

BRAIN DYNAMICS
AND
MENTAL
DISORDERS:

PROJECT FOR A SCIENTIFIC
PSYCHIATRY

AUTHOR
AVI PELED M.D.

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INTRODUCTION

The project for a scientific psychiatry is an ambitious endeavor. It opts to complete Freud's original effort to explain the physical (neuronal) roots of mental phenomena.

Achievements in biological psychiatry reflect the consensus that psychiatric mental disorders are brain disorders. However, we do not have enough knowledge about the exact processes underlying the different mental disturbances. Without understanding of the specific causes for mental disorders, their diagnosis is descriptive and subjective, thus unreliable and deceptive.

Two reasons for our shortcomings in this field. Firstly, not enough is known about how the brain works to enable high mental functions. Secondly, there are no good theoretical frameworks or models that can explain the underlying neurological pathology of mental disorders.

In 1895, Sigmund Freud attempted to explain mental phenomena and mental disorders based on neurological brain functions. He wrote in his manuscript titled *Project for a Scientific Psychology* "The intention [of this project] is to furnish a psychology that shall be a natural science" Figure 1. By natural science, Freud meant disciplines like biology and physics that deal with matter by using measurement and experimentation.

Since then psychology and biology evolved to form different languages, however, if one compares Freud's work in his project with new insights from modern neuroscience, an exciting picture emerges. It seems that it is time to continue Freud's quest in his "project" based on novel insights from modern neuroscience.

This manuscript goes back to Freud's original notion of the human brain as a physical system and uses combined updated neuroscience, modern physics of complex systems and psychoanalytic insights to advance the science of psychiatry. The basic approach of this manuscript refers to mental functions as emergent properties from brain complex organizations. Mental disorders are conceptualized as perturbations and disturbances to brain organization. Psychiatry is reformulated as a science of brain system dynamics.

The scope of the manuscript is to pave the way for a theoretical framework to explain mental disorders; this would be achieved by formulating a communicating language to bridge biological and psychological conceptualizations of mental disorders.

The manuscript begins with a simplistic representative outline of relevant concepts from the physics of complex systems. It is in no way comprehensive nor is it a profound tutoring of the subject, however it provides a general notion of the possible behaviors that may characterize complex systems such as the brain. Following are some relevant topics from the neurosciences that help understand the brain as a complex dynamic system. The author does not intend to give a comprehensive review of the field, as he assumes that potential readers have basic knowledge in neurobiology.

Future research findings based on the theoretical framework proposed by this manuscript would provide for the diagnostic tools of future psychiatry, meanwhile a communicating language between clinicians and brain researchers calls for a temporary diagnostic re-conceptualization of psychiatric diagnosis. This manuscript provides the clinical guideline to assess patients within the new neuroscience-oriented conceptualization, thus suggesting a new psychiatric diagnostic system. It is not merely a semantic modification, it is a theory-based conceptual advancement proposed to serve a new scientifically oriented terminology for psychiatry.

Theories and novel conceptualizations are useless unless they can provide groundbreaking scientific advancements. In the case of psychiatry, these advancements should relate both to diagnosis as well as to treatment of mental disorders. The manuscript concludes by describing some innovative diagnostic and therapeutic approaches to mental disorders. These are formulated as testable predictions relevant for future experimental efforts, which the author promotes and hopes to stimulate with this manuscript.

SYSTEMS BASIC CONCEPTS

“As far as the laws of mathematics refer to reality, they are not certain; and as far as they are certain, they do not refer to reality...” Albert Einstein (1879-1955)

1.1. Complexity, Systems, 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. Connection 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. In 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

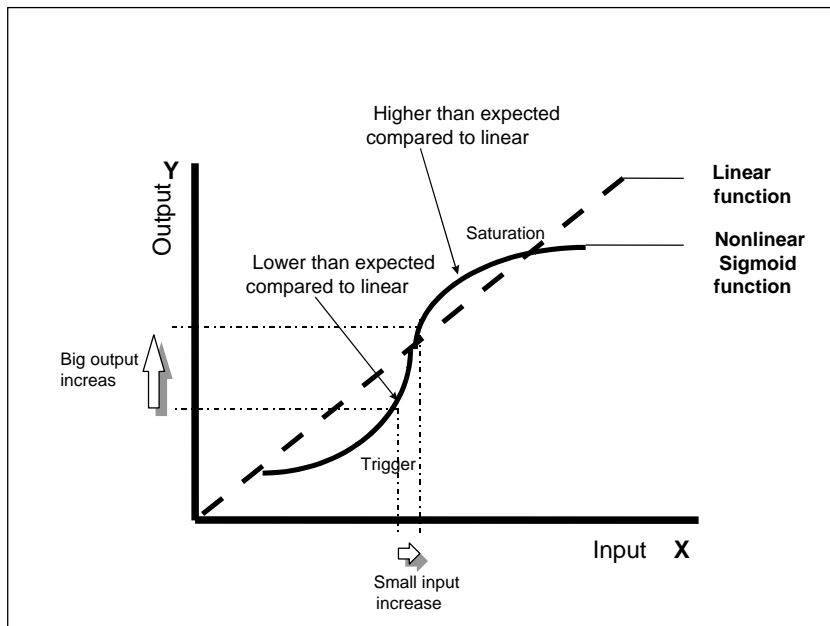
a perfect crystal the position of a molecule is completely determined by the positions of the neighboring molecules to which it is bound, and is an example of connection leading to fixed order. Complexity can only exist if both aspects are present. Complexity is therefore situated in between order and 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 as a whole 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.

