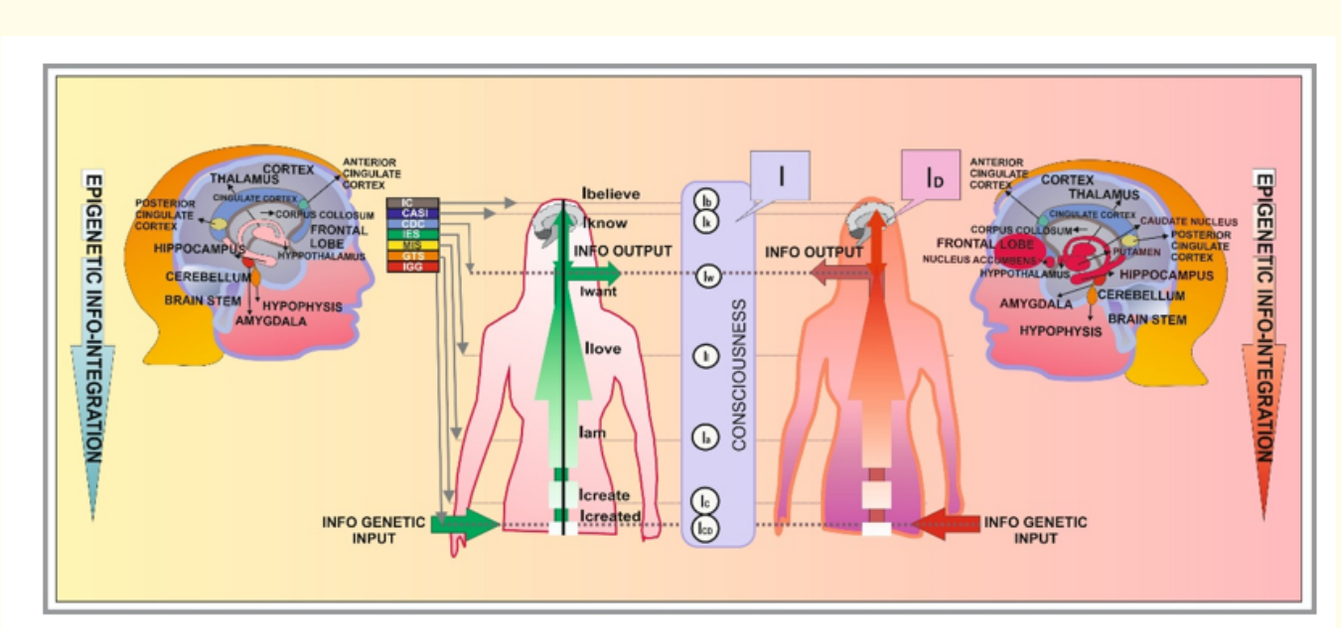

Figure 1: *Schematic representation of the informational system of the human body and of the cognitive projections in the mind under normal (I - central side) and abnormal disease (ID - right side) conditions; the relation between the info output behaviour and the info-integration/info-genetic input circuits are marked by corresponding arrows.*

A chain of such interactions on a specific informational pathway/circuit in the brain defines a function/functionality manifested/detected as information both provided by the inner and external environment and detected by the informational sensors. The function/functionality of more such micro-pathways/circuits is inter-correlated in the brain, both to interpret the perceived and to express the decisional response. The dysfunction of some circuits modulates therefore in a negative way the entire macro-level response, both at reception/interpretation info-input and at the info-output level, expressed by attitude. To be more explicit, the informational system of the human body could be described by seven informational components/modules, each of them with distinct and specific functions/functionality (Figure 1 left side): (1) CASI is the centre of acquisition and storing of information (represented by arrows to CASI on the human profile in figure 1), connected to external and internal sensors and detected in mind as memory (Iknow cognition centre), supported mainly by prefrontal cortex, hippocampus and cerebellum for acquired info-motor abilities; (2) CDC - the centre of decision and command, corresponding to Iwant/attitude in mind, is connected with the cortex in general, but with the prefrontal cortex in special for judgment processes, so the interrelation CASI<=>CDC is very close; (3) IES is the info-emotional system, composed by limbic system and the surrounding components (nucleus accumbens, putamen, caudate nucleus), as represented in red colours in figure 1 right side, and detected in mind/consciousness as the cognitive centre Ilove; (4) MIS is the maintenance informational system which manages the metabolic processes by connection with the middle brain and brain stem and detected in consciousness as Iam; (5) GTS - genetic transmission system, is connected mainly with hypophysis and is reflected in consciousness as Icreate; (6) IGG is the info-genetic generator, managing the inherited info-genetic input from parents, connected with hypophysis and basal ganglia and is reflected in consciousness by Icreated, expressed by predispositions, mentality; (vii) IC is the info-connection pole of the organism, connected with the anterior cingulate cortex, with a role to select among various possibilities which are to be transmitted to prefrontal cortex, and reflected in consciousness by Ibelieve.

