

## Neuroanalytic Manual 0.1

# NEUROANALYTIC MANUAL of MENTAL DISORDERS

First Edition

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## GENERAL INTRODUCTION

Psychiatric diagnosis based on the DSM is descriptive. The DSM is a set of descriptions (signs and symptoms) with a title. For example, if the patient is complaining about sadness, helplessness, insomnia, and lack of motivation he receives the DSM title of “Depression.” Unlike psychiatry, in other fields of medicine the diagnosis is etiological meaning that the name of the disease is the cause of the disease. For example, “Appendicitis” involves a location in the body, the Appendix, part of the intestine, and it is infected, as “itis” indicates. Another example, “Mitral Valve Prolapse” indicates valve insufficient closure, in the heart, again a location in the body and its related pathology. “Depression,” “Anxiety” and all other psychiatric diagnosis are not in any way body-locations or pathologies. This is because the aetiology of mental disorders is simply unknown thus psychiatry is stuck with a descriptive diagnostic approach of the DSM.

One may argue that changing nomenclature is only an unimportant semantic issue, however it is not, there is a serious consequence to not knowing the etiology of mental disorders. Therapy in medicine targets the etiology of disease, if you have “Appendicitis” the therapy is directed to the “Appendix” and is an anti-inflammatory agent such as antibiotics. However, as is the case in psychiatry, not knowing what is wrong with the patients has serious consequences to treatments. Not surprisingly the efficacy of psychiatric treatment is typically lacking, for example in Depression (Sinyor et al 2010).

It can be argued that because we do not know the etiology (causes) of mental disorders, then any attempt to reconceptualize mental disorders as brain-related disorders is premature. The author argues that such mindset hampers any chance for surmounting the etiology-discovery barrier in psychiatry, and overcoming the vicious cycle in which descriptive diagnosis impedes brain-related etiological diagnosis. An old Chinese proverb (Confucius) states that “wisdom begins by calling things by their correct name” Discovery of the causes of mental disorders will start by re-conceptualizing psychiatric phenomenology in terms of brain disorders. Off course the initial conceptualization of mental disorders as brain-related disturbances will inevitably begin as a hypothetical construct, but such construct will be the basis of a testable-hypothesis launching-pad for discovering the brain-related (etiological)

psychiatry. Furthermore, the hypothetical speculative reconceptualization proposed here can be kept at a desired minimum as there is already a large body of knowledge in Neuroscience of mental disorders. In fact, the scientific justification, to take this bold step of reconceptualizing mental-disorders as brain-disorders stems from the accumulation of knowledge that brings us to the doorsteps of discovery. For example, enough knowledge exists already to reconceptualize “Psychosis” as a “Disconnection Syndrome” or more specifically as a disturbance to the “Small World Network” (Bullmor and Sporns 2009) organization of the cortical Connectom (Schmidt et al 2015).

Here the author will attempt the daunting task of reconceptualizing mental-disorders as brain-disorders, or in other words substituting the DSM (Diagnostic Statistical Manual) with a NM (Neuroanalytic Manual), where “Neuroanalysis” is the title given to a vast set of testable hypotheses reformulating mental disorders as brain disorders (Peled 2000, 2009, 2012). In effect the author will base upon a unification of knowledge from “Phenomenological Psychiatry” with that of “Complex-Systems Neuroscience.”

The manual begins with some explanatory introduction and then for each of the major psychiatric disorders, Psychosis, Negative Signs, Anxiety, Depression, Mania & Bipolar, and Personality disorders. The manual registers the 1) phenomenology, the 2) brain dynamics, and the 3) new diagnostic formulation in short. With these three steps the reader is taken from descriptive psychiatry to the etiological (hypothetical) psychiatry. Some leads about diagnosis and treatment follow in the last chapter and an Appendix table offers a quick diagnostic format to use in the clinic for those who read the manual.

## AUTHORS INTRODUCTION

Psychiatry attracted me from the beginning, I went to medical school not for the conventional medicine but to become a psychiatrist. We psychiatrist deal with the most important and fascinating phenomena of human beings, the higher-level functions, those of mental functions. It is a fascinating field to research and a frustrating medical practice. This is because we do not yet know how mental functions arise thus, we are limited also in understanding how they breakdown and malfunction. A direct consequence of this is manifested in our serious limitation in helping our patients, alleviating their suffering, not to mention, curing them entirely.

As early as medical school some 40 years ago I understood that the major challenge facing psychiatry is discovering the causes (etiology) of mental disorders. Only by knowing what is wrong with the patient we have the chance to cure him. As I advanced with my professional career it became obvious that the task of discovering the causes of mental disorders is a colossal and maybe unsurmountable task. I understood that when dealing with the brain we are dealing with a physical complex system and that we should become professionals in complex-system-physics on top of all the rest that we need to know. But most importantly I realized we must reconceptualize mental disorders in terms of brain, neuroscientific conceptualizations. Avoiding this daring step fixates psychiatry to a descriptive non-etiological discipline hampering any way toward achieving effective treatments and cures. By criticizing the DSM descriptive format, one needs to be able to propose an alternative. I have dedicated my entire professional life investigating the developing fields of Computational Neuroscience and Complex System Theories to formulate a set of basic theoretical hypothesis to provide a preliminary launching-pad for the future of a real brain-related etiological psychiatry.

In the process of my effort, I have discovered that the term “psych” is unscientific and confusing and in search for a better name to substitute with the term “psych” of psychiatry I came up with the term “Neuroanalysis” which is scientifically informative about brain organizations and brain disorganized disturbances as the origin of mental disorders. It is just natural to incorporate “Neuroanalysis” into a diagnostic manual of psychiatry under the title of “Neuroanalytic Manual” (NM).

I have chosen to name NM - 0.1 because, as mentioned above, it is a preliminary introductory effort to be iterated multiple times and developed fully to become the etiological diagnosis for mental disorders. Thus, by numbering the manual 0.1 there are 9 more iterations until full development as NM 1 diagnosis for mental disorders. The iterations in the case of NM are discovery-based unlike the DSM where they are political, consensus-based, decided upon by a voting committee.

## BARD GENERATIVE A.I. INTRODUCTION

Dated August 2023 Neuroanalysis is already present on the web as to generate a summery using Bard Generative IA as follows:

“Neuroanalysis is a method of using neural network and neural computation models to bridge the divide between psychology, psychoanalysis, and neuroscience when diagnosing mental health disorders and prescribing treatment. It was developed by Avi Peled, a professor of psychiatry at the Technion in Israel.

Neuroanalysis views the brain as a complex system of interconnected units, and suggests that conscious experience, feelings, and mood are emergent properties arising from these complex organizations. Mental health disorders are therefore seen as perturbations to the optimal brain organization, and can be identified through a specific breakdown pattern of the brain's organization.

Neuroanalysis is still a relatively new field, but it has the potential to revolutionize the way we diagnose and treat mental health disorders. By providing a more objective and scientific basis for diagnosis, neuroanalysis could help to improve the accuracy and effectiveness of treatment.

Here are some of the benefits of neuroanalysis:

- It can provide a more objective and scientific basis for diagnosis.
- It can help to identify the specific brain areas that are involved in a mental health disorder.
- It can help to develop more targeted and effective treatments.
- It can help to improve the understanding of the causes of mental health disorders.

However, there are also some challenges associated with neuroanalysis:

- It is a relatively new field, and there is still a lot that we don't know about how the brain works.
- It can be expensive and time-consuming to conduct neuroanalysis studies.
- The results of neuroanalysis studies can be difficult to interpret.

Overall, neuroanalysis is a promising new field with the potential to revolutionize the way we diagnose and treat mental health disorders. However, there are still some challenges that need to be addressed before neuroanalysis can become a widely used tool.”





## INTRODUCTION TO BASIC CONCEPTS

The new diagnostic conceptualization of brain related psychiatry is heavily relying on modern neuroscience that of systems neuroscience and computational neuroscience. Thus the modern day psychiatrist has to invest in acquisition of this knowledge. Here a concise simplified introduction is described, and should be viewed as the basics upon the psychiatrist of the future should search to educate himself.

The brain is a complex system and the mental phenomenology generated by the brain is an “Emergent Property” thus it is crucial to understand these concepts of Complexity, Systems and Emergent Properties.

The Oxford Dictionary defines complexity as “comprehending various parts connected together; composite, compound-involved, intricate”. Thus, complexity is inseparable from the concept of “systems”. Systems have “elements” and “connections” between the elements. Parts, units, and processes are all elements of systems they are interconnected to, becoming interdependent, cooperating, or competing for organization. According to the dictionary, the primary sense of the verb “to organize” is “to form as or into a whole consisting of interdependent or coordinated parts, especially for harmonious or united action” and “organization” means “the state or manner of being organized”. Thus, the root idea in common speech has to do with the interdependence of parts and “united action”. Thus, the concept of organization is indivisible from the idea of systems.

The modes of interactions among the elements are crucial to the complexity of the system, for example, elements can interact at random or in a more orderly manner. This leads us to another known definition of complexity, the KCS (Kolmogorov-Chaitin-Solomonoff) definition which places ‘complexity’ somewhere between order and randomness; that is, complexity increases (the shortest algorithm which can generate a digit sequence, S) to equal the length of the sequence to be computed; when the algorithm reaches this incompressibility limit the sequence is defined as random. The KCS definition brings out the distinction

between “highly ordered” and “highly complex” structures. Highly complex systems are ordered, but approach randomness, placing these systems balanced between order and randomness.

Simply put, two aspects of complexity concern dissociation and connection. Dissociation denotes variety and heterogeneity, and to the fact that different parts of the complex behave differently and independently. Connections signifies constraint, redundancy, and the fact that different parts are not independent, but that the knowledge of one part allows the determination of features of the other parts. A gas where the position of any gas molecule is completely independent of the position of the other molecules is an example of disconnection leading to disorder and chaos. In a perfect crystal the position of a molecule is completely determined by the positions of the neighbouring molecules to which it is bound, and is an example of connection leading to fixed order. Complexity can only exist if both aspects are present. Complexity is therefore situated in between order and disorder, or, using a recently fashionable expression, “on the edge of chaos” (see next chapter).

Complexity is often defined as: “the way in which a whole is different from the composition of its parts”. This definition is crucial in understanding how mental phenomena arise from brain complexity. It explains how mental functions are “emergent properties” from the organization of the human central nervous system. Emergent properties relate to the expression, ‘the whole is more than the sum of its parts’. Simply put, the characteristics of the system are not explainable based on the characteristics of its isolated parts. In other words, emergent properties are those properties of a system that are part of the system as a whole and cannot be understood only from the characteristics of the elements considered in isolation. Thus, the characteristics of the system are more than the sum of the attributes of the elements of the system.

For example, in referral to our interest of mental functions as emergent properties from brain organization, in 1962 Rosenblat stated that “neurons have never been demonstrated to possess psychological functions (e.g., mood, awareness, intelligence). Such properties presumably emerge from the nervous system as a whole” (Rumelhart & McClelland, 1986). It is evident from brain research that microcircuits of neurons possess more properties than those that can be deduced from our understanding of the single neuron (King, 1991).

Similarly, the properties of activated brain regions are greater than the properties of microcircuits of neurons.

Emergent properties originate from nonlinear systems. Non-linear systems are those systems where there are no one-to-one relations between input and output, thus, the activity of these systems cannot be described by linear equations. In linear systems, the whole can be described by the sum of all parts. A change in the total system obeys an equation of the same form as the equation for the change in its elements. Thus, linear systems cannot demonstrate additional properties more than those of their components. Non-linear systems may result in responses (or properties) that are higher than predicted compared to linear estimations, thus achieving emergent properties. When systems transit from random states to ordered formations, emergent properties arise in the system that were not part of that system before organization occurred.

” Complexity” and” Emergent Properties” explain how a physical system such as the brain generates mental functions thus addresses the psycho-physics problem. To understand disturbances of the brain dynamic system characteristics are important, these are the concepts of “Criticality,” “Phase-transition,” “Trigger-saturation Effects and “Optimization,” “Constraint-satisfaction,” “State-space System Dynamics,” “Neural Complexity,” “Matching Complexity,” “Plasticity and “Internal\_Representations.”

In physics, a critical point is that where a system radically changes its behaviour or structure, for instance, from solid to liquid. In standard critical phenomena, there is a control parameter, which an experimenter can vary to obtain this radical change in behaviour. In the case of melting, the control parameter is temperature. A self-organized critical phenomenon, by contrast, is exhibited by driven systems that reach a critical state by their intrinsic dynamics, independently of the value of any control parameter. The archetype of a self-organized critical system is a sand pile. Sand is slowly dropped onto a surface, forming a pile. As the pile grows, avalanches occur which carry sand from the top to the bottom of the pile. At least in model systems, the slope of the pile becomes independent of the rate at which the system is driven by dropping sand. This is the (self-organized) critical slope. Generally, we can define criticality as a point where system properties change suddenly, e.g. where a matrix goes from non-percolating (disconnected) to percolating (connected) or vice

versa. This is often regarded as a phase change, thus in critically interacting systems we expect step changes in properties and phase transitions in dynamics.

To conclude, criticality may involve both levels as well as patterns of organization in systems. As mentioned above, phase transitions going from one level of organization to the other system may gain or lose emergent properties according to transiting to higher or lower levels of organization. For example, evolution is generally described as phases transiting from one level to a higher level of organization, thus systems of higher level have additional properties in respect to the previous level system. Properties of a system can change abruptly according to the change of organization pattern within the system. Nonlinear systems can react abruptly to small changes (trigger effect) or remain stable despite large perturbations (saturation effect).