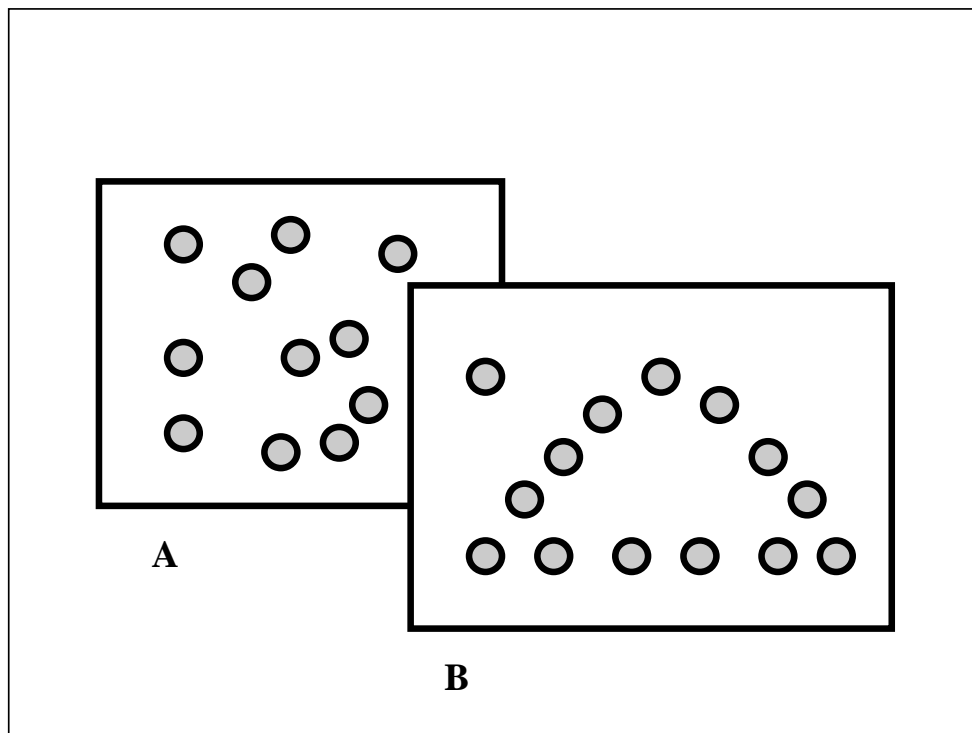
Emergent properties originate from nonlinear systems. Non-linear systems are those systems where there are no one-to-one relations between input and output, thus, the activity of these systems cannot be described by linear equations. In linear systems, the whole can be described by the sum of all parts. 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 (Figure 2).

Figure 2



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. Figure 3 provides a graphical illustration of emergent properties; in the first part of the illustration (Figure 3a), the round elements are randomly distributed on the page. In the second part of the illustration, the triangle is formed as an emergent property from the ordered distribution in space of the round elements (figure 3b).

Figure 3



This graphical example illustrates the fundamental importance of interrelations or organization (spatial in this example) for emergent properties (e.g., the triangle) in a system. Neither the elements in isolation, nor their summation, can account for the emergent property (the triangle). Without the additional organization, there could not be emergent properties in the system.

To conclude, in this work mental functions are conceptualized as emergent properties of brain organization. The brain is a highly nonlinear complex system. With its ten-milliard elements (neuronal units), each connected with seven milliards other units, the brain provides the computational power that allows for all our mental psychic functions. To understand mental functions the dynamic organization of the brain is addressed. Just as mental functions result from organized regulated and balanced brains, mental disorders probably emerge from perturbed and disturbed brain organizations.

1.2. Non-linearity, Criticality, Phase-transition, Trigger-saturation Effects and Stability.

As mentioned above, nonlinear systems are those where relations between input and output do not have a one-to-one relationship. Nonlinear systems are often described by a sigmoid graph (Figure 2). The initial portion of the graph can be viewed as a “trigger-effect” in which a small increase in input results in a large response in the output. The last portion of the sigmoid graph can be viewed as “saturation-effect” since the increase in input levels does not increase the output further.

