

# THE THERAPEUTIC MODEL OF GROUP ANALYTIC PSYCHOTHERAPY IN BRAIN'S PLASTICITY MODIFICATION AND EXPRESSION, IN PATIENTS WITH COGNITIVE AND PSYCHIATRIC DISORDERS: A HYPOTHESIS OF NEURON-IMMUNE-ANALYSIS AND NEURON-IMMUNE-MODULATION

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## SUMMARY

**Background:** Dementia-like situations and depressive symptoms can be caused by a specific neuron circuit blockage, related with remote organic causes that are not cited in the CNS. Excessive cytokine secretion during stress situations is one of these causes which can be related with onset of cognitive symptoms including or accompanied by depressive ones, sometimes in an overlapping way. In both cases, chronic inflammation is a common hidden mechanism causing a vicious circle with mechanisms of somatic chronic stress and vice-versa while the serotonin pathway seems not to get seriously involved.

**Materials and methods:** Psychotherapy could dynamically influence the brain's and synaptic plasticity by treating disorders in an analogue with life's emotional trauma and conflicts, and by altering current life's stimuli according to the restoration of memories in the prefrontal lobe and in deeper brain areas.

After neurological examinations, EEG, Mini Mental Scale and MRI control, Patients underwent personal and group psychotherapy with selective members of their choice participating in the group.

**Results:** The reduction of the cytokine's levels by participation and psycho-education inside the Group Psychotherapeutic Treatment, could lead to a regulation of IL-1, to the reduction of CRP, to the amelioration of the levels of cortisol thus regulating the inflammation of the brain. The function of the Psychotherapeutic environment as a "container" is strongly associated with stress relief and reduction of the hyper secretion of cortisol, with successful management of the cortisol blood levels, and with impact on the HPA Axis, with consequence to cortisol secretions in the body's organs and glands. EEG and Mini Mental Scale significantly change and improve after Psychotherapy. Medical treatment for depression and dementia failed in comparison with the benefits which emerged from the Psychotherapeutic method.

**Key words:** psychotherapy – depression - dementia-like symptoms - cytokines

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## INTRODUCTION

Symptoms related with cognitive disorders, are usually expressed or provoked during several psychiatric situations and vice versa. On a cognitive level particular produced cognitive deficits, express a rather quantitative than qualitative differentiation of symptoms and signs, based also on the phase of the development of each disease, which usually has an overlapping expression, thus producing serious diagnostic dilemmas. In depression the level of mood, the sense of guilt, despair, denial, resignation, isolation, the suicidal thinking, and other symptoms like anxiety, lack of interest for pleasure and activities usually influence the cognitive status. Cognitive deficits can lead patients to a feeling of loss of identity, to the lack of insight and to disorientation in time, space and persons.

In dementia-like situations, the brain region surrounding the hippocampus is crucial for memory forming and for processing of spatial information. Decreased effective connectivity between the right front- parietal and insula networks is present in participants with melancholic depression compared with those with non- melancholic depression (Mann-Whitney). Reduced effective connectivity between the insula and executive networks was found in individuals with melancholia compared with healthy controls.

Before the installation of depression, usually situations of resignation and isolation towards psychological problems and traumas have been observed that lead to a malignant psychological and biochemical regression at an organic level.

Denial as an ego defense mechanism towards stressing life factors provokes immune deficiency and suppression.

All the situations described above are related with disturbances in a level of mental organization like "split-brain" with consequences to the function of the sympathetic nervous system and with failure of the models of emotional communication thus leading to the formation of the "infantile personality".

On a level of neuron connectivity, there is a link between psychiatric symptoms and dementia-like situations. During psychotic situations sometimes related also with OCD characteristics, the loss of identity, of the Ego representation and insight can lead patients to a depressive situation with cognitive de-arrangement.

In terms of brain plasticity, that is the brains' capacity to be adapted to the environments' needs, it is a question to be answered whether cognitive deficits and depressive symptoms coexist or express a common mechanism of the brain, different in pathogenesis resulting after stressful situations which can sometimes lead to neurodegeneration.

Although the cognitive and psychiatric disorders usually have different traditional mechanisms of pathogenesis, from a dynamic point of view, they are sometimes strongly related. The impact of the brain's inflammation as a parameter that fosters the onset of these symptoms has to be also seriously considered.

Our hypothesis is based on the psychotherapeutic factors which could reverse the brain's neuro-degenerating process and inflammation, thus reversing the mechanism of the depressive symptoms and cognitive signs. The topic of our presentation is how psychotherapy could intervene regarding the treatment of some characteristics of psychiatric diseases such as lack of insight, depression, impulsive symptoms within the way of thinking with cognitive dysfunction and dementia-like situations.