Comparing the results found in the previous section with the above discussion, we may observe the following: (A) the dysfunctionality of the brain is mainly due to the imbalance of IES (stimulatory) vs. CASI/CDC (inhibitory) YES/NO system and of the associated stimulant/inhibitive neurotransmitters activity; (B) the susceptibility of addiction/mood disorders are mainly related with IGG, managing the inherited genetic information and schematically represented by the horizontal red arrow in the right bottom side of figure 1; (C) the external stress and life conditions as informational stimuli/factors can influence and/or activate/determine the pathological expression/symptoms of MD/addiction.

According to the above comparison, we can discuss in detail the three items highlighted above as below:

A. The compensation systems like stimulatory/inhibitory neurotransmitters and corresponding areas of the brain are characteristic features for functioning of the nervous system and metabolic processes in the body under a YES/NO type form, determining the homeostasis/equilibrium axis of the organism functionality and of the informational inter-connection with reality.

B. The susceptibility for MD/addiction is heritable feature and is related to IGG/Icreated, marked by the red arrow in the right-bottom side of figure 1, in comparison with the green arrow (info-genetic input) in the left-bottom side of figure 1 for non predisposed persons. However, this feature can be regarded as an acquired property for adaptation by means of epigenetic mechanisms, as a consequence of a repetitive/intensive process of stressing events and/or adoptive practices and negative experiences of the precedent generations, mainly from parents.

C. The epigenetic mechanisms explain the susceptibility of the organism to the external information and show how information can be integrated in the organism structure under a stable form, explaining actually the info-evolution of the brain in human and animals [37,38]. We can think therefore that an acquired trait can be inhibited/eliminated by implementation of a new controlled trait, consciously assumed, against a genetic inherited vulnerability/susceptibility, and how can be used this method as a preventive or palliative therapy.

According to the above discussion, information can be integrated into the informational system of the human body by epigenetic processes, contributing to the individual behaviour. Normally, the nervous system as well as the entire organism is set to function under quasi-equilibrium conditions, with deviations not too much faraway from the equilibrium axis of the organism [4], defined as a normal, healthy state, when the driven forces YES of excitatory impulses/processes are normally compensated/balanced by the inhibitory NO tendencies. The abnormal functionality can be defined by a deviation from the equilibrium state, which can become chronical, integrated into the info-genetic system of the cells by epigenetic mechanisms. If such a state was implemented into the informational system in this way, a contrary informational state can be implemented also, this time in a controlled manner, to compensate/inhibit/eliminate the undesirable previous negative state.

The epigenetic mechanisms function if repetitive/intensive processes induced by an external cue is followed. The information is integrated in the informational system gradually: a first stage is represented by info-reception from external (or internal) sensors, which transmit it to CASI for short-time (1 min.) storage in prefrontal cortex or for long-time storage in hippocampus. Such a process should be reversible, i.e. the stored informational can be recalled from memory (Iknow) by CDC decision (Iwant) and submitted for analysis/judgement for a new decision making. By frequent activation, this information becomes more and more stably integrated, serving as a decision/reference criteria, if this is important for the decision acts, especially if is also amplified by the emotional system IES/Ilove. This is already an advanced step of info-integration. A next step can be referred to the automatic memory, assisted by cerebellum, in which the integration is even deeper, because this includes motor-type abilities expressed like MIS/Iam. The last step of integration consists in the restructuration of the stable memory of the cells in GTS (Icreate), which is the gene structure, but without modification of the species memory.