In physics, a critical point is that where a system radically changes its behavior 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 behavior. 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 in spite of 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 'behavior' inherent to nonlinear systems.

1.3. Optimization, Constraint-Satisfaction, Connectivity, State-Space System Dynamics

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

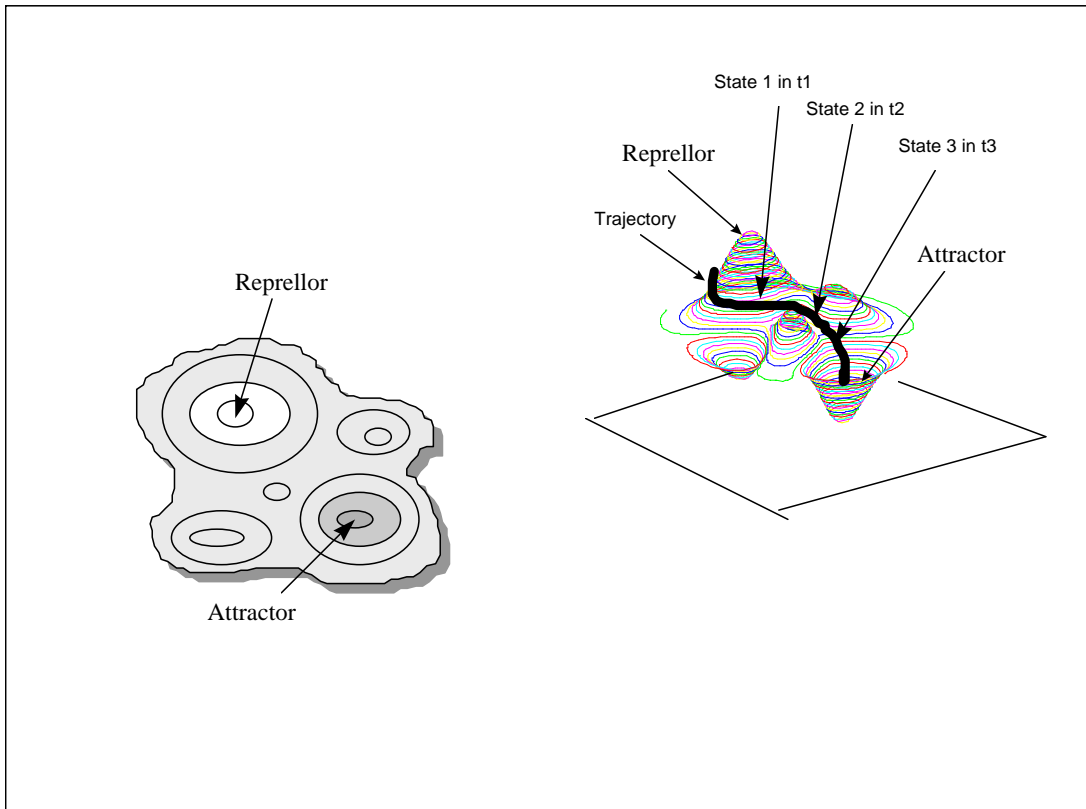
fixed, the more static “freezing” state will prevail. Thus, the connectivity patterns in the system are crucial to the optimization and complexity of the system.

“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 similar to 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” (figure 4).

Figure 4



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 of the possible states that the system is capable of assuming, (i.e., all the possible combinations in the activity of the elements). This configuration-space is sometimes termed “landscape” (Figure 4). 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 (Figure 4, states 1, 2 and 3, over time t1, t2, and t3).

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) in figure 4, it would be easy to see that peaks represent “repellers” (i.e., those states the system tends to avoid) and basins represent attractors (i.e., those states the system tends to assume).

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Brain Organization and Mental Functions

...all understanding consists of forming and manipulating appropriate representations, these representations could be analyzed into primitive elements (naturas simplices), and all phenomena could be understood as complex combinations of these simple elements....Descartes.