This approach will be related with:

- the brain's plasticity dimension that is the different way for the brain to be expressed and shaped by an external stimulus;
- the transcription and the way of transformation of life's past traumatic events and conflicts by the alteration of the memory's recalling function;
- the regulation of the key-lock psycho-immunologic marker, IL-1, that is participating in the brain's alteration with influence on the level of cellular memory and architecture and the function of the brain's circuits, via the mechanism of inflammation.

## CASE PRESENTATION AND ANALYSIS

A 64 years old female patient, suffering from Multiple Myeloma, Amyloidosis and Heart Amyloidosis (congo -red + and Amyloid P component +) in glands and vessels, with Hypothyroidism when she first came for examination in private practice, will be presented. She was accompanied by her children that described her mental situation as "completely lost", "disoriented in space and time", living in her "own world" thus preparing herself for the last stage of her life. Treatment with antidepressants (SSRIs) had no influence on her depressive signs of isolation and resignation. Medical treatment for her "dementia status" has made her physical and emotional situation worse.

In treatment the patient answered to all questions with great delay but it was evident that she understood every question posed to her. Her mood was mainly depressive, with a tendency for isolation and resignation, weakness and feelings of fatigue also related with her physical situation and inability, loneliness, and unhappiness. Chronic stress situations in her job and a violent symbiotic marriage have been referred in association to the memories of stressful situations which she had also experienced in her childhood. Pseudo-dementia, mainly expressed as depressive symptomatology with cognitive deficits, was the dominant clinical symptom with no significant response to

antidepressants. The influence of psychotherapy as a method to alter and to influence the above mechanisms was a question to be answered. Born in a migrant family coming from Armenia, the patient has suffered during her life time, from cultural conflicts and different habits in life and school, in society and in her marriage. Feelings of anger against her violent husband, memories of being suppressed and frustrated during years of her childhood and her marriage were mainly expressed.

In parallel, associating feelings of gratitude for the feelings of concern, understanding and care that she has experienced in return from her 4 children have been mentioned during the sessions.

These particular feelings and this specific life position matches with the research findings of the thesis that when we slow down and take the time to appreciate all the good in our lives - rather than what we are dissatisfied with - a radical change in our physiology occurs.

The patient described her over exposure to chronic stress situations during her life due to many demands coming from different parts of her life, such as the following:

- The rigidity of the attitude of her father during her childhood, not allowing to the patient the possibility for joy and amusement.
- Difficulty for physical exercise (running, playing, etc.) during childhood in school, due to a genetic abnormality of her hips area, for which she underwent two surgical operations, with in consequence the need to remain in bed for a long time.
- The culture of her husband's family did not allow socializing and amusement, thus reinforcing traumatic past experiences and conflicts of her childhood mainly with her father.
- Violent symbiotic relationship with her husband during her marriage.
- Stressful demands at her job.
- Stressful demands at home, having to take care of her four children, without any help, especially after the death of her parents, a particular period, when she felt "completely disconnected" from her past, thus being forced to accept an unhappy life's reality.

## MATERIALS AND METHODS

Every patient of the protocol including the patient under analysis underwent EEG, MMS and MRI Brain Scan with frequent blood tests.

The treatment included individual psychotherapeutic sessions of 50 minutes' duration in combination with group sessions including herself, her 4 children and the therapist. She did not want her husband to participate in the sessions.

In the case of our patient, when this thesis emerged, some immune blood markers have started decreasing.

The simple act of gratitude has been scientifically shown to balance the heart rhythms and the nervous system, leading to favorable changes in immunity and hormonal equilibrium. Further benefits of Psychotherapy included a significant reduction of stress, of the symptoms of anxiety, insomnia and depression. Considering that the damaging effects of stress contribute to a spectrum of diseases - including, but not limited to cardiovascular disease, cancer, mental illness and a variety of autoimmune disorders - it is of best interest to consider as a "whole" this health-destroying syndrome.