Instability can occur in all kinds of structures from solids to gases, from animate to inanimate, from organic to inorganic, and from constitution to institution. External and internal disturbances can cause stable systems to become unstable, but this instability does not necessarily happen just from some ordinary perturbation. Cambel says that it depends on the “type and magnitude of the perturbation as well as the susceptibility of the system” (Cambel, 1993), which must be considered before the system is rendered unstable. He adds that sometimes it takes more than one kind of disturbance for the system to transform into an unstable state.

Prigogine and Stengers speak of the “competition between stabilization through communication and instability through fluctuations. The outcome of that competition determines the threshold of stability” (Prigogine and Stengers, 1984). In other words, the conditions must be ripe for upheaval to take place. We could suppose this to many observable situations in areas such as disease, political unrest, family and community dysfunction but in psychiatry it is especially appropriate to conceptualize the idea of acute reaction to stress and adjustment disorders. Cambel used the old adage that it may be the straw that broke the camel’s back that finally allows the system to go haywire. This old saying reflects the idea of the trigger effect bringing us back to the instability as a ‘behaviour’ inherent to nonlinear systems.

Optimization is typically defined as the ability of a system to evolve in such a way as to approach a critical point and then maintain itself at that point. If a particular dynamic structure is optimum for the system, and the current configuration is too static, then the more changeable configuration will be more successful. If the system is currently too changeable, then the more static mutation will be selected. Thus, the system can adapt in both directions to converge on the optimum dynamic characteristics. Christopher Langdon speaks of the “edge of chaos” as the place where systems are at their optimum performance potential (Kauffman 1993). At the edge of chaos, there is a sublime balance between stability and instability. This sublimely balanced formation is the state where the system is at its optimum adaptation where it can naturally approach the more changeable configuration as well as the more static mutation. This balance is important for optimal adaptation to external and internal events as well as for “best solution” configuration toward these events. The ability of a system to optimize is related to the idea of complexity as well as connectivity. As mentioned above, if the elements of a system are disconnected from each other and act independently, the system will tend toward randomness and therefore to the more changeable configurations. If connectivity is dominant and fixed, the more static “freezing” state will prevail. Thus, the connectivity patterns in the system are crucial to the optimization and complexity of the system.

“Multiple constraint satisfaction” is the type of organization that accounts for the interrelations among multiple units in a system. Once the activity of unit A influences the activity of unit B connected to it in the system, the activity of unit B is constrained by unit A. This constraint depends on two factors, 1) the activity of unit A and 2) the “strength” of the connection to unit B. The strength of the connection conveys to what extent the activity in A constrains the activity in B. If the value of the connection-strength between the units is large, then the constraint of the activity in A on the activity in B is large. Conversely, if the strength of the connection is small, then the activity in B will be less constrained by the activity in A. In systems with numerous interconnected units, each unit simultaneously influences (i.e., constrains) several other units, thus the activity of each unit is a result of multiple parallel constraints. When the activity of a unit satisfies all the influences exerted on it by the other units connected to it, it achieves multiple constraint satisfaction. If the activities of all the units in the system achieve multiple constraint satisfactions then the system as a whole optimizes multiple constraint satisfaction.

To describe the dynamic activity of complex systems it is mandatory to understand the physics concept of “state-space”. Imagine a system formed from many elements. The arrangement of the elements in the system represents the “states” of the system. Each distinct arrangement in the system forms a different “state” for the system. If the elements are arranged randomly, all the states in the system are like each other. If the elements of the system can form many distinct patterns of arrangements, then the system has many possible states. If the system can form only one type of arrangement, then the system is represented by one state only. The “space” of a system is represented by all the possible states a system can assume. If the system changes over time, it is called a “dynamic” system. In this case, the system changes its arrangement from one point in time to the next. To visualize systems and their dynamics William Hamilton, the well-known physicist, and the mathematician Karl Jacob devised the concept of *state-space* necessary for describing dynamics in physical systems (Ditto & Pecora, 1993). A dynamic system is generally defined by a configuration-space consisting of a “topological manifold.” A point on the configuration-space represents the state of the system at a given instant. Each point is a combination pattern in the activity of the elements (i.e., the arrangement of the elements). The configuration-space of the system is given by all the possible states that the system can assume, (i.e., all the possible combinations in the activity of the elements). This configuration-space is sometimes termed “landscape.” As the dynamic state of the system changes over time, the combinations in the activity of the elements change (i.e., the points on the space change). The dynamics of the system are described in terms of state-space as ‘movement’ from one point to the next on the landscape, defining a trajectory, or curve, on the configuration space. If the system ‘prefers’ certain states (i.e., arrangement) over other states, it will tend to be ‘drawn’ or ‘attracted’ to form these states. Once certain states are preferred by the system, they form “attractors” (basins) in the topological surface (Herz *et al*, 1991). If a metaphorical ball were rolling on the surface (space) it would be easy to see that peaks of the landscape represent “repellers” (i.e., those states the system tends to avoid) and basins represent attractors (i.e., those states the system tends to assume). Now that we have described some basic concepts of systems that are relevant to the working of the brain it is time to relate to the brain and see how these concepts are relevant to brain plasticity adaptability and flexibility, and also to some phenomenology aspects of mental disorders.

Historically brain activity was formalized using the localised approach of brain centres, stating specialized functions for segregated neuronal regions. Later the integrated approach

argued against localised functions and evoked the non-localised approach of spread activation and functional connectivity across vast cortical regions. Today, it is recognized that nervous systems facing complex environments have to balance two seemingly opposing requirements. The need to quickly and reliably extract important features from sensory inputs and the need to generate coherent perceptual and cognitive states allowing an organism to respond to objects and events, which present conjunctions of numerous individual features. The need to quickly and reliably extract important sensory features is accomplished by functionally segregated (specialized) sets of neurons (e.g., those found in different cortical regions), the need to generate coherent perceptual and cognitive states is accomplished by functional integration of the activity of specialized neurons through their dynamic interactions (Tononi and Edelman, 1998).

The mathematical concept of “neural complexity” ( $C_N$ ) (Tononi, 1994) captures the important interplay between integration (i.e., functional connectivity) and segregation (i.e., functional specialization of distinct neural subsystems).  $C_N$  is low for systems whose components are characterized either by total independence or by total dependence.  $C_N$  is high for systems whose components show simultaneous evidence of independence in small subsets, and increasing dependence in subsets of increasing size. Different neural groups are functionally segregated if their activities tend to be statistically independent. Conversely, groups are functionally integrated if they show a high degree of statistical dependence. Functional segregation within a neural system is expressed in terms of the relative statistical independence of small subsets of the system, while functional integration is expressed in terms of significant deviations from this statistical independence (Tononi, 1994). One general characteristic of high mental functions is their capacity to flexibly adapt to the needed information processing. For example, working memory tasks involve shifting paradigms, the examined subject is required to choose from a set of stimuli (cards) according to a guiding rule (to colour shape or a specific number of stimuli). Choosing is performed based on the feedback of ‘correct’ or ‘incorrect’ from the examiner. After a certain number of stimuli presented to the subject, the examiner shifts category and the subject is required to change (adapt to) and choose according to the new rule. The adaptive performance is measured as the capacity to flexibly process the changing conditions in the task environment.

For a system to adapt to the environment it must master a degree of flexibility to change according to the demands of the environment (Ditto & Pecora, 1993). If the system is rigid

and unchangeable, it will not have the ability to modify according to altered environmental conditions. If a certain degree of randomness is introduced to the system, then the system is more susceptible to change and will modify according to the changes in the environment. Once change occurs in the system, it needs to be maintained over time for as long as it serves its adaptive function. If the system is totally random (changes continuously), modifications cannot be maintained for long periods. The system, therefore, has to have a certain degree of order that will maintain the acquired change. It is clear that for optimal adaptability, the system has to balance orderliness and randomness in its interaction with the environment. In neuronal terms, randomness involves segregation because the segregated neuronal systems will act independently of each other demonstrating non-organized, random activity. Orderliness in neuronal terms involves integration because each neural system constrains the activity of the other systems connected with it via integrative functional connections. In order to adapt and change according to the shifting paradigms required by high mental functions such as working memory it is likely that brain function requires integrative as well as segregative capabilities. As explained above, the balance between integrative and segregative functions in the brain is achieved when neural complexity is optimal.

The relevance of synaptic plasticity to the information processing of the brain was recognized as early as the beginning of the 20<sup>th</sup> century. Cajal (1911) was one of the first to realize that information could be stored by modifying the connections between communicating nerve cells in order to form associations. Thus, acquisition and representation of information basically entail the modulation of synaptic contacts between nerve cells (Kandel, 1991). Information is stored by facilitation and selective elimination of synaptic links between neuronal aggregates that represent discrete aspects of the environment. Memories are hence essentially associative; the information they contain is defined by neuronal relationships.

Hebb (1949) proposed that “two cells or systems that are repeatedly active at the same time will tend to become associated, so that activity in one facilitates activity in the other.” This is called “the principle of synchronous convergence” (Fuster, 1997). Through summation of temporally coincident inputs, neurons become associated with one another, such that they can substitute for one another in making other cells fire. Furthermore, connections between input and output neurons are strengthened by recurrent fibres and feedback. By these associative processes, cells become interconnected into functional units of memory, or Hebbian “cell



assemblies". Later, the formation of cellular assemblies in the brain were named under the general term of "neural plasticity"

Evidence for synaptic plasticity was presented as early as 1973 when a group of researchers published one of the first detailed reports on artificially induced modification of synaptic strength (Bliss & Gardner, 1973). They found that stimulation of certain neuronal fibers with high-frequency electrical pulses caused the synapses of these fibers to become measurably stronger (i.e., their capability to stimulate post synaptic potentials increased) and stay so for many weeks. Their observation, which they called long-term potentiation (LTP), was probably one of the first reports of synaptic plasticity.

One critical component of the induction of synaptic plasticity in virtually all experimental models is a change in post-synaptic (sometimes pre-synaptic) membrane potential, usually a depolarization. There are two other common features. First,  $Ca^{2+}$  typically plays an indispensable role in triggering synaptic change. The elevation of  $Ca^{2+}$  may arise via flux through membrane channels, release from intracellular stores, or both. Second, plasticity usually comes in two general forms: short-term plasticity which is dependent on post-translation modifications of existing proteins, and long-term plasticity which is dependent on gene expression and *de novo* protein synthesis.

Finally, it is increasingly apparent that for many experimental models a vital bridge between initial induction of plasticity and its maintenance over time is the activation of adenylyl cyclases and protein kinases A. One of the more studied mechanisms of regulating  $Ca^{2+}$  flux in synaptic transmission relates to the N-methyl-D-aspartate (NMDA) excitatory amino acid receptor. Over the years it has become apparent that many sub-cellular systems combine in a complicated way to regulate  $Ca^{2+}$  flux and levels, for example, the phosphoinositide system, G-protein systems, and the neuronal membrane currents (for detailed explanation of the relevance of these systems to synaptic plasticity *see* Wickliff & Warren, 1997).

In a series of experiments with the marine snail *Aplysia*, Kandel demonstrated how synaptic connections can be permanently altered and strengthened through the regulation of learning from the environment. Kandel (1989) found structural changes in neuronal pathways and changes in the number of synapses related to learning processes in the *Aplysia*. Essentially LTP is the mechanism by which *Aplysia* learns from experience at the synaptic level, and the

experience-dependent process then translates into structural, ‘hard-wire,’ alterations (Singer, 1995).

In another series of experiments, with monkeys, the map of the hand in the somatosensory cortex was determined by multiple electrode penetrations before and after one of the three nerves that enervate the hand was sectioned (Merzenich & Kaas, 1982). Immediately following nerve section most of the cortical territory, which previously could be activated by the region of the hand, enervated by the afferent nerves became unresponsive to somatic stimulation. In most monkeys, small islands within the unresponsive cortex slowly became responsive to somatic stimulation from neighboring regions. Over several weeks following the operation, the previously silent regions became responsive and topographically reorganized.

Studies of the primary visual cortex in mammals typically show experience-dependent activity (Kandel, 1991; Singer, 1995). The blockade of spontaneous retinal discharge prevents the segregation of the afferents from the two eyes into ocular dominance columns; this finding suggests that spontaneous activity may promote axon sorting. Ganglion cells in the developing retina engage in coherent oscillatory activity, which enables the use of synchronous activity as a means of identifying the origin and neighborhood relations of afferents. However, substantial fractions of neurons in the primary visual cortex, especially those in layers remote from thalamic input, develop feature-specific responses only if visual experience is available. Manipulating visual experience during a critical period of early development can modify visual cortical ‘maps’ in these layers (Singer, 1995).

The relevance of Hebbian synaptic plasticity to mental functions such as perception, memory, and language is best understood via artificial neural network models. Neural network models are simplified simulations of the biological neural networks spread in the brain. Units in the model are simplified representations of neurons (having input summation and threshold dependent output). The units are richly interconnected to resemble the massive synaptic connectivity found in neural tissue. These models abstract from the complexity of individual neurons and the patterns of connectivity in exchange for analytic tractability. Independent of their use as brain models, they are being investigated as prototypes of new computer architectures. Some of the lessons learned from these models can be applied to the brain and to psychological phenomena (Rumelhart, 1986).