2.1. Neural Complexity and Computational Cognitive Flexibility

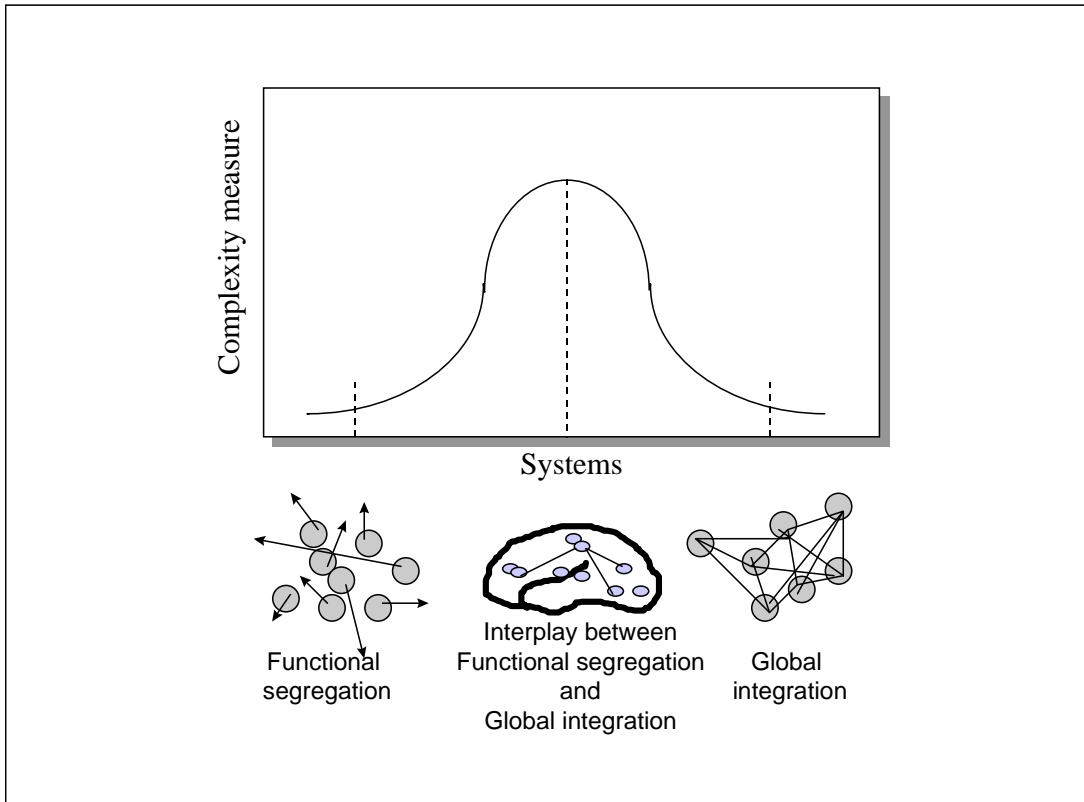
Historically brain activity was formalized using the localised approach of brain centers, stating specialized functions for segregated neuronal regions. Later the integrated approach argued against localised functions and evoked the non-localised approach of spread activation and functional connectivity 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). Figure 5 schematizes neural complexity levels (axis Y in figure 5) in relation to the balance between segregation and integration in the system (axis X in figure 5).

Figure 5



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.

2.2. Plasticity, Connectivity, Learning, Matching Complexity, and Internal Representations

The relevance of synaptic plasticity to the information processing of the brain was recognized as early as the beginning of the 20th 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 fibers 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 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 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 behavioral responses of the individual. In addition, reduced matching complexity will further reduce adaptability causing rigidity, reducing the repertoire of reactions available to the individual.

2.3. Hierarchical Organization Global Integrations and Consciousness

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.

Figure 6 presents the hierarchical organization of the brain as a centrifugal arrangement from transmodal to more unimodal systems and regions.