In the case of this patient under analysis the following remarks must be also highlighted:

- Mini mental score scale has been significantly improved when the patient started changing her life's attitude on focusing on the "nice part" of her life; The Mini Mental Scale examination showed a slight impairment of her mental situation, not corresponding to a dementia status. The Brain MRI was negative for any pathological lesion, thus excluding suspicious other diagnosis of metastasis, stroke, vascular inflammation in the brain or paraneoplastic situations. No pathological findings have been referred or found to her previous or current neurological examinations. During the psychotherapeutic sessions she has felt that she has finally found in life the space of her own to be freely and sincerely expressed and to create.
- The immune markers have been decreased in the serum measurement when she has started expressing feelings of gratitude and of solidarity for people surrounding her and supporting her, mainly her children. The patient underwent chemotherapy (6 sets) for multiple myeloma which, as time went by, has been transformed to a residual type of disease. Heart amyloidosis, from the other side, had a severe impact on the patient's quality of life thus later provoking cardiac failure and severe renal dysfunction with serum peritoneal fusion and severe electrolytic disorders. Although many factors could be considered as the reason of her depressive and cognitive impairment, the patient during individual psychotherapy presented an obvious amelioration in her orientation, in her concentration and in the velocity in answering to questions and making associations during the sessions.
- Amelioration of her physical and cognitive situation has been remarked when markers like CRP,  $\kappa$  chains, have been reduced, with reference to the treatment with chemotherapeutic agents and anti-inflammatory treatment. Creatinine and Urea and TSH titles in her Blood were high, while Sodium, Potassium, Magnesium titles were low. Impact on the morphology of her WBC and increase of the number of her PTL was evident too. Free monoclonal  $\kappa$  chains have been also initially detected and a short zone of monoclonal IgA $\lambda$  has been initially detected in the place of  $\gamma$  globulins

with increased titles of C4 (component), initially indicating a monoclonal " $\gamma$  - pathy", that is the definition of a gamma globulin dysregulation.

The creation of an "idealistic group matrix" based on the selection of the relatives from the patient's environment characterized by understanding, recognition, motives for life's change in the patient's current life, has been attempted.

Initially, the fear of loss of identity from the member occurred during her participation in the group, accompanied by panic attack and tendency for sub-grouping.

Through dialogue many ego-defense mechanisms became more mature and excessive narcissism and fear that was attributed to the psychosomatic disease was transformed in a social attempt to face the psychosomatic problem.

The participation of the member in the group-analytic process has transformed despair to a self-education of healing trauma associated with her problems and in the same time this process was reinforced through a neuro-modulating feedback.

The primitive frustration that the patient faced in the group has been transformed to sharing, partnership, collaboration and facing the psychosomatic disorder in the group. In the same time the group was considered and evaluated by the principles of Group Analysis (Foulkes), by the psychosomatic consideration of the body according to the principles of Goldstein, and finally by the psychosomatic estimation and evaluation of the communication and behavior as a result of an immune regulation and neuro-modulation.

The matrix of the psychotherapeutic group is considered as the hypothetical network/web of communication and relationship in a given group, and the common shared area/ground that ultimately determines the meaning and the significance of all events that occur in the group where all kind of communication and interpretations verbal and non-verbal, conscious or unconscious rest. Such a matrix can contain all the psychosomatic problems and life's traumatic experiences of a childhood related with organic diseases.

The matrix has roots that reach into the inner psychic experience of individuals binding them to the group-as-a-whole and makes roots to the neuromodulation of its member, where corrective emotional experience has the capacity to reinforce the immunological self-tolerance and mechanisms of the biological recovery. The matrix has been compared to a womb, a place in which something is bred or developed and frequently also related to some of the psychological functions of mothering.

The interaction of the matrix in the therapeutic group is an example of a network similar to the brain's neuronal network.

Foulkes considered matrix in an anatomical and physiological analogy with neuronal web in which neuron is a nodal point in the brain web which reacts and corresponds as a whole.

This phenomenon is bound-up with the concept of group matrix that is the operational basis of all relationships and communications. Inside this network the individual is conceived as a nodal point, in an aspect of an open and not closed system.

The psychotherapeutic factors based on the principles of group analysis, that contributed to the amelioration of the clinical course of the patient's symptoms by the combination of Individual and Group Psychotherapy in a family setting were the following:

- Creation of new safe boundaries (time orientation, new space for the meetings)
- Analysis in the "here and now situation"
- Holding
- Containing
- Sharing
- Mirroring
- Resonance
- Installation of Hope
- Corrective Emotional Experience
- Work on Trauma

## RESULTS

The results of the group, in psychosomatic terms gave an excellent model on the levels of:

- **psycho-education:** by participation in a small group through dialogue each member is reinforced for facing its psychosomatic problem, relieving chronic stress and managing situations of crisis: education and overall psychotherapy can influence the expression of the brain's left and right hemisphere in a balanced way thus negotiating with Hebb's hypothesis on the sets of neurons where a structural model of neural representations corresponds to elements of external reality.
- **support:** members inside a group are giving creation to "a psychosomatic foundation matrix" where the sense of "we-ness", "us-ness", is transformed to the "executive we" and a power of a world of caregivers is freely lovingly given to the member as an analogue to the mother's care for her infant. Inside the group, mechanisms related with family's relationships and functions emerged and were analyzed in association with the patient's current feelings.
- **neuron-modulation and immune alteration:** Plasticity of the neurones shows that the neuronal network remains open to change, enables the brain to register -in a lasting way- part of the information coming from the environment, thus making possible for the experiences undergone by each individual to leave a trace in the neuronal circuits.
- **creation** of a supporting psychotherapeutic ambience for understanding of conflict and conflict resolution with impact to the HPA axis and hormonal expression.
- **contribution** of Psychotherapy to the transformation and alteration of the organic trauma and symptom to a psychological one.
- **creation** of a safe container that relieves stress and CRH secretion with influence on the IL blood levels and to the brain's inflammation that is related with depressive symptoms. Excessive cytokine secretion during stress situations is one of the causes which can be related to the onset of Psychotic symptoms including or accompanied by Depressive ones, sometimes in an overlapping way. The function of the Psychotherapeutic group as a "container" is strongly associated with reduction of the hypersecretion of cortisol and with a successful management on its blood levels, on the influence of the HPA Axis, and on the consequence of its secretions in the body's organs and glands.
- **holding known** as a mechanism allowing several feelings to be expressed and understood, as well as feelings of shame provoked by and related with the disease. It provokes safety and cohesive feelings in the patient's life. The meanings of "holding" and of "containing" are strongly related and attributed with group matrix and as a consequence all the Ego defensive mechanisms such as multiple projective identifications as multiple transference can be analyzed and become conscious. Through holding and containing fears related to anxiety and depression these symptoms can be reduced (Rustomjee, Sabar, 2017)
- **acceptance** of traumatic experiences of childhood which can become conscious from a preconscious or unconscious level by memory transformation from implicit (by amygdala activation) to explicit (by cortical activation). Explicit memory enables us to learn about our environment through knowledge. It is sited in the Cortex and is mainly involved in conflict and trauma resolution. Implicit memory enables us to learn the way that we are doing, not consciously, related with early stages of life and is formed by different circuits of plasticity that can be differently changed. Behavior also can be recorded in implicit memory in an unconscious way. It is sited in areas close to the limbic system and it can be violently expressed, usually in front of a conflict, in an unconscious way and usually as a result of an accidental stimulus. It is related with social unconscious.

According to Le Doux neuron plasticity is expended in all human activities and experiences thus shaping our Emotional Memory which can influence also our cellular memory.

Eventually, the brain is constructed and shaped every moment according to its experiences and activities, by activating or drawing away neuron synapses in relation to their necessities and needs, to the traces shaped by a diversity of ways of memory function thus giving birth to new representations by selective neuron activation.

## DISCUSSION

### **The contribution of the group as a container with impact on the brain plasticity and neuron modulation**

Brain plasticity is the fundamental neuron activity of a constant change of the neuron circuits and synapses to the maintenance of the cellular memory. In many cognitive deficits and depressive symptoms, a lack of “container”, can be found during the earlier stages of childhood and a need of a caregiver occurs in both cases. The absence of the baby’s container when needed, is releasing high levels of cortisol that might expose the child to a somatic and psychic pain thus creating a somatic or psychological trauma seen in later life and expressed in terms of obesity, metabolic syndrome, cardiovascular diseases and diabetes mellitus. With “good enough parents” according to Winnicott and the presence of care-givers the baby’s anxiety is contained and the levels of cortisol are quickly reduced. The cortisol levels in the baby’s brain are related with its needs and demands and it can be modified by the presence or absence of a container (caregiver). The mother by responding to the baby’s signs of distress interpreting the baby’s needs as demands thus transports satisfaction to the place between need and demand. Life without the existence of a container for the inner and external conflicts cannot be a life without organic disorders. Here emerges the therapeutic impact of the Groups where experience leaves a trace on the neuronal network, modifying the efficacy of the transfer of information at the level of the subtlest of the system and the connections among neurons which are permanently modified thus provoking both structural and functional changes. Perception can leave a trace in the nervous system and become a memory and a sign inscribed in the neuronal circuits known as the Freudian concept of the sign of perception. The brain has mechanisms allowing the perception of the external world, the inscription of these perceptions in the neuronal network and the formation of our Memory.

Brain Plasticity is determined by the dynamic network of circuits and neuron adaptations with synapses that are constantly modified through the dendritic ends of the neuron, which many of them increase, thus making new adaptations, others decrease giving an end to the communication. As a matter of fact in any sensory or cognitive stimulus, the brain can respond and answer with a biological response that is equivalent with neuron activation, energy exchange and modification of the histo-chemic status of the neuron while in the same time it can be expressed as a psychological response.