One of the relevant models is the class of feed-forward layered network with added feedback connections. In the feed-forward layered network architecture, information is coded as a pattern of activity in an input layer of the model neurons and is transformed by successive layers receiving converging synaptic inputs from preceding layers. Added feedback connections transform the architecture of the network to a fully interconnected structure also termed after its inventor, the Hopfield network. In the Hopfield model, 'learning' is achieved by adjusting (strengthening) connections between the units to strengthen certain activation patterns in the model. Strengthening connections simulates synaptic plasticity and the Hebbian algorithm in the model determines higher activity to the units more strongly connected. Input is presented to the model in a form of an initial pattern of unit activation distributed over all of the units. The units in the model are then left to interact with each other. Due to the predetermined strengthening of connections the model "tends" to activate the pattern which is closest in configuration to the input pattern.

The distance between the input pattern and the activated pattern is measured in terms of "Hamming distance" which reflects the number of units with different activation values between the two patterns. In this manner, the Hopfield model achieves a computation of content addressable memory activation. The pattern strengthened by connection encodes the memory, just as Hebbian dynamics probably determines learning in real brains, and the input activates the relevant associated (nearest in hamming distance) memory, just as one memory is associated to with its relevant remainder. The content addressable computation has been successfully applied to problems of feature extractable and recognition of visual and other stimuli, thus simulating brain perception and perception-dependent memory activation (Rumelhart, 1986).

Using the state-space formulation (see above), a memory embedded in the Hopfield model forms an "attractor" on the space manifold of the model. The attractor represents the dynamic tendency of the system to activate the memory states just as a ball may roll toward a basin of a landscape. Thus, multiple attractor-formations in the space manifold of a system could provide for internal information embedded in that system. In other words, the manifold topography of a dynamic system could well simulate internal representations achieved by that system.

The internal representations in the brain probably follow the general rules of Hebbian plasticity. Since the brain operates on the border of chaos, balanced between orderliness and randomness, the internal representations are probably subject to continuously changing influences. A more complete characterization of the functional connectivity of the brain must therefore relate it to the statistical structure of the signals sampled from the environment. Such signals activate specific neural populations and, as a result, synaptic connections between them are strengthened or weakened. In the course of development and experience, the fit or match between the functional connectivity of the brain and the statistical structure of signals sampled from the environment, tends to increase progressively through processes of variation and selection mediated at the level of the synapses (Edelman, 1987).

Tononi and coworkers introduced a statistical measure, called “matching complexity” ( $C_M$ ), which reflects the change in  $C_N$  observed when a neural system is receiving sensory input (Tononi *et al*, 1996). Through computer simulations, they showed that when the synaptic connectivity of a simplified cortical area is randomly organized,  $C_M$  is low and the functional connectivity does not fit the statistical structure of the sensory input. If, however, the synaptic connectivity is modified and the functional connectivity is altered so that many intrinsic correlations are strongly activated by the input,  $C_M$  increases. They also demonstrated that once a repertoire of intrinsic correlations has been selected which adaptively matches the statistical structure of the sensory input, that repertoire becomes critical to the way in which the brain categorizes individual stimuli (i.e., perceives stimuli).

In plain words, the internal representations embedded as statistically input-matching patterns are continuously altered by the configuration of external influences. Once altered, the consecutive inputs are “interpreted” by the recently altered internal representations. Piaget using the terms of “assimilation” and “accommodation” described this idea (Piaget, 1962). Roughly defined, assimilation is when new patterns of experience are incorporated, and accommodation is the use of the assimilated experiences for the manipulation of the environment. Piaget described how the interactive assimilation-accommodation feedback drives human mental development.

The famous psychologist Carl Rogers (1965) suggested that the best vantage point for understanding behaviour is from an “internal frame of reference” of the individual himself. He called this frame of reference the “experiential field”, and it encompasses the private

world of the individual. Neuroscience demonstrates that the brain uses internal “maps” to represent information. One example is the “homunculus” of sensory and motor representations spread over the cortex (Roland, 1993). Just as the homunculus is probably formed from the strengthening of synaptic pathways, the experiential field probably results from experience-dependent plasticity in the brain (Kandel, 1979; Friston, 1996). In terms of space-state formulation (see above), the experiential field can be conceptualized as a configuration of attractor systems in the brain.

According to Rogers, “organismic evaluation” is the mechanism by which a “Map” (i.e., the internal configuration) of the experiential field assesses the psychological events of everyday life (Rogers, 1965). Using the description of state-space configuration organismic evaluation can be re-conceptualized as convergence into, or activation of, relevant experience-dependent attractor configurations of the internal map. If the incoming experience is identical to the previous internal representation of that experience, no change will occur and the map of internal representation will activate familiar past experiences. On the other hand, if the new experience is slightly different from the past experience, this will be enough to ‘reshape’ the topological map and add attractor configuration to the internal map of references.

Activation of the internal map organizes the incoming stimuli into a meaningful perception. The newly perceived experience is meaningful when it relates to the previous experience already embedded in this map. This is a circular process where the map of internal representation is both influencing and being influenced by the incoming stimuli at the same time. In other words, the brain sustains a map of internal representations that is continuously updated through interactions with the environment. Recently, this type of interaction between internal representations and perception of environmental stimuli has been referred to as “context-sensitive processes” (Friston, 1998). Due to this interaction, internal representations can be viewed as approximated models of reality.

It is reasonable to assume that a “good match” between internal representations (of the psychosocial world) and external psychosocial situations will enable efficient adaptive interpersonal relationships. On the other hand, a “mismatch” between the psychosocial events of the real world and their internal representation may “deform” the perception and the behavioural responses of the individual. In addition, reduced matching complexity will

further reduce adaptability causing rigidity, reducing the repertoire of reactions available to the individual.

In addition to the massive connectivity organization of the brain, connectivity offers hierarchy. As early as 1881, Wernicke regarded the cerebral cortex as constituting, in its anatomical arrangement of fibers and cells, the organ of association (Wernicke, 1906). Wernicke perceived a hierarchy of evermore-complex arrangement of reflexes in the brain. With this formulation he preceded later insights of brain organizations achieved by studying sensory and motor brain functions.

According to Fuster (Fuster, 1997) there is a hierarchy of perceptual memories that ranges from the sensorial concrete to the conceptually general (Fuster, 1997). At the bottom resides the information on elementary sensations; at the top, the abstract concepts that, although originally acquired by sensory experience, have become independent from it in cognitive operations (Fuster, 1995). This information process is most likely to develop, at least partially, by self-organization from the bottom up, that is, from sensory cortical areas towards areas of association. Memory networks, therefore, appear to be formed in the cortex by such processes as synchronous convergence and self-organization.

In the higher levels, the topography of information storage becomes obscure because of the wider distribution of memory networks, which link scattered domains of the association cortex, representing separate qualities that however disparate, have been associated by experience. Because these higher memories are more diffuse than simple sensory memories, they are in some respects more robust. Only massive cortical damage leads to the inability to retrieve and use conceptual knowledge, the “loss of abstract attitude” described by Kurt Goldstein (Fuster, 1997).

Like sensory information, motor information on planning and deciding has also been hierarchically described. As first suggested by Hughlings Jackson (1969), the cortex of the frontal lobe computes the highest levels of motor information. At the lowest cortical level is the primary motor cortex, representing and mediating elementary motor acts. The prefrontal cortex, conventionally considered the association cortex of the frontal lobe, represents the highest level of the motor hierarchy (Jackson, 1969; Feinberg & Guazzelli, 1999). This position connotes a role not only in the representation of complex actions (concepts of action,

plans and programs) but also in their enactment, including those such as working memory (Goldman-Rakic, 1987).

The prefrontal cortex develops late, both phylogenetically and ontogenetically, and receives fiber connections from numerous subcortical structures, as well as from other areas of the neocortex (Perecman, 1987; Weinberger, 2000). This extensive connectivity links reciprocally the perceptual and conceptual information networks of the posterior cortex with prefrontal motor networks, thus forming perceptual-motor associations at the highest level (Fuster, 1997).

Mesulam M-M (1998) reviewed brain organization leading from sensation to cognition. Unimodal association areas make part of the lower hierarchical organization; they encode basic features of sensation such as colour, motion, and form. They process sensory experience such as objects, faces, word forms, spatial locations and sound sequences. More Heteromodal areas in the midtemporal cortex, Wernike's area, the hippocampal-entorhinal complex and the posterior parietal cortex provide critical gateways for transforming perception into recognition, word\_formation into meaning, scenes and events into experiences, and spatial locations into targets for exploration. The transmodal, paralimbic and limbic cortices that bind multiple unimodal and the higher more Heteromodal areas into distributed but integrated multimodal representations occupy the highest connectionist levels of the hierarchy. The transmodal systems with their complex functional inter-connectivity actualize (see emergent properties above) the highest mental functions.

Via the different sensory systems, information is continuously sampled from the environment. Simultaneously the environment is subject to continuous manipulations via the motor systems. This cycle of continuous sampling and intervention in the environment is governed by the ever more complex circuits which characterize the hierarchical organization of the brain. This hierarchy enables the associative transformations needed to support the cognition typical of high mental functions and is heavily dependent on neuronal connectivity.

The transmodal connectionist level of brain organization plays an important role in shaping the characteristics of high mental functions. If prior to establishing a connection two neuronal systems could act independently one from another, now that their activity is interdependent, the activity of one neural system or network will influence the activity of the other. This

might explain the internal consistency we experience in our mental functions, and why reality is perceived as being coordinated audibly, visually and tactually. Planning, thinking and acting also have consistency; thoughts and reactions are goal-directed to the stimuli at hand, and match situational events. Finally, our entire conscious experience seems united in one complete logical and meaningful continuity.

Building on a 'contrastive analysis' that compares conscious versus unconscious processes across numerous experimental domains, Baars (1988) presents an integrative theory of consciousness called "global workspace" (GW) Theory. Baars' theory is founded on the view that the brain is composed of many different parallel "processors," (or modules) each capable of performing some task on the symbolic representations that it receives as input. The modules are flexible in that they can combine to form new processors capable of performing novel tasks, and can decompose into smaller component processors. Baars treats the brain as a large group of separable "partial processors", very specialized systems that function at the unconscious levels much of the time. At least some of these partial processes can take place at the conscious level when they organize to form "global processes." Global processes carry the conscious information and are formed from competing and cooperating partial processors (Baars, 1988). According to Baars, conscious awareness is subject to "internal consistency." This implies that multiple-constraint-satisfaction characterizes the interacting partial processors when they participate in the global process. This model of the brain is well supported by evidence from brain studies (see above) and studies of patients with brain damage (Roland, 1993). The model also complies with the notion that the brain is composed of interacting elements (i.e., information processors) and is multiply constrained.

To explain the differences between conscious and unconscious processes, Baars turns to the popular models of distributed-processing systems (i.e., neural network models; (Herz *et al*, 1991). Baars proposes that a similar structure exists in the human brain, and that it supports conscious experience. The structure, which he terms the global workspace, is accessible to most processors, meaning that most processors potentially can have their contents occupy the working memory. The global workspace can also "broadcast" its contents globally in such a way that every processor receives or has access to the conscious content. Significant, though, is the idea that only one global process can be conscious at one instant. In other words, consciousness is a serial phenomenon even though its unconscious pre-determinants are parallel processes. Baars' important claim about consciousness is that it has internal



consistency, a property not shared by the collection of unconscious processes in the brain. Baars cites as an example of this property the experience of viewing a Necker-cube, an optical illusion which we can consciously see in one of two different orientations. The two views of the cube can "flip" back and forth, but we cannot entertain both of them simultaneously. In other words, our conscious experience of the cube is consistent. A similar situation is found with ambiguous words. People seem to be capable of having but one meaning of a given word in mind at one time. There is evidence, though, that the alternative meanings are represented unconsciously in the brain at the same time as the conscious meaning, in that the other meanings of such words often show priming effects on sentence comprehension (Manschreck, 1988; Neely, 1977). This indicates that, while conscious processes are consistent, the collection of unconscious processes are not.

To summarize, Baars postulated a theoretical workspace where global processes are formed from the interactions of many partial processes. He postulated that the global formations in the workspace carry the global dominant message of conscious awareness (Baars, 1988). Partial processes are specialized processes, each processing its information in an independent fashion. They function in parallel and if not involved in any global organization, they proceed disconnected from other processes. Partial processes compete, cooperate and interact to gain access to and participate in global organizations. The global formation may be viewed as a complex network of partial processes. In global formations, there are internal consistencies and thus multiple constraints are formed between the partial processes. When partial processes participate in the organization of a global process, they are constrained by the activity patterns of the global formations. Thus, partial processes can no longer function (i.e., process information) regardless of the message. Partial processes are fast, highly specialized and aimed at handling certain specific types of information. They are, however, limited in the extent of the information they can process, and they lack the flexibility and adaptability acquired when many partial processes combine and cooperate to act together. Global formations have the advantage of both complexity and flexibility needed for efficient and elaborate information processing.