Figure 6

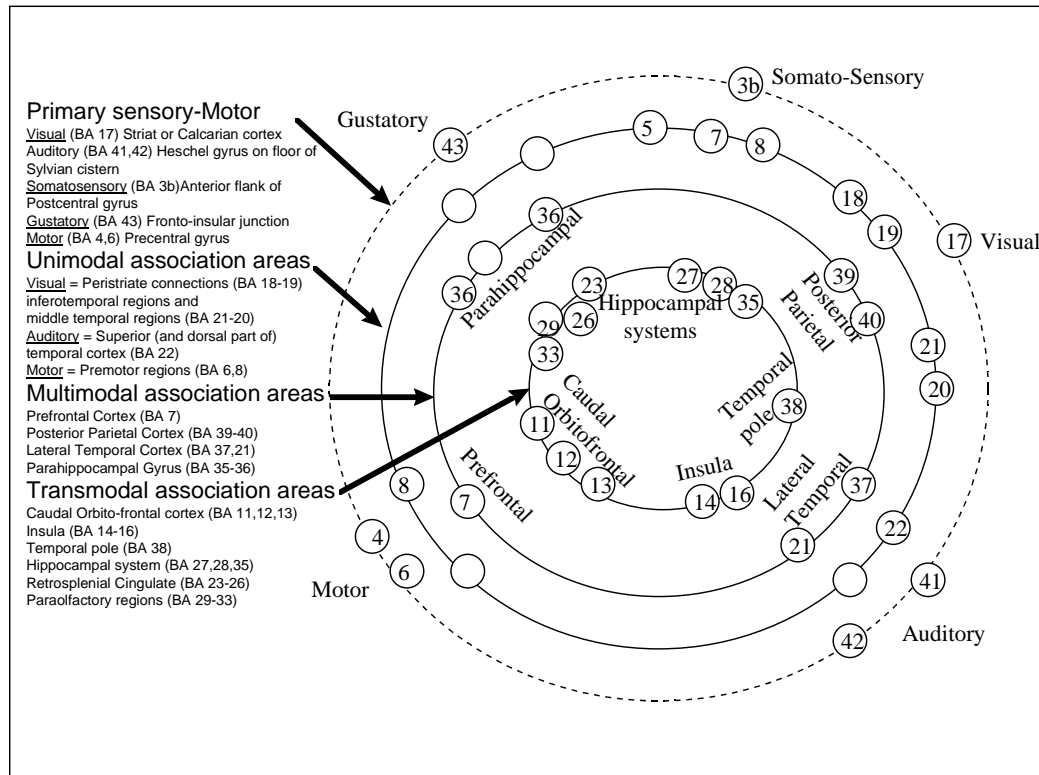
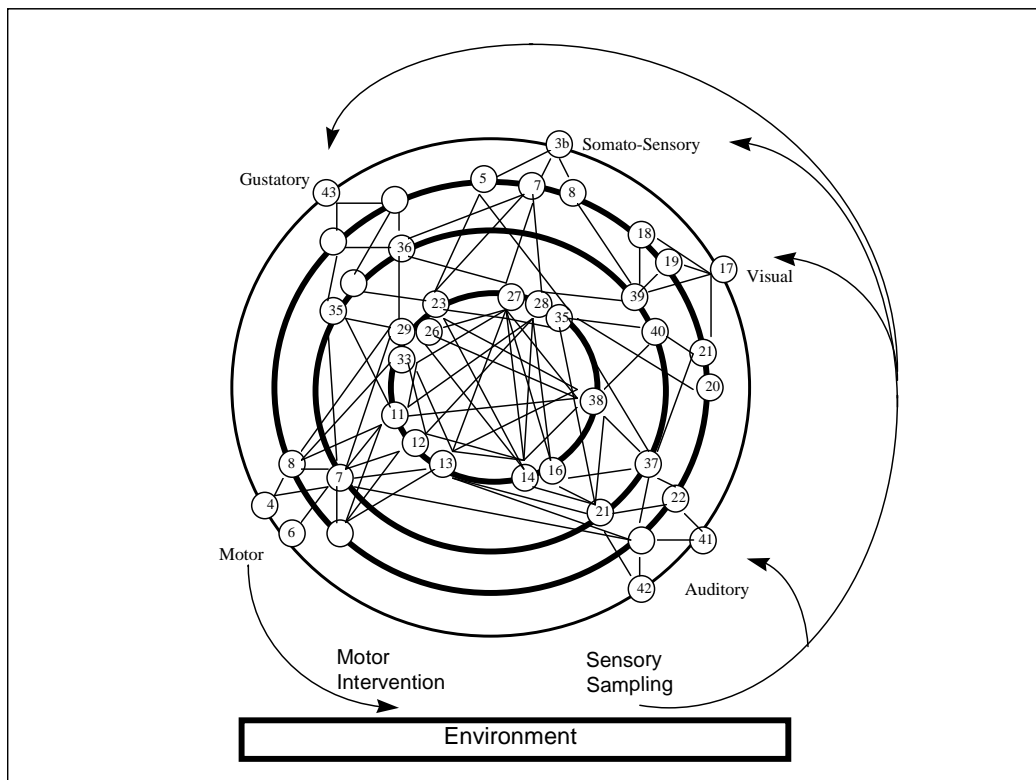