Some of the most important criteria and factors that characterize the Group- Analytic spirit according to Rappaport are: Democracy, Permissiveness as the tolerance of any deviating behaviour, Realistic Confrontation and Communalism as the result of the sharing of

the “whole” in the context of the previous other three factors.

The application of the above in the clinical practice of group psychotherapy occurs as the free communication, flattening of hierarchy, common decision, sharing of responsibilities, the study of the roles and relationships in the group. Democracy helps different people of different ideology and problems, in different ways and in different situations to integrate an open system of theory and application. It contributes to the transformation of the creative traits of the individuals participating in a group therapy to creative elements of the community environment .Some of these creative traits are sensitivity, flexibility, adaptation, ability to share, interest in reflective thinking, confidence, healthy scepticism , emotional-mental and physical drive ,risk-taking, objectivity, non-conformism, reciprocal trust and respect, emotional drive, positive social learning and criticism, resolution of conflicts.

Changes occur when things become connected with each other in a synergic way and operate at higher levels of creativity. The fear of the individual of “loosing identity” after a period of exploration leads to a stage of transformation and to a synergic mature system.

The group identity in a supportive setting of an open system contributes to positive thinking and living in a protective way against familial, political and social problems.

The therapeutic counterculture of the group as a natural transition of the open system based on creation and integration is proposed. This counterculture is nourished by the elements of matrix composed by the members that participate in the group in an administrative Group model as well as in a model faced to the other open systems.

Kurt Goldstein first mentioned that the human organism behaves as a whole and not as a process of disorders of its differentiated parts.

As a result the symptom is faced as a product of dysfunction of the whole and not as a partial disorder. This concept gives the chance to all of us to move on beyond the Cartesian consideration and discrimination of the body separately from the soul and to move on to the theory of the thinking matter of expressed by James Clerk Maxwell according to whom the norms of the matter are mentally made, and vice versa mental norms are made from matter. William James referred to the specific situation that occurs when in a specific situation of the brain there corresponds a certain situation of information.

Stress is a common factor in all familial and social situations and vice-versa stress is a factor inducing symptoms leading sometimes to an exhaustion of cortisol receptors thus provoking immune deficiency and depression.

Affective and cognitive disorders are related with immune states and particular personality characteristics and they may be sometimes associated with differences

in immunological reactivity which are influenced by behavioral processes via neuro-endocrinal and psycho-immunological pathways. But how could the above elements of a group influence brain plasticity?

### **Group Psychotherapy and Brain circuits of immune regulation and neurotransmission**

Affective states and personality characteristics may be sometimes associated with differences in immunological reactivity. As a matter of fact, behavioral processes that influence immunologic reactivity and the immune state of an organism can have consequences for behavior, in the frame of different neuro-psychiatric disorders. The regulation of synaptic plasticity supports optimal information processing and storage and highlights the unique role this region plays in learning processes and memory formation. On the other hand, patients suffering from melancholia, report a distinct and intrusive dysphoric state during internally generated thought. Melancholia has long been considered to have a strong biological component, but evidence for its specific neurobiological origins is limited. The distinct neurocognitive, psychomotor, and mood disturbances observed in melancholia do, however, suggest aberrant coordination of frontal-subcortical circuitry, which may best be captured through analysis of complex brain networks. The brain has mechanisms allowing the perception of the external world, the inscription of these perceptions in the neuronal network and the formation of our Memory.

### **The Group in Trauma transformation and immune tolerance regulation.**

The neuroendocrine state, constitutes the internal environment, within which immune responses take place. Normal and abnormal affective states, different prenatal and early life experiences and social interactions, and environmental circumstances over which the individual has no control, are all associated with neuroendocrine changes that are implicated in the modulation of immune responses. The immunological changes associated with stressful stimulation or different affective states involve complex interactions among neural, endocrine and compartmentalized immune responses. Activation of the immune system will in turn, alter levels of circulating hormones and neurotransmitters. Complex feedback and feedforward mechanisms characterize the interactions within and between these systems. Many parameters can influence a patient's capacity for dealing or coping with that altered state. These variables include: i) genetic makeup ii) general health iii) sex iv) age v) intactness and functioning of the nervous system vi) growth and development experience vii) culture viii) psychological processes and self-image ix) the specific "outside-of-self" resources (e.g. family, work, school, community)

x) stress-producing life events (death, divorce, job-change, moving, promotion).

The verbal codes that come to be represented by the pre-frontal cortex can be transformed to an 'internal' speech originally derived from the perceptual cortex and therefore ultimately from the outside world.