The new acquired traits can be transmitted to the new generation as IGG (Icreated), as it is schematically represented by the vertical green interrupted arrow in figure 1 left side for not predisposed organism, and in the right side for susceptible organism (red vertical

arrow). It is therefore extremely important what kind of information we accept, determining the judgement process, leading finally to an info-genetic (automatic) response/expression. Such a control is as well important, as the kind of the foods we consume. The organism is connected to two main poles: matter-pole corresponding to metabolic processes, and informational pole, corresponding to informational "nourishment". In other words, a healthy informational nourishment (suggestively represented by the green vertical arrow) determines the healthy functionality of the nervous system, as well as a healthy feed determines the corporal health. From this perspective, it results that human nourishes with feed, but also with information, as a bipolar info-matter system. The human organism is a learning adaptive system to the external conditions, which adapts its behaviour and micro-structure by using the informational pathway/circuit CASI/Iknow => CDC/Iwant => IES/Ilove => MIS/Iam => GTS/Icreate (=> IGG/Icreated in offspring), so depends on what kind of information is received. The human maintains/adapts also his body, the "hardware" supporting the informational system, by using the food pathway/circuit CASI/Iknow => CDC/Iwant => MIS/Iam.

We have to observe therefore that using the concept of info-integration, starting from the information reception (CASI/Iknow) and continuing with the info-operational processing (CDC/Iwant), assisted by the emotional system (IES/Ilove) and a repetitive/intensive process to transform it into an automatic stereotype (MIS/Iam) it is obtained an informational reactive chain/pathway stabilized into the genetic system (GTS/Icreate), automatically triggered when a triggering factor is detected or recalled from memory. Once triggered, such a process is difficult to be stopped, because of low contribution of the inhibitory prefrontal cortex circuit.

The info-integration epigenetic process is sustained by the cellular biochemical mechanisms in three main phases [37]: (1) the initial signal interacting by multiple cascade reactions with the body cell, sensitive to the external environmental changes, is defined as epigenetor (CASI/CDC+IES activation); (2) the epigenetor triggers the initiator, which by repetition and/or intensity induces a chain-type signal insistent/high enough to initiate the epigenetic process (MIS-type activation); (3) the maintainer is the informational signal which preserves the changes in the DNA structures, which will be manifested by acquired new traits (GTS intervention), transmissible to the next generation (inherited IGG).

Opposite emotions like desire (attachment)/apathy, pleasure/displeasure, happiness/sadness, love/hate were found to be driven by antagonistic pull-push (informational - YES/NO) mechanisms in the brain circuits [39,40], supporting our statement concerning the YES/NO type mechanisms driving the brain functionality. The "love circuit", belonging to the reward circuitry, and the "hate circuit" contain insula and putamen, as two common components. The love/reward circuit is composed mainly by medial insula, anterior cingulate cortex, and hippocampus in the subcortex, parts of the striatum and the nucleus accumbens [41]. Putamen is involved in the perception of contempt and disgust and part of the motor system of movement/action, and insula is involved in decision making, anxiety, addiction, pain perception, cognition, mood [42]. The hate circuit is directly involved in various phases of bipolar disorder [43], so an info-therapy procedure must involve the love circuit as a prevalent leading manager of the life.

In the same opposite situation are the neurotransmitters: the increase in dopamine is coupled to a decrease in another neuro-modulator, serotonin. Oxytocin and vasopressin as neuro-modulator, are particularly linked to attachment and bonding, opposing to negative emotional expressions like fear [44]. These neurotransmitters, intimately linked to dopamine as reward factor, which is also involved in memory and learning processes, are generated in hypothalamus, released/stored in hypophysis (GTS/IGG info-systems), discharged into the blood, particularly during the orgasm/satisfaction process of both sexes, and during child-birth and breast-feeding in females and social behaviour in males, particularly in aggression toward other males [41]. The implication of the love biological factors (IES) in GTS/IGG informational systems shows not only the power of emotions, but also their deep involvement into the roots of the life (info-genetic system), indicating love as a driving force, expressed by IES/Ilove informational systems. The increase of the positive/loving-type emotions induces a decrease of the activity of the central component of the limbic system amygdala, which normally engages IES in the fearful negative feelings. As an opposite reaction, the activity of the inhibitory/control/judgment areas of the brain like prefrontal/parietal/temporal cortex involved usually in control/critic operations is decreased, relaxing/inhibiting their vigilance and fear activation [41].