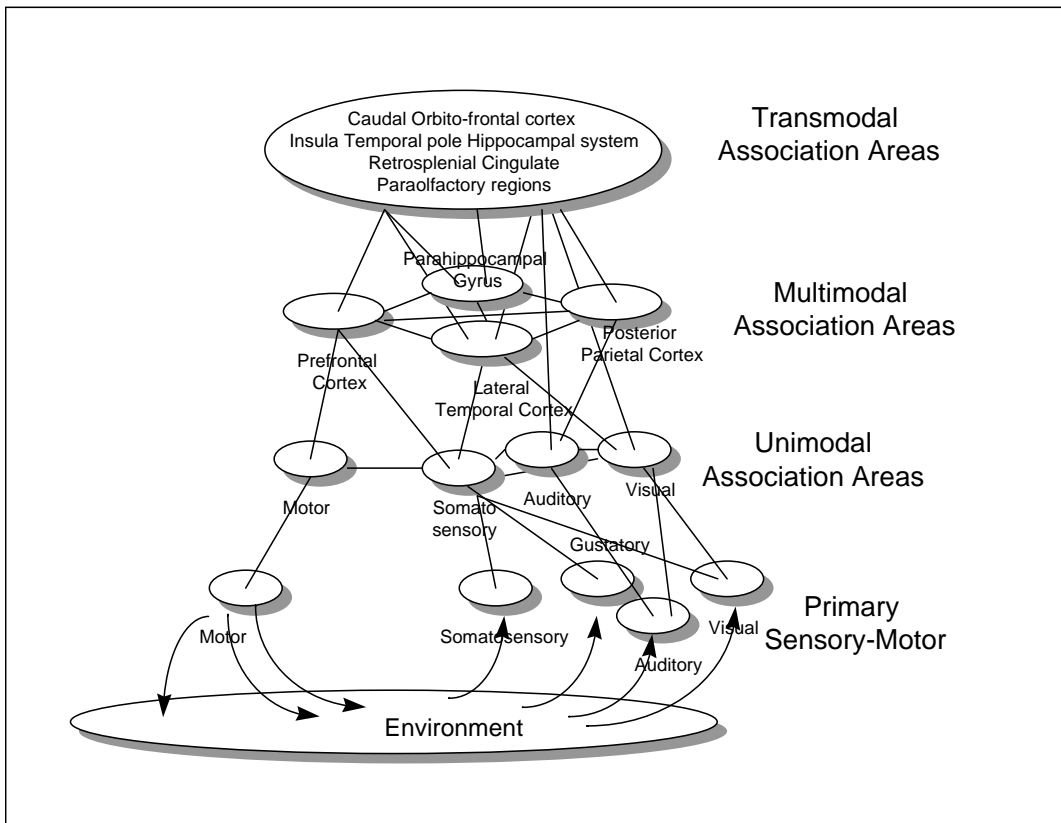
Figure 7 shows how the hierarchical arrangement of connectivity in the brain interacts with the environment thus forming constraints between the brain and the environment.

Figure 7



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. Figure 8 schematizes the hierarchical structure of the brains.

Figure 8



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 fairly 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.

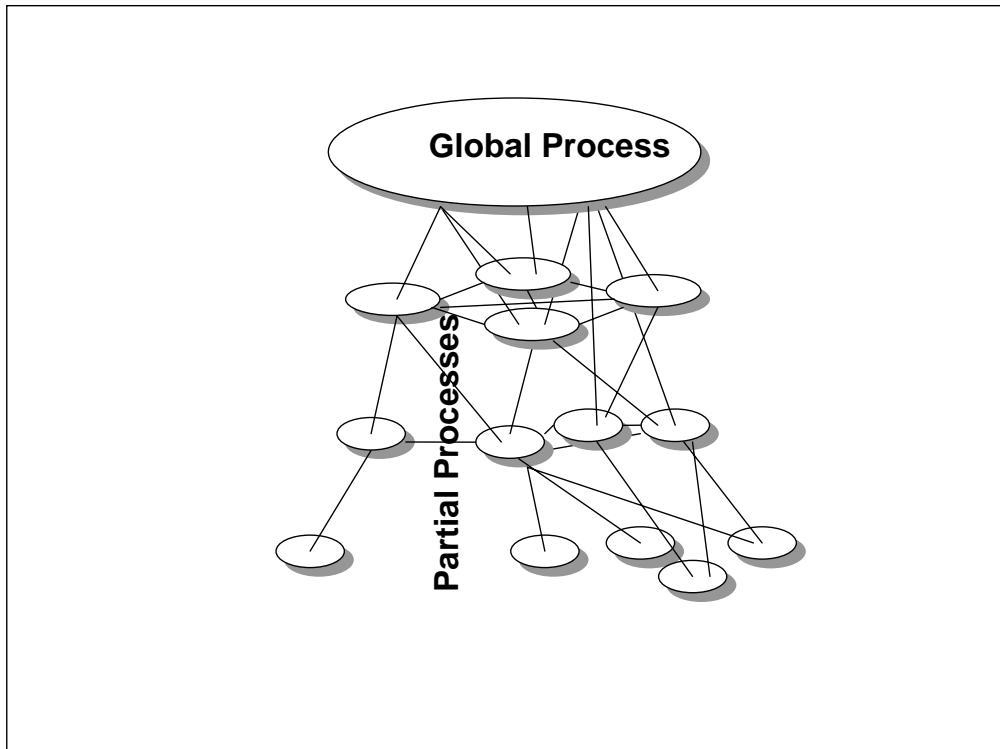
To explain the differences between conscious and unconscious processes, Baars turns to the popular models of distributed-processing systems (i.e., neural network models; (Herz *et al*, 1991). Baars proposes that a similar structure exists in the human

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 (Figure 9).

Figure 9



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 demonstrate 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).