Mnemonic traces derived from these reality perceptions gradually structuralize a portion of the Id into the psychic organization known as Ego. Implicit memory which recalls unconscious events influences the pre-frontal cortex not only in the way of thinking but also in the formation of many needs and demands. In our current needs and demands, unconscious past experience and traumas are "living". Although the mechanisms creating cognitive deficits in stress related neuro-psychiatric disorders has been obscure, pre-frontal cortical dopaminergic dysfunction is involved. The pre-frontal lobe is also related with Ego formation and in correlation with the dopaminergic circuits.

The prefrontal lobe represents the deepest and last layers of Ego formation and is organized as a set of internal prepositions, which were originally modeled on the concrete utterances of the parents.

Following a certain critical maturational period, the dependent relations between inside and out-side reverse themselves and the pre-frontal lobe comes to control the highest executive functions of the mind.

Reduced levels of dopamine (DA) neurotransmission in the pre-frontal cortex is associated with depression and schizophrenia, mainly with symptoms and signs such as: negative defect symptoms, withdrawal, and impaired insight and judgement, low volition and working memory.

It seems that we are carrying our past in ourselves even before the restoration of the initial representations of the Ego in the Prefrontal cortex.

Even more in our later life, trauma leaves traces in our memory, either through an explicit or in an implicit way. Research has shown, that trauma is coming to consciousness as knowledge when explicit memory functions, but other times it is expressed in an unconscious, blind, sudden, sometimes violent way, as in the case of implicit memory's function when the traumatic quantity cannot be bound and it overwhelms the Psychic Apparatus.

The relation between the trauma and the self-representation is also important. Many times in the psychic trauma a representation of the traumatic experience exists and a structuring transformation organizes the psyche; in the pre-psyche or early trauma such transformation does not function, there is only a sensorial mark that emerges with compulsion to repetition seeking binding or meaning. This lack of representation leads to a state of helplessness.

Trauma can separate the present from the past, the healthy part from the suffering one in microcosmic and macrocosmic terms. Its expression in treatment and in

the group, with the expression of its accompanying feelings and thoughts, usually creates a "chorus" of witnesses shaped from the need to "tell it to someone".

A brain-mind that is not attempting constantly to suppress concepts and memories can easily learn to "turn-off" signals from traumatic memories and pain neurons.

### **The Cytokines' expression: a Psycho-neuro-immunologic point of view**

On a neuroendocrine state which constitutes the internal environment, within which immune responses take place in normal and abnormal affective states, different prenatal and early life experiences and social interactions, and environmental circumstances over which the individual has no control, are all associated with neuroendocrine changes that are implicated in the modulation of immune responses. The immunological changes associated with a stressful stimulation or different affective states involve complex interactions among neural, endocrine and compartmentalized immune responses. Activation of the immune system will in turn alter levels of circulating hormones and neurotransmitters. Complex feedback and feed forward mechanisms characterize the interactions within and between these systems.

In chronic stress, there is a major role for glucocorticoids that are preparing the organism for strenuous activity by increasing the availability of energy substrates.

It is obvious that the relationship between depression and the immune system is much more complex dictate the conceptual frameworks for future research on the immune system and depression. Cytokines are a family of protein mediators-messengers of both natural and acquired immunity and they are involved in a "key-lock" mechanism in the homeostasis of human beings. They play a major role in mediating inflammatory and immune responses/processes by activating either protective or destructive processes of the brain's plasticity, immune-regulation and auto-immunity.

Cytokines may be involved in relationships between disease, stress or psychological status and immune or endocrine status in several ways:

#### **1. Directly involved in the local inflammatory responses of the brain.**

#### **2. Participating in acute and chronic psycho-neurological diseases:**

- IL-1 immuno-reactive nerve fibers have been described in the human brain especially in the hypothalamus, as well as the hippocampus and specific peri-ventricular hypothalamic structures.
- IL-1 mediates acute inflammatory and neuro-degenerative response to brain trauma, infection, heat stroke and excitotoxic insults without overt neuronal death as well as in stroke IL 1 is also activated in

psychological stress (academic stress, stress in depression) or during physical stress (infection, trauma).The increase of IL 1 can produce sickness behavior.