Combining Baars' theory with notions about hierarchical organization of information (memories) in the brain (see above), it is reasonable to consider that lower-level partial processes in the nervous system interact to form higher level neural global organizations. In addition, the idea of internal consistency in global formations captures the basic notion of

multiple constraint organization. It is assumed that the dynamic activity of partial processes demonstrates both hierarchical and multiple constraint organizations. For example, once the partial process makes part of the global organization it is interconnected with all the other processes (i.e. is broadcast globally). Thus, it contributes to, or influences, the global organization by virtue of its connections, i.e., by exerting its output through the connections to the rest of the system. On the other hand, because it is a multiple constraint system, many other processes will constrain (through the connections) its activity. One may conclude that from the information processing point of view, the information delivered by partial processes influences and is influenced by the global message at the same time. Due to internal consistency, if the information structure (i.e., activation pattern) of the partial process “contradicts” (i.e., markedly differs from) the information being represented in the global formation, the partial process will have “difficulty” gaining access to (or fitting with) the global process. This is due to the multiple constraints between the partial process and the global formation, which will not be satisfied in this case. Since global formations are higher levels of organization (from the hierarchical point of view), by constraining partial processes which are probably of lower levels, top-down control blocks access of partial processes to global formation (i.e., “repression”). Partial processes compete for access to global formation, creating the bottom-up procedure. Thus, a balance between bottom-up and top-down processes becomes crucial for the contents that reach global formations and consciousness.

Tononi and Edelman (1998) combine the above insights with other findings of theirs and formulate the concept of the “dynamic core.” The dynamic core explains which neural processes underlay conscious experience. Tononi and Edelman conclude that a group of neurons can contribute directly to conscious experience only if it is part of distributed functional cluster of high millisecond range integration as well as a highly differentiated complexity (i.e., ability to choose from many different states). The dynamic core is a functional cluster of neurons in the sense that the participating neuronal groups are much more strongly interactive among themselves than with the rest of the brain. In addition, the dynamic core must also have high complexity in that its global activity patterns must be selected within less than a second out of a very large repertoire. The dynamic core would typically include posterior corticothalamic regions involved in perceptual categorization interacting reentrantly with anterior regions involved in concept formation, value-related memory, and planning. The dynamic core is not restricted to an invariant set of brain regions; it continuously changes composition and patterns over time. The formulation of the “dynamic

core” as presented by Tononi and Edelman (1998) summarizes many of the ideas about consciousness and brain organization presented so far. Firstly, it incorporates the idea of global workspace as a globally distributed functional cluster of neuronal groups. Secondly, it refers to the brain organization at the edge of chaos (balanced between orderliness and randomness) by introducing the idea of the simultaneous need for integration and differentiation within the dynamic core. Finally, the dynamic core refers to the transmodal connectionist systems at the highest levels of brain hierarchical organization pointing to the relevant formulations about memory and mental functions by Fuster (1997) and Mesulam (1998).

In complex systems the dynamics of constraint satisfaction among the units is in continuous flux of change in time and can proceed in two directions; 1) optimization, when more constraints become satisfied over time; and 2) deoptimization, when fewer constraints are satisfied over time. It is proposed here that optimization correlates with the emergent property of elevated mood and deoptimization dynamics correlates with depressed mood. Thus, it is speculated that mood is an emergent property related to the level of optimization dynamics within the dynamic core. Optimization-dynamics takes into account the configurational space of internal representations because optimized are the various configurations and arrangements of state-space. Optimization-dynamics also involves sets of incoming stimuli (from environmental and psychosocial events) because their interpretation involves activations and optimizations of the configuration map with its various internal representations. Normally, optimizations and deoptimizations occur mixed together. The information processing in the brain optimizes certain internal configurations and deoptimizes others in a parallel manner. The overall dynamics is thus stabilized between numerous optimizations and deoptimizations. In such balanced conditions the emergent property of mood is balanced. However, if many configurations are deoptimized and a shift of balance toward deoptimization takes over the system, this will result in the emergent property of depression of mood. Homeostatic mechanisms will probably act to balance this dynamic shift by triggering optimization-dynamics to counter-act the deoptimizations in the system. If the system is taken over by oscillatory dynamics between optimizations and deoptimizations, mood will also oscillate between mania and depression resulting in the well-known psychiatric entity of manic-depressive disorder.

Whenever constraint satisfaction in the brain tends to be disturbed, “frustration” of the connection between the elements in the system occurs. Frustration is the term used to indicate that connections are only slightly unsatisfied. In other words, frustration of constraints implies that the elements of the system act barely in ‘disagreement’ with the multiple connections among them. The elements in such a system will change their states (i.e., values) in an attempt to reach full satisfaction of the constraints, and continue to change as long as frustration of constraints characterizes the system.

Since the brain is a dynamic system (Globus, 1992), once connections are satisfied, the system has already changed, and a new set of constraints needs satisfaction. As such, a certain degree of ongoing frustration is typical to the system of the dynamic core. If the frustration of the constraints increases, the dynamic process of constraint-satisfaction increases, causing the elements to change their states more abruptly. If the frustration of constraint increases even more, surpassing the dynamic ability of the elements to change their states, a ‘danger’ of breakdown threatens the connections. Since the dynamic core has a massive connectivity structure, multiple constraint frustrations can “spread” over many connections in the cluster system, and to some extent be “absorbed” by the interconnected structure of the system. This process of absorbing the frustrations of the constraints maintains the stability of the global integration within the dynamic core. It is suggested that whenever the degree of frustrations applied to the multiple connectivity of the system exceeds the level where it can be absorbed, the system is “destabilized,” and the risk of rupture to the connections becomes prominent. At this level of disturbance, elements in the system change rapidly in a “desperate” attempt to satisfy their connections. It is suggested that anxiety is the emergent property from this type of instability in the neural systems especially in those neural systems that are involved in global formations such as transmodal processing systems of the dynamic core.

To comprehend how optimization of internal representations can be relevant to mood changes let us assume that based on past experience (i.e. experienced dependent plasticity) the brain has acquired a set of internal configurations (attractor formation in the space manifold) to represent “succeeding in an examination” in which there is a socially favoured achievement. Now let us assume that the person with such internal representation has performed an important examination and has just received the news (i.e., the information stimulus) that he has passed the examination. The interaction of such information with the map of internal

configuration will shift part of the system dynamics towards an optimization mode of activity. Such a shift would emerge as a feeling of satisfaction elevated mood. In the unfortunate case of failing the exam, the same internal configurations would be deoptimized, resulting in a depressed feeling of disappointment. This example is oversimplified. There is a need to consider both the complexity of internal representations as well as the dominant patterns of dynamics in the system. The internal representation of succeeding in the exam could be interconnected with many other internal representations that may extremely amplify the effect of optimization. For example, if the internal representative configuration of succeeding in the exam is linked to the internal representative configuration of love from a parent, then feeling loved by the parent can be associated with the optimization dynamics of success in the exam, amplifying substantially the mood effect of this achievement.

Another example associates conflicting information processing and anxiety. Let us assume that a population of neurons processes certain information assuming an activation pattern relevant to that information. During the information processing constraints among neuronal ensembles, become satisfied toward the relevant information-dependent pattern of activity. Now imagine that another set of information is applied simultaneously to the system, however, this other information contradicts the original information pushing the system to an opposing configuration in comparison to the original information patterns. The result is that units in the system are simultaneously constrained to “comply” with opposing patterns of activity. Opposing patterns of activated units will disturb the process of constraint satisfaction taking place in the system causing augmented frustration to the constraint satisfaction processes among units in the system.

Assuming that anxiety is the emergent property from constraint frustration in the system, it is comprehensible why conflicting information processing increases the sensation of anxiety. Conflicting information processing involves experiencing opposing stimuli as well as confronting opposing actions in decision-making. In effect, our environment as well as our brain system are dynamically changing to provide continuous frustration on constraints in our brain system, thus allowing for a continuous physiological life-long level of anxiety to characterize our psychic awareness.

Now that brain dynamic processes have been reviewed, it is important to see if they can be relevant also to psychoanalytic formulations described by psychologists. The first concepts

introduced by Freud in his “topographic model” (Freud, 1953) related to the levels of consciousness. We now have the tools to define his description of conscious, unconscious and subconscious as levels of integration that partial processes achieve to form the global organizations of the dynamic core. Conscious awareness is the property of global integrations, while partial processes that do not make part of the global organizations present unconscious information. Those processes that are about to make part of, or drop out of, the global formations characterize the subconscious. In the “structural model”, psychic ‘compartments’ such as the “ego” and “id” were added (Freud, 1953). The ego develops from where initially all was id in the infant. The id is described as a disorganized system where concepts are disconnected or dissociated in every ‘strange’ possible way. Freud named this form of inconsistency “primary thought process.” From the point of view described so far, primary thinking can be conceptualized as a feature of a system without internal consistency, or in other words, where multiple constraints are abolished. This enables conflicting ideations and nonsense concept-formations to coexist and predominate consciousness. Biological evidence shows that in infants synaptic connectivity is premature (Roland, 1993). Thus, the neural substrate cannot support the needed multiple-constraints organization that forms the basis of ordered mental activity. Ego development involves the formation of “secondary thought process” (Freud, 1953); a process described by Freud as normal thinking. In other words, secondary thinking emerges from multiple-constraint-satisfaction organization of the neural system and in fact, synaptic connectivity matures from infancy to adulthood. By introducing the concept of superego, Freud suggested internal representations of social and interpersonal norms. It gave the ego (i.e., its superego portion) not only the scope of organizing the disordered id processes but also the entire responsibility of representing and adapting to psychosocial reality. Introduction of the “dynamic model” (Freud, 1953) added an interplay of “drives” among the psychic compartments of Freud’s model. “Defense mechanisms” are probably the dynamic factors most accounted for in this model. According to Freud, the ego makes use of an unconscious domain of mental activity (the id) into which undesirable drives and ideas are repressed. “Repression” has been described as the mental mechanism that “guards” the conscious awareness from the intrusion of inadequate and intolerable ideas or drives. Freud indicated that the intruding ideas and drives from the unconscious threaten ego integrity. Repression can be re-conceptualized as the dynamics of participating, as well as non-participating processes in the global formations that support conscious phenomena. Partial processes that do not gain access to the global process remain unconscious, (i.e., repressed). Due to the multiple-constraints that characterize global

organizations, certain partial processes may encounter “difficulty” in accessing the global formations. This is especially true if the partial processes carry information (i.e., arrangement pattern) that is entirely removed from, or contradictory to, global messages (see above). Based on these assumptions it is possible to conceive what type of information will be denied access to the global organization; it will be the contradictory and unfitting messages. In neuronal terms it will be the partial arrangement pattern that does not satisfy the constraints of global arrangements. In fact, Freud described the repressed contents as “conflicting” topics or unbearable ideas. Here, unbearable stands for the partial process that is removed from (i.e., “unfitting” to) the information pattern presented by the pattern of the global integration. The partial process cannot be incorporated in the general message without damaging its internal consistency and integration, therefore, it is bound to be excluded. For example, to a mother of a newborn baby the idea of killing her baby is extremely contradictory to the regular loving and “caring state-of-mind” typical to a new mother. If inadequate partial processes somehow gain access to the global organization they are inclined to destabilize or even disrupt it. If many conflicting and disrupting processes gain access to the global formation, the whole global message may be destroyed and the neural system representing it is bound to destabilize. Indeed, the types of thoughts which involve killing one’s newborn baby often emerge in mentally disturbed patients. It is thus conceivable that in fact certain partial processes actually do threaten the integrity of global formations and the actual stability of the dynamic core. This description conforms to Freud's notion of ego integrity that is being threatened by repressed mental processes of conflicting ideas or drives. Occasionally, inadequate partial processes may gain access to the global organizations and are ‘transformed’ in order to accommodate the global pattern. For example, immoral ideation is contradictory to the dominating content of a moralistic conscious awareness. Transforming the wish to behave in an immoral way into moralistic ideation may accommodate the dominating global organization of a “puritanical message.” This type of transformation is known in the psychoanalytic literature as “reaction-formation.” Another transformation of unbearable ideation is known as “isolation.” Here, the ideation is not excluded from awareness, only certain relevant parts of it are “neutralized.” These are the parts that are incompatible with the rest of the conscious message. The partial process is included in the conscious awareness only to the extent (i.e., it is isolated) that it is removed from certain contents of the conscious awareness. If isolation is not enough to satisfy the message of the global integration then “dissociation” might occur and certain contents of awareness would be ignored or experienced as independent and unrelated. The “transformations” described

above are needed in order to protect the global formation from being disrupted by contradicting partial processes. Therefore, it is conceivable that these transformations justify the term “defense mechanism.” They protect the global formations and prevent destabilization of the dynamic core. From the biological point of reference, this may translate into destabilization of the interrelations between groups of neurons, which presumably has direct neuro-pathological outcomes on transmitter-receptor activity.