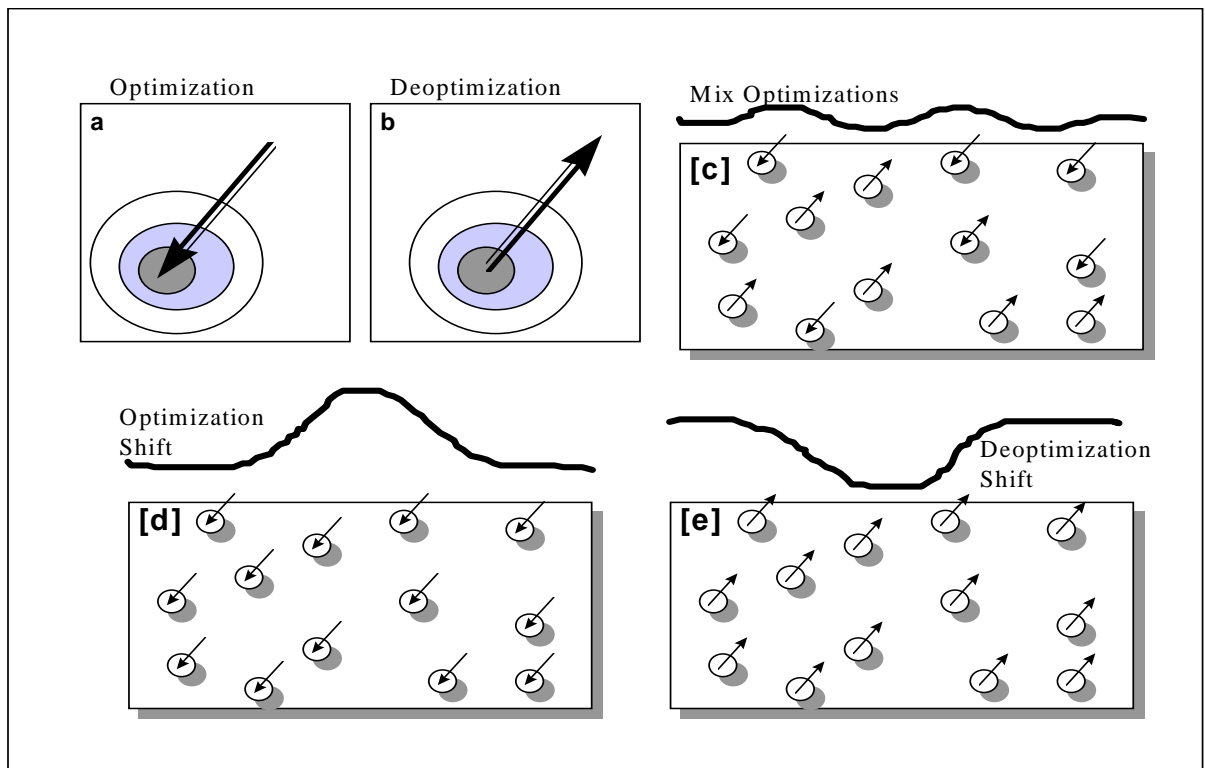
2.4._Optimization of Representational Dynamics, Conflict and Mood.

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 (figure 10c). 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 depression of mood (figure 10e). 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 (figure 10d) resulting in the well known psychiatric entity of manic-depressive disorder. Figure 10 is a schematic illustration of the optimization and deoptimization dynamics.

Figure 10



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 favored 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.

2.5. Neuro-system Analysis and Psychoanalysis

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 actually 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 arraignment pattern that does not satisfy the constraints of global arraignments. 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 Winnicott, 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 center 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 behavior.

Sometimes a current experience is so far removed from any context of past 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.

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Perturbations of Brain Organization and Mental Disorders.

The beginning of knowledge is the discovery of something we do not understand.Frank Herbert (1920 - 1986)

3.1. Disruption of Global Integration and Psychosis

Psychosis is a term reserved for mental conditions that involve gross deviations from normal general perception of reality. It is also referred to as a disturbance of “reality-testing” as it presents mental states that are greatly removed from the regular experience common to most individuals. Psychiatrists tend to diagnose psychosis when the patient is experiencing delusions and hallucinations. Delusions are unshakable false beliefs, and hallucinations refer to perception without stimulus. It is thus conceivable that a patient who is experiencing false ideas about what is occurring, and that is perceiving non-existent sensations would be living in a world that is greatly different from the regular shared experience of most persons. Psychosis is typically accompanied also by behavioral disturbances.

Typically, the psychotic patient acts on his environment according to his delusional and hallucinatory experience. The ‘mismatch’ between the environmental occurrences and his reality experience causes his behavior to be incoherent in relation to what is transpiring around him. An external observer would then diagnose odd and non-adjusting behavior. Many times psychosis is also accompanied by restlessness and even violent behavior.

Medical experience indicates that psychotic symptoms such as delusions and hallucinations may accompany gross injury to cerebral functions. Brain pathology such as trauma, infections and tumors with extensive damage to cortical and subcortical brain tissue is often the cause of psychosis. In other cases, transient conditions such as aberrant electrophysiological activity (epileptic seizures) or biochemical metabolic shifts could also cause psychosis.