- IL-1 also increases the production of serotonin, dopamine, and norepinephrin and stimulates the production of IL-2, IL 6 and TNF factor, the latest been involved in mechanisms of neurodegeneration, cell death and apoptosis.
- IL-1 is elevated in Alzheimer's disease in both brain and serum, in major depression and in panic disorders and in OCD.
- In depression there is an increase in the plasma of the concentration of IL-1 and IL-6
- In many cognitive Disorders like Alzheimer Disease there is elevation of IL-1 , IL-6 and TNF in the serum and in brain extracts.
- In chronic stress, there is a major role for glucocorticoids, that are preparing the organism for strenuous activity by increasing the availability of energy substrates.
- They suppress also the immunological function per se and increase the brains' inflammatory response that is also related with depression, thus involving alterations in both T and B-cell function and Interleukin release.
- The immunosuppression during stress may be protective, at a time where maximal mobility may be important, but also may explain the increased incidence of infection after injury.
- Prolonged stress may also suppress thyroid and GH activity, as well as sexual and reproductive behavior, altering the "umbrella" under which, brain plasticity functions.
- The hypothalamus-pituitary-adrenal axis has long been known also as the region of the expression of stress, through the catecholamines.
- Lesions in various brain regions have revealed the role of distinct areas in immunomodulation and development of the Immune System.
- CRH has been recognized as the principal organizer of the neuroendocrine stress response and plays a major role in coordinating the endocrine autonomic, behavioral and immune responses to stress through actions in the brain and the peripheral tissues.
- CRH causes behavioral arousal, sympathetic stimulation and a decrease in appetite. CRH release from the hypothalamus is subject to stimulatory serotonergic control.
- CRH receptors are localized in highest densities in the anterior and intermediate lobes of the pituitary, the olfactory bulb, cerebral cortex, amygdala and cerebellum and the spleen.
- The timing that stress occurs, seems to be the most important regulator for the immune response: stress before antigen administration has a beneficial

influence while stress during and after infection can be devastating to the health of the subject.

- In cases of depression many abnormalities in neuro-endocrine functioning related with the hypothalamic-pituitary-adrenal (H.P.A.) axis have been mentioned.
- Immune cells have receptors for molecules derived from the H.P.A. axis, including corticotrophin-releasing hormone (CRH), corticotrophin (A.C.T.H.), beta-endorphin and cortisol.
- Endogenous glucocorticoids may play an important and complex role in the regulation of the immune response. Depression and stress are both associated with abnormalities in adrenal steroid secretion along with the idea that adrenal steroids may modulate immune function, indicate that depression vis-à-vis the H.P.A. axis may serve as a cofactor in the development and course of immune related disorders.
- This multisystem inflammatory function is characterized by exacerbations and remissions. Other situations are an example of a B cell mediated autoimmune disease in which depressive features are frequently involved and are related to a variety of circulating anti-self-antibodies that occur. Levels of anti-neuronal antibodies in the CSF are elevated in patients who have "organic mental disorders".
- Measuring inflammation levels could move physicians toward personalizing depression treatment. Until then, doctors will likely continue to treat people with depression with an antidepressant, and if the first one fails, they try another version every few months, hoping to find one that relieves symptoms. As Pariante says, "It's about not wasting all this time if an anti-inflammatory can tackle the biological mechanism of depression" thus underlying the double nature of cytokines and inflammation factors in neurodegeneration.
- Cytokines are a family of protein mediators-messengers of both natural and acquired immunity and they are involved in a "key-lock" mechanism in the homeostasis of human beings.
- They play a major role in mediating inflammatory and immune responses/processes by activating either protective as well as destructive processes of the brain's plasticity immune-regulation and auto-immunity. In fact they can modulate both neural and immune responses, they are involved in immune-related disorders such as infection, allergy, auto-immune disorders, cancer and in parallel they intervene in the break of blood-brain barrier. Depression is related with inflammation of the brain.
- Although cytokines in the past were more usually associated with peripheral immune and inflammatory responses virtually every cytokine so far identified, has been found also in the brain.
- These molecules act as important mediators of many neuro-immune interactions and responses to systemic inflammation and disease that are controlled by the CNS.

Cytokines may be involved in relationships between disease, stress or psychological status and immune or endocrine status in several ways:

**1. Directly involved in local inflammatory responses in the brain.**

**2. In many acute and chronic psycho-neurological diseases.**

- IL-1 immuno-reactive nerve fibers have been described in human brain especially in the hypothalamus, as well as the hippocampus and specific periventricular hypothalamic structures. IL-1 increases the production of serotonin, dopamine and norepinephrine. IL-1 is elevated in Alzheimer's disease in both brain and serum, in major depression and in panic disorders and in OCD.
- IL-1 also mediates acute inflammatory and neurodegenerative response to brain trauma, infection, as in stroke IL 1 is also activated in psychological stress (academic stress, stress in depression) or during physical stress (infection, trauma). This increase of IL 1 can produce sickness behavior.
- IL-1 stimulates the production of IL-2, IL 6 and TNF factor, the latest been involved in mechanisms of neurodegeneration, cell death and apoptosis.
- Tissue damage in the brain is related with marked increase in expression of IL-1, IL-6 AND TNF.
- HPA activation that leads to hyper cortisolaemia creates a positive feedback to the excessive inflammatory response initiated by the chain of cytokines.