Followers of Freud such as Winnicot, Klein and Mahler developed what was later termed “object relation psychology.” They concentrated on the study of the dynamics of internal presentations and their relevance to personality and personality disorders. Personality traits are enduring patterns of perceiving, relating to, and thinking about the environment and oneself. They are exhibited in a wide range of social and personal contexts (Sadock, 1989). Specific configurations of internal representations have first-hand impact on personality traits. For example, internal representations regarding hygiene, punctuality and precision, are more pronounced for some individuals, while for other individuals other representations are prominent; e.g., vanity and pride. The first example is typical of individuals who give special importance to order and strive to achieve perfection. These individuals are often referred to as having “obsessive” personality traits. The second example is more typical of individuals who regard themselves as special and important. They are often referred to as having “narcissistic” personality traits. Individuals who attribute importance to hygiene (i.e., optimize these internal representations of context), will perceive a stimulus carrying information of dirt and filth differently than individuals who do not have this type of attribute. Once “decoded,” the map of internal representation can both explain and predict the reaction of the individual to certain stimuli. In the case of “personality disorders”, the optimization of particular internal representations of context may be enhanced to the extent where certain stimuli may be perceived with incredible distortion. For example, someone with an obsessive personality disorder may perceive even a little dust on the table as extreme filth. An individual with a narcissistic personality disorder may interpret even slight disapproval as an extreme insult. The formation of specific configuration maps in different individuals depends on the background of the individual. Individuals reared in families that give emphasis to being sanitary will probably encode this “emphasis” through experience-dependent-plasticity. Individuals reared in environments in which they were considered of prime importance and were the centre of attention will probably incorporate these attitudes by optimizing the need to receive affection and attention (narcissistic traits). The experience-dependent processes



responsible for the formation of internal representations may involve deviations from the ‘normal itinerary’ of internal representations needed for ‘regular’ psychosocial function. These deviations may form internal representations that are greatly removed from psychosocial reality. A large mismatch between the internal representations and the environmental reality is likely to provoke distortions that lead to disturbances in perceiving and reacting to the environment (i.e., personality disorders). To a certain extent, incoming information from environmental stimuli may be conceptualized as partial processes competing to gain access to global organizations of conscious awareness (see above). A large mismatch between the internal map of representation and the pattern of environmental stimuli is likely to create the same difficulties that conflicting partial processes may encounter when trying to gain access to global organizations of conscious awareness. This mismatch may distort the incoming information. A good example of this distortion is seen in the phenomenon of “transference.” Transference is a distortion within interpersonal relations, it occurs when people are perceived not as they are, but rather as somebody who resembles them from the past (Michael, 1986). Thus, the perception of an individual is distorted to ‘fit’ the internal representation of a similar person encountered in the past. Since incoming stimuli are “evaluated” by the internal representations that are formed by experience, it is only natural that many of the perceptions we have are related to past experience. When sets of stimuli from a new interpersonal event interact with the neural system, they activate a set of attractors representing past experience similar to the new interpersonal situation. If there is substantial mismatch between the internal representations from the past situations and the actual psychosocial event, a distortion of the actual situation may occur (i.e., transference). Matching complexity (see above) may be the future mathematical tool that will predict to what extent transference is likely to determine one’s behaviour.

Sometimes a current experience is so far removed from any context of experience that it becomes entirely unperceived by the individual. This is defined by psychodynamic terminology as “denial”. An individual with narcissistic personality traits may not perceive signs suggesting that he is not desired. This is because in his map of internal representations there is no context (i.e., attractor system) that represents rejection. Since the representation of rejection will not be activated at all, it will not manifest in the global organization of state-space and will remain entirely out of any conscious awareness (denial).

To summarize, unifying the theoretical considerations detailed so far, it is assumed that: 1) Consciousness arises as a property (i.e., emergent property) out of the global organizations. 2) Different levels of consciousness and awareness correlate with different levels of organization in global formations. 3) Since partial processes in their segregated forms do not support conscious phenomena, they remain in the ‘unconscious domain.’ Thus, the unconscious is simply a lower level of information processing that has no access to global formations. 4) The subconscious is the level of information on the border of gaining access to, or dropping out from, the global formations that are part of higher-level organizations. 5) Higher-level neuronal organizations supporting consciousness are on-going processes simultaneously influencing lower level processes (top-down modulations) and being influenced by incoming stimuli (bottom-up processes).

The entire set of conscious awareness results from the ongoing dynamic connectivity of the brain (the dynamic core). The history of this awareness involves a gradual but phase-transition evolution of brain development. First, the brain organization shows weak connections. Gradually, as the nervous system matures it provides both for increasing integration of sensory inputs and more complex reactions and manipulations of the environment.

The increasingly complex interactive relations with the environment (see above) via experience-dependent plasticity and matching complexity provides for the evolutionary process that culminates with the formation of normal mental functions. Simple environmental events, as well as more complex interpersonal psychological occurrences, organize by the dynamic core into normal mental awareness.

In mental disturbances, such as psychosis and schizophrenia, awareness is much different and reality is perceived differently, both at the lower level of perception (e.g., auditory hallucinations) as well as at relatively higher levels of conception of thinking (e.g., delusions of persecution). This different organization of reality is non-adaptive causing dysfunction, handicap and suffering, thus justifying the definition of “illness.”

In mental disturbances, overly optimized or deoptimized internal configurations could be relevant to the emergence of mood shifts and affective disorders. Personality disorders involve specific “sensitivities” which cause inflexible non-adaptive suffer-generating reaction

modes within interpersonal settings. These “sensitivities” probably result from distorted awareness of psychological interpersonal events (i.e., poorly matching experience-dependent internal-representations or maps of organismic evaluation).

Applying the above terminology from complex system theories to psychiatric neuroscience proposes that mental disorders could one day be understood better in the context of brain dynamics. Such understanding would provide for better and more reliable etiology-oriented diagnosis in psychiatry. Ultimately better etiology-directed therapeutic interventions may develop. The following chapters will attempt to develop a new approach to psychiatric diagnosis and therapy.

## TRANSLATING DSM INTO NM

The phenomenology described in this chapter is based on items of commonly used rating scales (PANSS, HAMD, HAMA, YMRS see References) which themselves are based on the DSM approach of descriptive psychiatry

### PSYCHOSIS

#### **Phenomenology of Psychosis**

Psychosis with predominantly thought disturbances and hallucinations. Generally, has difficulty in organizing thoughts, as evidenced by frequent irrelevances, disconnectedness. or loosening of associations even when not under pressure. Agitation or over arousal is clearly evident episodic outbursts occur sporadically, Movements are notably awkward or disjointed. Hallucinations occur frequently but not continuously. These may involve more than one sensory modality, and tend to distort thinking and/or disrupt behaviour. As symptoms increase then, thoughts are disrupted to the point where the patient is incoherent. There is marked loosening of associations, marked excitement delimits attention, and affects personal functions such as eating and sleeping Frequent repetition of bizarre rituals, mannerisms, or stereotyped movements. Hallucinations are present almost continuously, causing major disruption of thinking and behaviour. Patient treats these as real perceptions, and functioning is impeded by frequent emotional and verbal responses to them.

Psychosis with predominant Delusions. Presence of numerous well-formed delusions that are tenaciously held and occasionally interfere with thinking, social relations, or behaviour. When delusions become more severe then, distrustfulness is clearly evident, Patient shows marked distrust, there are clear-cut persecutory delusions that have impact on interpersonal relations and behaviour. Ideas are frequently distorted and seem quite bizarre. As the psychosis with delusions becomes more severe, presence of a stable set of delusions which are crystallized, possibly systematized, tenaciously held, and clearly interfere with thinking, social relations, and behaviour. These frequently result in inappropriate and irresponsible action, which may even jeopardize the safety of the patient or others. These can become

clear-cut pervasive delusions of persecution which may be systematized and significantly interfere in interpersonal relations. Patient expresses many illogical or absurd ideas or some which have a distinctly bizarre quality

### **Brain Dynamics of Psychosis**

The 'disconnection syndrome' as described by Friston (1995) and has been replicated many times since then. Some of the early findings supporting a disconnection syndrome for schizophrenia psychosis are: (1) Principal component analysis of PET data suggests that the normal inverse relationship between frontal and temporal activation on a verbal fluency task is disturbed (they show weak positive correlation). This finding may suggest disintegration between the two areas in schizophrenia patients (Frith et al. 1991). (2) Studies with Functional MRI replicate these findings (Yurgelun-Todd et al. 1995). (3) Subjects imagining another person talking activate left inferior and left temporal cortices (McGuire et al. 1995). Schizophrenia patients not suffering from hallucinations have the same activation pattern as normal subjects. Schizophrenia patients suffering from hallucinations show a reduction in activity of the left temporal cortex, despite normal activation of the left inferior frontal region (McGuire et al. 1993). (4) Phencyclidine (PCP) is a psychomimetic drug that induces schizophrenia-like symptoms (Allen and Young 1978). PCP is a potent inhibitor of N-methyl-D-aspartate (NMDA) glutamate receptors. Glutamate neurotransmission is the mainstay of the excitatory cortico-cortical interactions (Friston and Frith 1995). (5) Reduced EEG coherency between frontal and temporal electrodes are highly correlated with reality distortion symptoms in schizophrenia, suggesting disruption of fronto-temporal connectivity (Norman et al. 1997). More recent findings that support the disconnection hypothesis involve EEG coherence task-locked to the delay-response epochs of a working memory test. Schizophrenia patients showed less coherent activity during the delay period of the working memory task (Peled et al. 1999). Previous work with gamma-complexity also showed loosened cooperation in the anterior brain regions of schizophrenic patients (Saito et al. 1998) and in acute neuroleptic-naive first-episode schizophrenia patients. Dissociated complexity levels partially regressed, similar to premature brains at an earlier, age were found in schizophrenia patients during a study of the neurodevelopmental hypothesis of schizophrenia (Koukkou et al. 2000). These findings started to indicate that psychosis may result, or is an emergent property, from global disintegration of the dominant brain organization, as this

neuro-system disconnection fragments conscious experience. The specific clinical patterns of psychosis relate to the different neuronal subsystems which are affected.

As consciousness is a result of global brain connectivity organizations, It is thus conceivable that disturbances to connectivity in the brain will fragment the higher-level conscious experience with sensations and concepts disconnected and statistically independent from each other. Thus, thoughts organized as interdependent neuronal activations will become disconnected and unconstrained, causing the individual to suffer from loosening of associations. Since logic is built on semantic integrated network concepts, logical thinking becomes impaired, causing biased erroneous ideas to form (delusions). With the spread of disconnection dynamics loosening of associations in the form of disordered speech is evident and biased erroneous conclusions form. The hierarchal top-down processes may become overly active and constrain information via top-down shifts and thus maintain and increase erroneous conceptualizations (delusions) by damage to the error-prediction and correction processes known to occur normally in the brain.

Disconnection-dynamics spreading in the cortex, causes also more macro-network disintegration that may cause entire neuronal systems to disconnect from whole brain organization. For example, the auditory cortex with its speech-related adjacent cortical network can become disconnected from the brain with the emergent property of experiencing talking voices emerging from the disconnected brain systems while there is no real auditory input to the brain and regardless of other brain systems such as the visual one. The experience of the patient in such a case will be that of auditory complex hallucinations as they are typical manifesting in schizophrenia.

The above description indicates how positive symptoms of functional psychosis are explained by disconnection dynamics both in general as well as hierarchal in the brain. This description is supported by many papers in the literature that discuss disconnection and small-world disturbances in psychotic and schizophrenic patients (Guye et al., 2010). In addition, neuronal network models simulating psychosis and schizophrenia-like phenomenon support this notion (Peled & Geva, 2000; Geva & Peled, 2000).

As the phenomenology of psychosis happens in the millisecond range (thoughts, perception cognition is fast millisecond range occurrences) and are related to functions described for the

Central Executive Network (Fabian & Martial 2002), it is assumed that the formulations of brain dynamics underlying psychosis are located in the CEN and millisecond range time window.

### **New Neuroanalytic Diagnosis of Psychosis.**

Psychosis is the result of disconnection dynamics in the brain, meaning that different neuronal networks which normally function in synchronization and optimized harmony are disintegrated disconnected and act statistically independent from each other. As seen when the global workspace of transmodal organization fragments conscious experience is likewise fragmented. This causes experience to fragment and patient to become disorganized. Speech is fragmented as different semantic associations become disjointed. Logic collapse and erroneous activations form delusional conceptions.

Hallucinations happen when entire brain processors such as speech language processors become disconnected from the global brain organization and from environmental external inputs.

With disconnection brain hierarchal organization is altered and Top-Down shift may overrun normal error correction fixating top-down erroneous configurations thus fixating and increasing delusional contents.

All this happens in the neuronal networks of the Central Executive Networks responsible for the integrative conscious experience. As thoughts and perceptions are millisecond-range phenomena then the disturbances of connectivity and hierarchy are also millisecond range time-scale disturbances.

Optimal brain dynamic connectivity organization is that of Small World Network (Basset Bulmore 2016) organization thus it is expected that the disconnection syndrome of psychosis is a disturbance to Small World Network organization for example the Cluster Coefficient of nearby connections compared to far away connections. The implications on state-space global workspace and dynamic core are all a result of disconnection and fragmentation dynamics

## NEGATIVE SIGNS

### **Phenomenology of Negative Signs Alogia & Avolition**

In cases with predominant Alogia, thinking is rigid and repetitious thus conversation is limited to only two or three dominating topics. The patient deals primarily in a concrete mode, exhibiting difficulty with most proverbs and many categories. Conversation lacks free flow and appears uneven or halting. marked lack of spontaneity and openness, replying to questions with only one or two brief sentences. Affect is generally flat, with only occasional changes in facial expression and a paucity of communicative gestures. As symptoms worsen thinking, behaviour, and conversation are dominated by constant repetition of fixed ideas or limited phrases, leading to gross rigidity, inappropriateness, and restrictiveness of patient's communication. The patient can use only concrete modes of thinking. Shows no comprehension of proverbs, common metaphors or similes, and simple categories. Patient's responses are limited mainly to a few words or short phrases intended to avoid or curtail communication. Conversation is seriously impaired as a result. Marked flatness and deficiency of emotions exhibited most of the time. Patient seems constantly to show a barren or "wooden" expression. In severe cases patient is highly indifferent, with marked interpersonal distance. Eye and face contact are frequently avoided.