According to the above discussion, it is already evident that we can speak about info-therapy mechanisms and about an info-therapy procedure, which can be applied consciously in the day by day activity. This consists in the careful selection of the information which we accept to enter into our informational system, rejecting the negative and favouring the positive information. Such a procedure stimulates the pro-health activity by new objectives and projects and inhibits the abnormal functionality as much as the (CASI/CDC + IES) system, defined as operational informational system (OIS), reflected in mind by (Iknow/Iwant+ Ilove), becomes the master of own life, of conscious decisions and controlled behaviour. Such a procedure allows not only the preventive short-time control, but also assures long-time effects, taking into account the epigenetic processes of info-integration.

The change of mind operability based on new projects and positive thinking and decision criteria, on the complete elimination of criticism, aggressive mode to approach the social inter-relationships and partnership, will change the inner mood and will open the normal dialog with himself/herself, with family and with the society. The cultivation of beauty, in all its aspects, including art and culture, is the mental field where the cultivated seed will bear fruits. The use/exercise/practice of mind on such a field, especially at the old age, increases/maintains the brain healthy and its circuits, just like the sporting activity increases/maintains the muscles of the body, by intervention of the growth factor. The movement and sport activities induce also a wellbeing state by the improvement of the irrigation with blood of the brain regions. The mind should be occupied permanently with good and attractive projects and trained like the body muscles. Just as the right food is necessary for a healthy body, as well a right information is necessary to nourish a healthy mind. The nutrients of the mind are information and its healthy depends on what kind of information is provided to it. Therefore, the info-therapy should consist in: (1) connection to reliable/healthy sources of information and their selection in a YES/NO type system, equivalent with the activation of Iknow/Iwant/Ilove in a selective (Ibelieve) mode; (2) repetitive/intensive process of info-connection, including repetitive self-commands (Iwant), which must substitute the obsolete/negative patterned/"encrusted" habits; (3) the confidence, trust and patience (Ibelieve) in the favourable results. Within such procedure, the music-based therapy [16] or laughter therapy [45] may be included.

The external stress and life conditions as informational stimuli/factors determining on medium and long-time period the mood and addiction tendency, can be controlled favourably by an attentive/careful conscious info-selection, once it is understood their decisive influence on brain functionality and operational mechanisms, not only for preventive but also as a palliative therapy, particularly in elders, for a correct maintenance of the connection with reality.

Conclusion

The pathological expression in addiction and mood disorders (anxiety, depression, bipolar disorder, schizophrenia) were analysed, highlighting their correlation with the limbic/amygdala as excitatory system and prefrontal cortex as inhibitory area of the brain, dedicated to the judgment and short-time memory. An important role is complied by the associated excitatory/inhibitory - type neurotransmitters in the brain, showing the bipolar functionality (YES/NO Bit-unit) of nervous system, operating between such two poles to assure the mental equilibrium. The pathological expression of addiction and mood disorders were analysed, showing that the susceptibility/vulnerability is related with genetic inheritance (IGG/Icreated), but also induced by the stress/cues conditions, which determine the dysfunction of the brain area and the triggering of stereotypical behaviour (MIS/Iam), trans-generationally transmissible (GTS/Icreate).

The approach of pathological expression and circuits in informational terms, allow to distinguish seven modules of distinct functionality of the brain, showing that the addiction and the mood disorders are engaged by the imbalance of IES/Ilove (stimulatory) vs. (CASI/Iknow)/(CDC/Iwant) (inhibitory) YES/NO type processes and of the stimulant/inhibitive neurotransmitters, the disorder susceptibility/vulnerability being correlated with IGG/Icreated. The info-integration epigenetic mechanisms could be consciously controlled by application of adequate info-therapy, consisting in the repetitive/intensive practice of new adequate information using primarily the love-type thinking/circuit against the negative hate-type thinking/circuit, to stimulate the wellbeing states and the substitution of the obsolete/older info-stereotypes patterned/engraved in the genetic system by epigenetic mechanisms. The mind should be occupied with good and

attractive projects, trained continuously like the body muscles, particularly at the old age, when the correct connection with reality should be maintained in a right sense.

Conflict of Interest

No financial interest or conflict of interest exist.

Acknowledgement

The author thanks this Journal and Managing Editors for the kind invitation to contribute with this paper to this issue and for professional publication.

To Adrian and Ana-Maria Gaiseanu, with love.

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