Many studies correlate the impact of IL6 in the pathogenesis of Depression caused after chronic stress situations. The relationship among the neural, endocrine and immune process, is significant for the maintenance of human homeostasis in the adaption of the individual and the species.

## CONCLUSION

According to Foulkes man is a social being and can only be understood as such in the context of his environment. Every individual mind reflects and represents the social model where he lives and is a complex network of interacting processes (communications). These processes interact in the communications network of the group, the group matrix or group dialogue. The personal mind is capable of interacting processes, thus in the group what is reproduced is basically the matrix of involving personality. The psychotherapeutic method could help in situations of anxiety and depression by facing matrix as a neuron analogue and in the same time as the place of realization of dreams, thoughts and delusional thoughts as "acting-in" phenomena occurring during sessions. The definition of an individual framework of predisposing and disease-provoking factors would further have an immediate impact on the application of the psychotherapeutic interventions, which could alter the status of immune tolerance. Synapses

between neurons process different information and function thus forming what is known as Synaptic Plasticity. In cognitive deficits the brain region surrounding the hippocampus is crucial for memory forming and for processing of spatial information. Lesions in this area could be reversible when local inflammation is treated by reducing the levels of cortisol and by creating autoantibodies that reverse the lesions.

The distinct neurocognitive, psychomotor, and mood disturbances observed in depression do, however, suggest aberrant coordination of frontal-subcortical circuitry, which may best be captured through analysis of complex brain networks. Trying to find the mechanism that interplays the key role in these disorders according to Meriel Jane Waissman and I. Stock, depression is related to a seemingly unrelated condition that is inflammation, which can be described as the body's natural response to stress. Inflammation could result from injury or infection, but also emotional issues like an unhappy marriage or problems at work. Some amount of inflammation is generally beneficial, as it ramps up production of cytokines. High levels of cytokines could contribute to depression and anti-inflammatory drugs could reduce those cytokine levels and help people recover from depression. Depression alters immune tolerance and immune regulation by weakening the immune system, making it harder for people to fight off infections and recover from an injury. Researchers started noticing that the levels of cytokines and T-cells, which help drive immune responses and secrete cytokines, were higher instead of lower in blood samples from people diagnosed with depression. Cytokines can reach the brain several ways: directly through the blood-brain barrier or indirectly by binding to nerve fibers elsewhere, which send signals to the brain to produce the inflammation molecules. In the brain, cytokines can disrupt the production and release of several important signaling chemicals, including serotonin, dopamine and glutamate, which help control emotion, appetite, sleep, learning and memory.

Cytokines also have been shown to activate stress hormone signaling in the brain, which may also prime some to develop depression. In Miller's study, researchers measured levels of C-reactive protein (CRP), which our bodies make in response to high levels of cytokines. Blood tests for CRP are already a routine part of monitoring and treating inflammation-related diseases, such as heart disease and arthritis, and Miller predicts that the same will one day be true for depression.

The psycho-neuro-immunologic pathway through a complex chemical code of communication reflects the group synthesis and structure of the human nervous tissue and provides spontaneously human's living, function and evolution in a group biological and social dimension. Behaviour at each moment during the life of each living system presupposes these complex and parallel interactions and emerges out of them.

Facts and issues occurred in any group can be observed as a result of transference according to Freud and transference results from the process of projection and re-introjection of infantile object relationships that leads to a fantastic world which is re-experienced in adulthood. The psychotherapeutic group as a container in combination with its democratic ambience serves in favour of the regular function of the above mechanisms with impact to the cytokine, cortisol and CRH levels.

A group therapeutic milieu forces of the social environment and creates bridges between members and based on the principles of group analysis and psychotherapy problems can be resolved leading to a creative and integrating dialogue producing many solutions.

So the psychosomatic problem is faced according to the internal world of each member, its internalized relationships of early childhood restored to the prefrontal lobe and their modification by the familial, social, physical and political structures of later life and mainly with focus to Brown's theory concerning the early infantile relationship of the baby with its mother. Malcolm Pines says that the group has the potentiality to develop as maturational environment, reducing the need for defensive patterns which are being built as defenses against anxiety. New patterns of relating emerge which are more mature, meeting the creative needs of the individual and for the collective creativity of the group. The dialogue in the psychotherapeutic milieu reflects to another dialogue of the neuron web called neurotransmission, a dialogue of exchange of energy between neurons and channels of ions in the cellular membrane and a dialogue of hormones in the whole body. In our brain deep structure and processes do evolve more or less over time. Everything in the mind is connected.

The task of Psychotherapy seems to start where important change is possible.

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