In cases with predominant Avolition patient shows pronounced indecision that impedes the initiation and continuation of social and motor activities, and which also may be evidenced in halting speech. Patient is clearly detached emotionally from persons and events in the milieu, resisting all efforts at engagement. Patient appears distant, docile, and purposeless Patient typically is aloof, act bored, or express disinterest. Dis-involvement is obvious and clearly impedes the productivity of the interview. Patient may tend to avoid eye or face contact. Passively participates in only a minority of activities and shows virtually no interest or initiative. As Avolition becomes worse it interferes in the execution of simple, automatic motor functions such as dressing and grooming, and markedly affects speech. Failure of volition is manifested by gross inhibition of movement and speech, resulting in immobility and/or mutism. Patient is almost totally withdrawn, uncommunicative, and neglectful of personal needs as a result of profound lack of interest and emotional



commitment. Apathetic and isolated, participating very rarely in social activities and occasionally neglecting personal needs.

### **Brain Dynamics of Negative Signs**

There is less literature about the probable opposing dynamics of Over-Connectivity in the brain. It is well known that increase of connection-strengths in a network model causes the dynamic activity of that model to constrain and even stop. This is typical of a fully connected Hopfield Network (1982) that shows local minima dynamics of restricted activity halting at the attractor base of local-minima. Other work showed (Geva & Peled, 2000) that increasing connectivity dynamics in network models constrain their activity to few attractors in space state and also shows tendency to repeat and get “stuck” in attractors. This is metaphorically similar to the reduced thought process of negative-signs schizophrenic deficient patients with their tendency to perseverate, which is actually the activation of the few repeated states in the model. Thus, the poverty of thought and perseverations are naturally simulated by over-connectivity dynamics in the brain models.

Another possible aspect of Over-connectivity relates to hierarchy because with fixated connections the bottom-up brain hierarchal organization is hampered. Higher-level construct cannot be formed and this curtails higher-level hierarchal organizations in the brain also resulting in Avolition, loss of motivation, which is one of the more debilitating manifestations of negative-signs schizophrenia. In all, the Over-connectivity dynamics in the brain can begin to explain the negative and deficient signs and symptoms of schizophrenia.

Schizophrenia is probably an “oscillating disorder” starting with positive symptoms and progressing over time to deficiency, negative signs and symptoms. Thus, from the point of connectivity conceptualizations, patients' brains oscillate between disconnection and over-connection dynamics. As the disease progresses the connectivity organization is progressively damaged, with progression of negative symptoms increasing over-time. In a very general manner, the spectrum of schizophrenia phenomenology manifestations can be re-conceptualized as disorders of brain-connectivity organization broken down to disconnection over-connection and hierarchical top-down and bottom-up disturbances.

Similarly to psychosis also the brain dynamics described for negative signs are presumably located in the CEN and millisecond range time window extended over time to deteriorating progressive dynamics.

### **New Neuroanalytic Diagnosis of Negative Signs**

In Negative Signs schizophrenia-like conditions over-connectivity dynamics takes over the activity of the Central Executive Networks. Connections are strengthened and fixated causing increase of mutual constraints among networks. Consequently, the space state of the brain is reduced (poverty of thought) the brain dynamics tends to limit and fixate in “Local Minima” i.e., preservations Alogia.

Higher-level transmodal optimization is hampered and the emergent property of Volition is damaged and even eliminated

## ANXIETY

### **Phenomenology of Anxiety**

Significant physical and behavioural consequences, such as marked tension, poor concentration, palpitations, or impaired sleep. Moderate worries, anticipation of the worst, fearful anticipation, irritability. Feelings of tension, fatigability, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax. Moderate fears of dark, of strangers, of being left alone, of animals, of traffic, of crowds. Moderate difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors. Moderate combined somatic symptoms

With more severe anxiety the patient experiences subjective state of almost constant fear associated with phobias, marked restlessness, or numerous somatic manifestations. At times reaches panic proportions or is manifested in actual panic attacks. Marked worries, anticipation of the worst, fearful anticipation, irritability. Feelings of tension, fatigue, startle response, moved to tears easily, trembling, feelings of restlessness, inability to relax. Marked fears of dark, of strangers, of being left alone, of animals, of traffic, of Crowds. Marked difficulty in falling asleep, broken sleep, unsatisfying sleep and fatigue on waking, dreams, nightmares, night terrors. Marked combined somatic symptoms

### **Brain Dynamics of Anxiety**

In order to analyse the emergent phenomena of anxiety we go back to refer to the idea of constraints among brain units (and states) caused by connectivity and mentioned above. In a system, “connection” signifies constraint and the fact that different parts are not independent.

As already mentioned, “Multiple constraint satisfaction” accounts for the interrelations among multiple units in a system. If the value of the connection-strength between the brain units is substantial, then the constraint of the activity in one brain unit on the activity in the other brain unit is substantial. Conversely, if the strength of the connection is small, then the activity in a brain unit will be less constrained by the activity in the relevant brain unit. In the brain with numerous interconnected brain units, each brain unit simultaneously influences

(i.e., constrains) several other brain units, thus the activity of each brain unit is a result of multiple parallel constraints.

When the activity of a brain unit satisfies the input exerted on it by the other connected brain units it, it achieves multiple constraint satisfaction. If the activities of all the units in the system achieve multiple constraint satisfactions, then the system optimizes multiple constraint satisfaction.

Whenever constraint satisfaction in the brain tends to be disturbed, “frustration” of the connection between the elements in the brain occurs. Frustration indicates that connections are only slightly unsatisfied and implies that the elements of the system act barely in ‘disagreement’ with the multiple connections among them. The elements in such a system will change their states (i.e., values) to reach full satisfaction of the constraints, and continue to change if frustration of constraints characterizes the system.

Since the brain is a dynamic system (Globus 1992), once connections are satisfied, the system has already changed and a new set of constraints needs satisfaction. As such, a certain degree of ongoing frustration is typical to the system of the dominant dynamic state. If the frustration of the constraints increases, the dynamic process of constraint-satisfaction increases, causing the elements to change their states more abruptly. If the frustration of constraint increases even more, surpassing the dynamic ability of the elements to change their states, a "danger" of breakdown threatens the connections.

Since the dynamic dominant brain trajectory results from a massive connectivity structure, multiple constraint frustrations can “spread” over many connections in the brain system, and to some extent be “absorbed” by the interconnected structure of the entire system. This process of absorbing the frustrations of the constraints maintains the stability of the global integration within the dominant brain state.

It is suggested that whenever the degree of frustrations applied to the multiple connectivity of the system exceeds the level at which it can be absorbed, the system is “destabilized,” and the risk of rupture to the connections becomes imminent. At this level of disturbance, elements in the system change rapidly in a “desperate” attempt to satisfy their connections. It is suggested that anxiety is the emergent property from this type of instability in the neural systems

especially in those neural systems that are involved in global formations such as transmodal processing systems of the dynamic dominant brain state.

This model can explain possible relations between conflicting ideas, actions or motivations and anxiety. Let us assume that a population of neurons processes certain information assuming an activation pattern relevant to that information. During the information processing constraints among neuronal ensembles become satisfied toward the relevant information-dependent pattern of activity. Now imagine that another set of information is applied simultaneously to the system. However, the new information contradicts the original information pushing the system to an opposing configuration in comparison to the original information patterns. The result is that units in the system are simultaneously constrained to “comply” with opposing patterns of activity. Opposing patterns of activated units disturb the process of constraint satisfaction that takes place in the system and causes augmented frustration to the constraint satisfaction processes among units in the system.

Assuming that anxiety is an emergent property of constraint frustration in the system, it is comprehensible that conflicting information processing increases the sensation of anxiety. Conflicting information processing involves experiencing opposing stimuli and confronting opposing actions in decision-making. In effect, our environment as well as our brain system is dynamically changing to provide continuous frustration of constraints in our brain system, thus allowing for a continuous physiological life-long level of anxiety to characterize our psychic awareness.

From the above we can learn that neuronal networks in constant flux of activation inhibition and reconfiguration are constantly changing and are thus unstable. Stability is perturbed by the stimulated activity from the environment and by the “computational load” that characterize neuronal networks activities. These are stabilized by the slightly longer plasticity, the “Reactive Plasticity”, which is responsible for maintaining the constraints among working networks and their elements. Frustration of constraints implies that the elements of the system act minimally when in “disagreement” with the multiple connections among them. The elements in such a system will change their states (i.e., values) to reach full satisfaction of the constraints, and will continue to change as long as frustration of constraints characterizes the system.

The networks that are stabilizing brain connectivity typically those of slower plasticity, i.e., the DN and the DMN are typically perturbed more than usual when anxiety occur, this has been recently confirmed by a review made by Van Oort (2017) he found that the acute stress response is consistently associated with both increased activity and connectivity in the salience network (SN) and also with increased activity in the default mode network (DMN), These results confirm earlier findings of an essential, coordinating role of the SN in the acute stress response and indicate a dynamic role of the DMN and are in line with the Neuroanalytic theory.

### **New Neuroanalytic Diagnosis of Anxiety**

Anxiety is an emergent property from a globally spread perturbation of brain neuronal networks. The hubs of such network are the Salient Network subcortical Basal Ganglia with their connections to both the Central Executive as well as to Default Mode Networks. As the brain faces cognitive computations and external interactions it is perturbed because the multiple constraint satisfaction dynamics is challenged by the everchanging cognitive computational demand on brain networks. The perturbation of multiple constraint satisfaction generates Anxiety. This can be continuing for perturbations that result from constant stress. Perturbing events can be also in the timescale of minutes as is typical for panic attacks.

## DEPRESSION

### **Phenomenology of Depression**

Distinctly depressed mood is associated with obvious sadness, pessimism, loss of social interest psychomotor retardation, and some interference in appetite and sleep. The patient cannot be easily cheered up. Patient expresses a strong sense of guilt associated with self-deprecation or the belief that he deserves punishment. The guilt feelings may have a delusional basis, may be volunteered spontaneously, may be a source of preoccupation and/or depressed mood, and cannot be allayed readily by the interviewer. Patient is clearly slow in movements, and speech may be characterized by poor productivity, including long response latency, extended pauses, or slow pace. When depression worsens depressive feelings seriously interfere with most major functions. The manifestations include frequent crying, pronounced somatic symptoms, impaired concentration, psychomotor retardation, social disinterest, self-neglect, possible depressive or nihilistic delusions, and/or possible suicidal thoughts or action. If depression becomes severe to the extent of psychotic depression then strong ideas of guilt take on a delusional quality and lead to an attitude of hopelessness or worthlessness. The patient believes he should receive harsh sanctions for the misdeeds and may even regard his current life situation as such punishment. Movements are extremely slow, resulting in a minimum of activity and speech. Essentially the day is spent sitting or lying down.

### **Brain Dynamics of Depression**

We have already described (above) that adaptation is related to "optimization" in dynamic systems. Optimization is typically defined as the ability of a system to evolve until it approaches a critical point and then maintain itself at that point. If a particular dynamic structure is optimal for the system, and the current configuration is too static, then the more changeable configuration will be more successful. If the system is currently too changeable, then the more static mutation will be selected. Thus, the system can adapt in both directions to converge on the optimal dynamic characteristics.

In complex systems the dynamics of constraint satisfaction among the units is in continuous flux and can proceed in two directions; 1) optimization, when more constraints become satisfied over time; and 2) deoptimization, when fewer constraints are satisfied over time.

Previously, we assumed that the emergent property of anxiety results from constraint frustrations; now let us assume that depression is the emergent property whenever brain state dynamics is subjected to deoptimization.

Deoptimization shifts in the brain system could be triggered by the alterations of the neural substrate itself (i.e., neurohormonal and neurotransmitter activity). Probably the hormone or neurotransmitter directly alter the transfer functions of the neurons, or their connectivity patterns, and directly alter the space-state topology of the internal configurations. In this manner, configurations that were “normally” optimized could now be deoptimized triggering a deoptimization shift that induces a depressed mood.

To support the idea of neural network alterations in mood disorders there is growing evidence in recent studies that anti-depression treatment is related to plasticity and connectivity of neurons in hippocampal and prefrontal brain regions (Laifenfeld et al; 2002; Manji et al. 2003; Coyle and Duman 2003). Recent research into depression has focused on the involvement of long-term intracellular processes, leading to abnormal neuronal plasticity in brains of depressed patients, and reversed by antidepressant treatment (Laifenfeld et al. 2002). There is growing evidence from neuroimaging and postmortem studies that severe mood disorders, which have traditionally been conceptualized as neurochemical disorders, are associated with impairments of structural plasticity and cellular resilience (Manji et al 2003). Postmortem and brain imaging studies have revealed structural changes and cell loss in cortico-limbic regions of the brain in bipolar disorder and major depression (Coyle and Duman 2003).

In extremely stressful events, such as grief, or calamity, the external constellation of life events changes dramatically. The change typically involves “loss” (certain regular patterns of incoming stimulations are lost) these are the information patterns that represent the lost person or the lost factor. In other words, a loss of a significant figure or factor in one’s life leaves the individual without the “regular” usual environmental inputs which that person or factor had generated. Certain configurations that were normally optimized by usual



environmental inputs will now suffer the loss of the optimization dynamics and will be deoptimized. This deoptimization can be enhanced by loss of connecting spines and marked pruning of dendrite arbors. Widespread deoptimization of many internal representations could shift the dynamics of the dominant system trajectory toward deoptimization and trigger the emergent property of a depressed mood.

The optimization dynamics can also be described as “Adaptive Plasticity.” While fast plasticity continually shapes the internal memories the slower adaptive plasticity makes them become permanent. The fast Hebbian dynamics caused by calcium flux and synchronized electrical ion-channels activation potentials, with repeated experiences, training, and skill acquisitions depend on longer processes of Hebbian dynamics, that of actual structural plasticity with generation of new synapse pathways and even neurons. These processes take place in time-scales of days to weeks and act as adaptation mechanisms to the changing fluctuating environmental occurrences. The actual experience embedded as memories forms internal representations of the active external world.

As already mentioned above, Tononi and colleagues introduced a statistical measure, called “Matching Complexity,” which reflects the change in connectivity observed when a neural system receives sensory input (Tononi et al., 1996). Through computer simulations, they showed that when the synaptic connectivity of a simplified cortical area is randomly organized, Matching Complexity is low and the functional connectivity does not fit the statistical structure of the sensory input. If, however, the synaptic connectivity is modified and the functional connectivity is altered so that many intrinsic correlations are strongly activated by the input, Matching Complexity increases. They also demonstrated that once a repertoire of intrinsic correlations has been selected which adaptively matches the statistical structure of the sensory input, that repertoire becomes critical to the way in which the brain categorizes individual stimuli (i.e., perceives stimuli).

Thus, the internal representations embedded as statistically input-matching patterns are continuously altered by the configuration of external influences. Once altered, the consecutive inputs are “interpreted” by the recently altered internal representations (see Rogers, “organismic evaluation below).

Recently the fact that adaptive plasticity involves the interactions of the SN and the DMN have been confirmed by a review from Mulders et al 2015 where they find increased connectivity within the anterior default mode network, increased connectivity between the salience network and the anterior default mode network and changed connectivity between the anterior and posterior default mode network. All indicating connectivity formations in the DMN related to the SN activity just as predicted by the neuroanalysis approach.

plasticity and synaptogenesis become relevant for brain activity in mood alterations. Karl Friston (2012) provided a good understanding of the process in his article on dynamic brain activity, which he calls the 'Bayesian brain,' or Bayesian brain dynamics. Friston claimed that the brain continuously predicts occurrences in the environment and adapts to them, in the sense that when it adapts to environmental occurrences, it is actually reducing a factor called 'Delta,' which is the difference between the occurrences in the environment, and the internal states of the brain. There is a continuous attempt for the brain to reduce the 'Delta function,'. This kind of reduction is also called 'Free Energy (Friston 2012).' The Delta reduction is a Free Energy reduction, which is a term taken from entropy measurements, where the entropy measurements of the internal states of the brain are continually reducing the free energy, i.e., the differences between internal states and environmental occurrences.

In order for the brain to effectively reduce the free energy, it should be more flexible, i.e. more synaptic. Increasing synaptic capacity, the increase of plasticity in the brain, offers the brain changeability and with it the capability to reduce free energy more effectively.

If the emergent property of depression is to be connected to plasticity, it should be assumed that the dynamic going from high-level free energy to low-level free energy, has an elevating-mood antidepressant effect. The dynamic itself, the reduction of free energy dynamics has an emergent property of improved mood. If the free energy increases, meaning there is an increase in the difference between the internal states of the brain and the environmental occurrences, then increase of free energy dynamics occurs, moving from more adaptable to less adaptable states, thus causing the emergent property of a depressed mood.

We can also adapt terms taken from optimization theory and optimization dynamics, meaning that the brain optimizes the environmental occurrences by reducing free energy. So,

optimization dynamics would have an anti-depressant effect, while de-optimization dynamics, increasing the free energy will cause an emergent property of a depressed mood.

The major findings: increased plasticity with its antidepressant effect (Peled 2013), whole brain dynamics, as a whole brain adaptability state (Peled 2013), and adapting to the environmental occurrences and the Delta Free Energy reducing dynamics connected to the emergent property of mood.

### **New Neuroanalytic Diagnosis of Depression**

In depression plasticity is reduced. The changeability and adaptability of the brain is reduced. This hampers Bayesian brain dynamics i.e., the ability of the brain to predict and adapt to new everchanging constellations. Matching complexity is reduced. Error prediction is hampered and Free Energy (Sikora 2022) Delta, increases. This triggers a deoptimization (see above) dynamics at whole-brain level of organization. The deoptimization dynamics of the brain generates the emergence of depressed mood.

External occurrences (computed by the Central Executive Network) matched to internal representations (computed by the Default Mode Network) define the optimization and de-optimization dynamics thus is intermediated by the Salient Network. The adaptability and reduction of free energy depend on plasticity inducing processes that take weeks to months timescale.

To conclude, depression emerges from deoptimization dynamics related both to external occurrences and internal representations within the framework of the Bayesian Brain with its “free Energy” dynamics. All, related to the activity of the Salient Network within week to months timescale.

## MANIA & BIPOLAR

### **Phenomenology of Mania (& bipolar)**

Consistently increased rate and amount of speech, difficult to interrupt Content Grandiose or paranoid ideas; ideas of reference Feels distinctly and unrealistically superior to others. Some poorly formed delusions about special status or abilities may be present but are not acted upon. Elevated; inappropriate to content; humorous Excessive energy; hyperactive at times; restless Elaborates on sexual matters; hypersexual Decreased need for sleep  
Sever Mania with psychosis. Pressured, uninterruptible, continuous speech. Content marked Delusions, paranoid grandiose. Clear-cut delusions of remarkable superiority. Thinking, interactions, and behaviour are dominated by multiple delusions of amazing ability, wealth knowledge, fame, power, and/or moral stature. Euphoric; inappropriate laughter; singing Motor excitement; continuous hyperactivity (cannot be calmed) Sexual interest involves overt sexual acts. Hostile, uncooperative; interview impossible. Denies need for sleep

### **New Neuroanalytic Diagnosis of Mania (& bipolar)**

Deoptimization and depression are the opposite of what transpires in Mania.

Mania emerges from hyper-optimization dynamics related both to external occurrences and internal representations within the framework of the Bayesian Brain with its “free Energy” dynamics. Free energy reduction triggers antidepressant and manic emergent properties.

Also, here all is related to the activity of the Salient Network within week to months’ timescale.

When corrective balance effects trigger contradicting deoptimization and hyper optimization oscillatory dynamics bipolar phenomenology emerges.

## PERSONALITY DISORDERS

### **Phenomenology of Personality Disorders**

Rigid predictable restricted behaviours attitudes childish immature personality egocentricity dependency is marked. Special sensitivity to criticism, need for attention low impulsive threshold. In other cases, may presents an overtly hostile attitude, showing frequent irritability and direct expression of anger or resentment. Patient exhibits repeated impulsive episodes involving verbal abuse, destruction of property, or physical threats. In other cases, dependent immature personality dependency is marked to extent that hampers any functional challenge. In other more severe cases unstable, impulsive, inability to regulate or control emotions. Tends to split (all-or-none-all good all bad attitude) when under stress becomes paranoid (brief psychotic episodes)

Uncooperativeness and verbal abuse or threats are typical and seriously impact upon social relations. Patient may be violent and destructive and is physically assaultive toward others. Patient frequently is impulsive aggressive, threatening, demanding, and destructive, without any apparent consideration of consequences. Shows assaultive behaviour and may also be sexually offensive

### **Brain Dynamics of Personality Disorders**

Combining Baars' theory with notions about hierarchical organization of information (memories) in the brain, it is reasonable to consider that lower level partial processes in the nervous system interact to form higher level neural global organizations. In addition, the idea of internal consistency in global formations captures the basic notion of multiple constraint organization. It is assumed that the dynamic activity of partial processes demonstrate both hierarchical and multiple constraint organizations. For example, once the partial process forms part of the global organization it is interconnected with all the other processes (i.e. is broadcast globally). Thus, it contributes to, or influences, the global organization by virtue of its connections, i.e., by exerting its output through the connections to the rest of the system. On the other hand, because it is a multiple constraint system, many other processes will constrain its activity (through the connections). It can be concluded that from the information

processing perspective, the information delivered by partial processes concurrently influences and is influenced by the global message.

Due to internal consistency, if the information structure (i.e., activation pattern) of the partial process “contradicts” (i.e., markedly differs from) the information being represented in the global formation, the partial process will have “difficulty” gaining access to (or fitting with) the global process. This is due to the multiple constraints between the partial process and the global formation, which will not be satisfied in such a situation. Global formations are higher levels of organization (from the hierarchical perspective). Thus, by constraining partial processes that are most likely of lower levels, top-down control blocks access of partial processes to global formation (i.e., “repression”). Partial processes compete for access to global formation, creating the bottom-up procedure. A balance between bottom-up and top-down processes then becomes crucial for the contents that reach global formations and consciousness.

The first concepts introduced by Freud in his topographic model were related to the levels of consciousness. We now have the tools to define his description of conscious, unconscious, and subconscious as levels of integration that partial processes achieve to form global organizations. Conscious awareness is the property of global formations. Unconscious information is presented

as partial processes that do not contribute to the global organizations. The subconscious is characterized by those processes that are about to contribute to, or drop out of, the global formations. In the structural model, psychic “compartments” such as the ego and id were conceived. The ego is described as developing from what was initially the id in the infant. The id is described as a disorganized system where concepts are disconnected or dissociated in every “strange” possible way. Freud named this form of inconsistency “primary thought process.” From the system point of view described so far, primary thinking can be conceptualized as a feature of a system without internal consistency, or, in other words, where multiple constraints are not satisfied. This enables conflicting ideations to coexist and concept formations that do not make any sense to predominate. Biological evidence shows that in infants, synaptic connectivity is just beginning to develop. Thus, the biological neural correlate at this phase of development cannot support the needed multiple constraints organization that forms the basis of ordered mental activity. Ego development involves the formation of a secondary thought process. This process is described by Freud as the normal

thinking that characterizes each one of us. In other words, secondary thinking emerges from multiple constraint satisfaction organization of the neural system; and in fact, synaptic connectivity fully matures from infancy to adulthood. By introducing the concept of superego, Freud suggested what were later to be developed as internal representations of social and interpersonal norms. This line of thinking gave the ego (i.e., its superego portion) not only the scope of organizing the disordered id processes, but also the entire responsibility of representing, and adapting to, psychosocial reality. Introduction of the dynamic model added the interplay among the psychic compartments of Freud's model. "Defense mechanisms" are probably the most described dynamic factors in this model. According to Freud, the ego makes use of an unconscious domain of mental activity (also referred to as id) into which undesirable drives and ideas are repressed. "Repression" has been described as the mental mechanism that "guards" the conscious awareness from the intrusion of inadequate and intolerable ideas or drives. Repression keeps them unconscious. Freud indicated that the intruding ideas and drives from the unconscious actually threaten ego integrity.

Based on the formulation described so far, repression can be re-conceptualized as the dynamics of participating, as well as nonparticipating, processes in the global formations that support conscious phenomena. Partial processes that do not gain access to the global process remain unconscious (i.e., repressed). Because of the multiple constraints that characterize global organizations, certain partial processes may encounter difficulties in accessing the global formations. This is especially true if the partial processes carry information that is entirely removed from, or contradictory to, global messages. Based on these assumptions it is possible to conceive that information comprised of contradictory and unfitting messages (i.e., partial patterns that do not satisfy the constraints of global patterns) will be denied access to the global organization. In fact, Freud described repressed contents as conflicting topics or unbearable ideas. Here, "unbearable" refers to information (of the partial process) that is removed from (i.e., unfitting with) the information presented by the global formation. The unbearable partial process cannot be incorporated into the general message without damaging its internal consistency (i.e., its multiple constraint satisfaction organization) and therefore it is bound to be excluded. For example, to a mother of a newborn baby, the idea of killing her baby extremely contradicts the normal loving and caring state of mind typical of a new mother. If inadequate partial processes somehow gain access to the global organization, they are inclined to destabilize or even disrupt it. If many conflicting and disrupting processes gain access to the global formation, the entire global message may be destroyed and the neural system representing it is bound to destabilize. Indeed, the types of thoughts that involve

killing one's newborn baby often emerge in mentally disturbed patients. It is thus conceived threatening to the integrity of global organizations and the actual stability of neural systems. This description conforms to Freud's notion of ego integrity being threatened by repressed mental processes of conflicting ideas or drives. Occasionally, inadequate partial processes may gain access to the global organizations and be "transformed" in order to accommodate the global pattern. For example, immoral ideation is contradictory to the dominating content of a moralistic conscious awareness. Transforming the wish to behave in an immoral way into moralistic ideation may accommodate the dominating global organization of a puritanical message. This type of transformation is known in the psychoanalytic literature as "reaction formation." Another transformation of unbearable ideation is known as "isolation." Here the ideation is not excluded from awareness, but certain relevant parts of it are "neutralized." These parts are incompatible with the rest of the conscious message. The partial process is included in the conscious awareness only to the extent that it is removed from certain contents of the conscious awareness (i.e., isolated). If isolation is not enough to satisfy the constraints of global formations, then *dissociation* might occur, and certain contents of awareness will thus be ignored or experienced as independent and unrelated. The transformations described above are needed in order to protect the global formation from being disrupted by contradicting partial processes.

Therefore, it is conceivable that these transformations justify the term "defense mechanism." They protect the global formations and prevent destabilization of multiple constraint activity in the neural system. From the biological point of reference, this may translate into destabilization of the interrelations between groups of neurons, which presumably has direct neuropathological outcomes on transmitter-receptor activity.

The psychologist Carl Rogers (1965) suggested that the best vantage point for understanding behavior is from an "internal frame of reference" of the individual himself. He called this frame of reference the "experiential field," and it encompasses the private world of the individual.

Neuroscience teaches us that experience dependent plasticity creates internal "maps" to represent information. One of the more famous examples is the homunculus of sensory and motor representations spread over the cortex. Just as the homunculus is probably formed from the strengthening of synaptic pathways (i.e., Hebbian dynamics), the experiential field



probably results from experience-dependent plasticity in the brain. In terms of space-state formulation (see above), the experiential field can be conceptualized as a configuration of attractor systems in the brain.

According to Rogers, “organismic evaluation” is the mechanism by which a “map” (i.e., an internal configuration) of the experiential field perceives the psychological events of everyday life. Using the formulation of state-space for internal representations, organismic evaluation can be re-conceptualized as convergence into, or activation of, relevant experience-dependent attractor configurations of the internal map. If the incoming experience is identical to the previous internal representation of that experience, no change will occur and the map of internal representation will activate familiar past experiences. On the other hand, if the new experience is slightly different from the previous experience, this will be enough to “reshape” the topological map and add attractor systems to the internal configuration. Activation of the internal map organizes the incoming stimuli into a meaningful perception. The newly perceived experience is meaningful when it relates to the previous experience already embedded in this map. This is a circular process in which the map of internal representation simultaneously influences, and is influenced by the incoming stimuli. In other words, the brain sustains a map of internal representations that is continuously updated through interactions with the environment.

This type of interaction between internal representations and perception of environmental stimuli has been referred to as context-sensitive processes (Tononi et al 1994). Owing to this interaction, internal representations can be viewed as approximated models of reality. It is reasonable to assume that a “good match” between internal representations (of the psychosocial world) and external psychosocial situations will enable efficient adaptive interpersonal relationships. On the other hand, a “mismatch” between the psychosocial events of the real world and their internal representation may “deform” both the perception and the behavioral responses of the individual. The concept of matching complexity (see above), further indicates that mismatch will be related to reduced neural complexity in the relevant neural systems and thus will be responsible for more adaptation problems on the neuro-computational level.

The process of creating the specific maps of attractor configuration in different individuals depends heavily on the background experiences of the individual. The developmental

experience-dependent processes responsible for the formation of internal representations of context may involve deviations from the “normal itinerary” of internal representations needed for “regular” psychosocial function. These deviations may form internal representations that are greatly removed from psychosocial realities. A large mismatch between internal representations and environmental reality is likely to provoke distortions that lead to disturbances in perceiving and reacting to the environment (such as personality disorders).

To a certain extent, incoming information from environmental stimuli maybe conceptualized as partial processes competing to gain access to global organizations of conscious awareness. A large mismatch between the internal map of representation and the pattern of environmental stimuli is likely to create the same difficulties that conflicting partial processes may encounter when trying to gain access to global organizations of conscious awareness (see above). This mismatch may distort the incoming information similar to the way unfitting partial processes that attempt to access the global workspace are distorted; they have to be transformed before they can participate in the dominant message of conscious awareness.

A good example of this distortion is seen in the phenomenon of “transference.” Transference is regarded as an attitude toward an event or individual that is based on previous experience with similar events or people that is not congruent with the current situation. Thus, the incoming stimuli from the psychosocial event are distorted to “fit” the internal representation of similar events already dominating the global processes in conscious awareness. Since incoming information is “evaluated” by internal representations, and since these are formed by experience, it is only natural that many of the perceptions we have are related to past-experiences. When a set of stimuli of a new psychosocial event enters the system and causes it to converge to a set of attractors that represents similar past experiences, that set of attractors activates the past-experience in the global organization, bringing it to a conscious level. The conscious awareness regarding the individual or event that provoked this process will be perceived in many connotations as being the past-experience. If there is a substantial mismatch between the internal representations and the actual psychological event, the transference (i.e., the perception as past-experience) may distort the perception of that psychological event.

Matching complexity may be the future mathematical tool that will predict to what extent transference is likely to determine one’s behavior. Sometimes the set of environmental stimuli

is so removed from any context of internal representation that it is totally unperceived by the individual. This is defined in psychodynamic terms as “denial.”

Considering the above, we can redefine the process of developing personality traits and maturation as a life-long process of Adaptive Plasticity, which gradually incorporates the experiences of an individual (i.e., experience-dependent-plasticity) to create memories-dependent internal representations. Such internal representations incorporated by Hebbian dynamics can be also defined as internal objects. They represent not only the physical environment but also complex presentations of peoples' attitudes and behaviours, our self-representations (self-objects) and the relationships formed among others and ourselves. This past psychosocial experience once internalized in the form of internal-maps becomes the point of reference for our understanding and familiarity, and thus serves as an evaluation-map (“organismic map” according to Rogers (1965)). Our psychosocial experience will determine how we perceive and react psychosocially, and will determine our personality styles.

Distortions, immaturity, and biases in developmental plasticity will cause maladaptive constant predictable pervasive behavioural problems typical to those suffering from personality disorders. In short, personality disorders are disorders to developmental plasticity networks.

### **New Neuroanalytic Diagnosis of Personality Disorders**

Personality disorder is related to experience dependent plasticity thus a lifetime-scale developmental process that generates internal representations from experiences and memories. The representations are formed by Hebbian dynamics and shape the way we interpret others and ourselves. The experience of other and ourselves determine our feeling and behaviour within psychosocial settings thus defining our personality traits.

Experience dependent internal representations have been described as “Organismic maps” by Carl Rogers (see above) and as “Object Relationships” by Object Relationships psychologists. The Default Mode Network, resting network is active during self-contemplation and is presumed to represent the construct determining our personality traits.

Personality disorders are emergent property from immature and / or biased development of the Default mode Network.



## DNM - SOME FUTURE LEADS FOR DIAGNOSIS AND TREATMENTS

To diagnose Psychosis means to detect disconnection dynamics both structural and functional connectivity must be assessed. One common way to evaluate connectivity is by using correlation matrices where structurally actual pathways form the correlations, and synchronized activity form the functional correlations. Thus, network activities can be connected functionally even though they are not structurally related. The correlations calculated can be simple linear or more complex nonlinear. The more complex ones are preferable as they address brain complexity better. It is useful to reconstruct Graphs from the correlation matrices as they lend themselves better to organizational assessment such as small worldliness. On a whole brain level, it is required to assess brain hierarchy according to “Unimodal” “Multimodal” and “Transmodal” brain processors. Because Negative signs also result from disturbance of connectivity the same diagnostic connectivity assessments apply as in psychosis and disconnection. Only that in the case of Negative signs overconnectivity is diagnosed. The overconnectivity will show by opposing correlation values to those of psychosis and the hierarchy evaluation will show insufficient “Transmodal” formations. If Anxiety -related brain dynamics is investigated then connectivity dynamics (as explained above) evaluated in the time domain should be most sensitive to perturbations of Multiple Constraint Satisfaction. Here electrophysiological assessment can have an advantage, that of temporal resolution. Markers for perturbations can be developed by Entropy measurements of the signals. For the assessment of disturbances to plasticity and optimization dynamics in mood disorders (Depression and Mania), Bayesian dynamics as evaluated by “Dynamic Causal Modelling (DCM)” is most suitable. Entropy measurements such as “Free Energy” is expected to increase in Depression. Bayesian dynamics as explained above is also relevant for hyper optimization measurements only that “Free Energy” is expected to decrease in manic and antidepressant effects.

With personality disorders Measuring lifelong changes of brain DMN is an insurmountable challenge for common diagnostic practice. Thus “markers” of immature network organizations could be enough to determine immaturity or biased DMN organizations. These in turn pointing toward a maldeveloped malfunctioning DMN. Such assessments should

involve both configurations and dynamics of connectivity matrices of distributed resting state brain networks

The general target of intervention in psychosis according to the Neuroanalytic approach is that of the Central Executive Network targeting the frontal lobes as the relevant hubs of this network. Increased Gamma Oscillations (30-100 Hz) has been correlated with positive symptoms (Lee et al 2006; Mulert et al., 2010; Spencer 2009) thus Slightly desynchronized gamma transcranial Alternating Current stimulation (tACS) will reduce Gamma Oscillations and may help treat positive signs. This can also be attempted with Deep Brain Stimulation (DBS) or other nano-particles-dependent future technology.

The general aim is to restore and optimize Small Worldliness within the Central Executive Network organization spread in the brain.

Concomitantly frontal-lobe functions should be strengthened using stimulation of experience-dependent plasticity. Thus, Virtual Reality (VR) gaming can be used if game condition are designed to activate frontal lobe functions such as Go-No-Go and Wisconsin sorting challenges.

Negative Signs also involve Central Executive Network targeting the frontal lobes as the relevant hubs of this network. The assumption here is over-connectivity and to disconnect the network slightly is the challenge here

Regarding current stimulation, here the opposite may function therapeutically. Synchronized Gamma tACS entrenchment stimulation will increase Gamma Oscillations and may help treat negative signs. As alogia is characterized by perseverations and poverty of thought then the VR gaming stimulation should involve associations tasks that stimulate wide range of associations like in matching games. Also, multimodal gaming challenge can be useful in this case. with 'avolition' frontal lobe stimulation and Gamma synchrony by entrenchment is the therapeutic rule. In the VR gaming challenge again frontal lobe stimulation can help higher-level brain hierarchal organizations improve thus functions such as Go-No-Go and Wisconsin sorting challenges are again relevant.

For Anxiety, the target of treatment is that of the Salient Network and the widespread whole-brain plasticity induction. The time-window of therapeutic action is that of months and weeks. The plasticity increases ease the constraints within neural networks with rapid effect

and anxiolytic results. Plasticity can be generated with medication as is traditionally treated with SSRI's. VR can be used here traditionally as is used for phobias. In depression the target of treatment is that of the Salient Network and the widespread whole-brain plasticity induction. The time-window of therapeutic action is that of months and weeks. The goal is to increase plasticity that offers the Bayesian brain the ability to change adapt and optimize internal representations. Plasticity can be generated with medication as is traditionally treated with SSRI's.

The scope is to induce wide spread cortical plasticity and tDCS rtDCS and tACS over multiple changing scalp locations are all legitimate.

VR can be used here traditionally as is used for phobias or CBT related corrective experience. In addition, the VR stimulation should encourage wide-spread network activations thus involve associative multimodal challenges. Psychotherapy modalities can also be added to this VR stimulation (explained below)

In cases diagnosed with personality disorders, targeted are the hubs of the Default Mode Network (DMN) with tDCS maximum stimulation. Once plasticity is induced dynamic open-ended psychotherapy is applied to achieve the relevant 'corrective 'experiences.' the plasticity induction allows for change to happen and psychotherapy brings these changes in the network configurations.

## APPENDIX

### DSM NM DIAGNOSIS

DSM	NM
Psychosis Delusions Hallucinations Loosening of associations	Millisecond range disturbances Disconnection dynamics disintegration of conscious experience reduced clustering coefficient of Small World Network organization Top-down imbalance with constraining distortion of higher-level transmodal schemata (ideations) upon bottom-up evidence. A disturbance to error-correction millisecond range Bayesian dynamics. Location Central Executive Network Frontal parietal hubs. Hierarchical transmodal organization
Negative Symptoms Dementia precox Poverty of thought	Over-connection dynamics Increase clustering coefficient of Small World Network organization. Constraint state-space dynamics Hierarchical collapse with insufficient transmodal optimization Location Central Executive Network Frontal parietal hubs. Hierarchical transmodal organization
Anxiety	Perturbation to Multiple Constraint Satisfaction Dynamics over distributed whole-brain networks. Consequence of computational brain dynamics. The dynamics of perturbation to Multiple Constraint Satisfaction takes place in the timescale of minutes as is evident from anxiety-related manifestations. Location Salient network with subcortical basal ganglia hubs acting upon massively distributed general cortical whole-brain networks.
Depression	Distributed hypoplasticity governed by Salient Network hubs resulting in reduced Bayesian brain dynamics, with deoptimization dynamics of internal representations, with overall increase of free energy. The dynamics of deoptimization takes place in the weeks to months' timescale as is evident from antidepressant plasticity-dependent processes Location Salient network with subcortical basal ganglia hubs acting upon massively distributed general cortical whole-brain networks.
Mania Bipolar	Distributed hyper plasticity governed by Salient Network hubs resulting in increased Bayesian brain dynamics, with hyper optimization dynamics of internal representations, with overall decrease of free energy.



	<p>Hyper plasticity and hyper optimization can trigger balancing effect that can result in oscillating hyper-hypo dynamics which will induce a bipolar phenomenology.</p> <p>The dynamics of hyper optimization takes place in the weeks to months' time-scale as is evident from stabilization of plasticity-dependent processes</p> <p>Location Salient network with subcortical basal ganglia hubs acting upon massively distributed general cortical whole-brain networks.</p>
Personality disorders	<p>Default-Mode Resting-State Network develops within a lifetime scale from birth to adulthood and beyond. It is configured by Hebbian dynamics as an “Experience – Dependent Plasticity” process where experience activates representative neuronal networks creating memories, internal representations via strengthening experience dependent connections. Experience continually moulds and reshape the brain network organization, while optimizing and deoptimizing the internal configurations thus relating our experiences to mood.</p>

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