Here, psychosis is viewed as an incoherent and aberrant conscious experience of reality. Psychosis is hypothesized to involve fragmentation of global integration processes with disturbance of connectivity patterns among neuronal ensembles and fragmentation of conscious awareness. A distributed malignant process in the brain or an electrophysiological upheaval within acting neural networks spread in the cortex would probably disrupt brain organization, more specifically, breakdown within neuronal ensembles in the brain is conceivable. Thus, it is intuitively comprehensible

that the pathological foundation of psychosis could be a disorder of connectivity breakdown within neural network systems in the brain.

Patterns of psychotic symptoms vary. They involve visual hallucinations when the brain damage is from drug intoxications or inter-cranial malignancy. Tactile hallucinations have been referred to certain intoxications such as in cocaine abuse. Metabolic disturbances as in diabetes may cause persecutory delusions. Auditory hallucinations and bizarre delusions have been described in schizophrenia psychosis. In schizophrenia psychosis there is no known cause that disrupts global brain organizations, however, there is evidence to support connectivity disturbances such as a “disconnection syndrome” (Friston, 1996).

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 schizophrenic 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). Schizophrenic patients not suffering from hallucinations have the same activation pattern as normal subjects. Schizophrenic 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 & 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 & Frith, 1995). (5) Reduced EEG coherency between frontal and temporal electrodes was highly correlated with reality distortion symptoms in schizophrenia, suggesting disruption of fronto-temporal connectivity (Norman *et al*, 1997).

More recent findings accumulated to support the disconnection hypothesis involve EEG coherence task-locked to the delay-response epochs of a working memory test. Schizophrenic 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

schizophrenics. Dissociated complexity levels partially regressed in a similar manner to premature brains at earlier age, were found in schizophrenics during a study of the neurodevelopmental hypothesis of schizophrenia (Koukkou *et al*, 2000).

In summation it is assumed that psychosis results (emergent property) from global disintegration of the dynamic core, neuro-system disconnections fragment conscious experience while the specific clinical patterns of psychosis relate to the different neuronal subsystems which are infected. These systems and the brain dynamics in psychosis are further explained in the following section.

3.2. Decreased Neural Complexity and Schizophrenia

Schizophrenia is a complex disease involving many clinical symptomatic patterns. It is assumed that disturbances of connectivity involving the organization of the dynamic core are at the basis of schizophrenia symptoms (Tononi and Edelman, 2000). It is proposed that the concept of neural complexity described above can account for most if not all of schizophrenia pathology. Following, is an attempt to link events at the biological levels relevant to neuronal connectivity with psychological levels relevant to schizophrenia experience.

Normal mental functions and normal coherent integration of conscious experience relays on optimization of connectivity patterns and hierarchical organization of the brain as captured by the idea of neural complexity (see previous chapters). Schizophrenia arises when these brain organizations are perturbed to the extent that neural complexity is reduced. The initial perturbation is of the “disconnection type” in the sense that psychosis occurs first. The balanced activity between orderliness and randomness shifts toward randomness. The elements in the system become loosely connected and neuronal group activity becomes statistically independent. This in itself reduces the optimization of connectivity dynamics allowing for a reduction in neural complexity.

The system tends to stabilize as well as resume optimization of neural complexity. In the process of stabilizing, the system shifts towards increasing connectivity dynamics. This is probably a compensatory move to balance the system, however, this swing of connectivity-dynamics pushes the system toward the overly connected activity allowing for orderliness to prevail and fixed connectivity patterns

to spread in the brain. Neural complexity stays low since optimization of connectivity dynamics was not achieved. This overly connected fixated dynamics is characteristic of poverty schizophrenia and residual symptoms (Peled, 1999). Since the brain system probably strives to optimization of neural complexity then at this point a tendency toward randomness is favored leaving the system prone to recurrent connectivity breakdown and psychosis. In an attempt to reconstitute optimization of neural complexity, the brain system becomes unstable, “oscillating” between “excessive” orderliness and randomness. This oscillating dynamics is reflected in the clinical shifting between positive symptoms and negative symptoms during the course of schizophrenia (Andreasen, 1982).

Balanced connectivity is probably continuously regulated by neural systems that have wide spread distribution and influence many cortical systems simultaneously. Neural systems known to have regulatory effects as well as wide global cortical distribution are the catecholaminergic systems (e.g., the adrenergic, serotonergic or dopaminergic systems). It has been repeatedly shown that the dopaminergic system is involved in schizophrenia (Snyder, 1976; Goldman-Rakic, 1987; Davis *et al*, 1991; Grace, 1991; Goldman-Rakic, 1994; Andreasen, 1997).

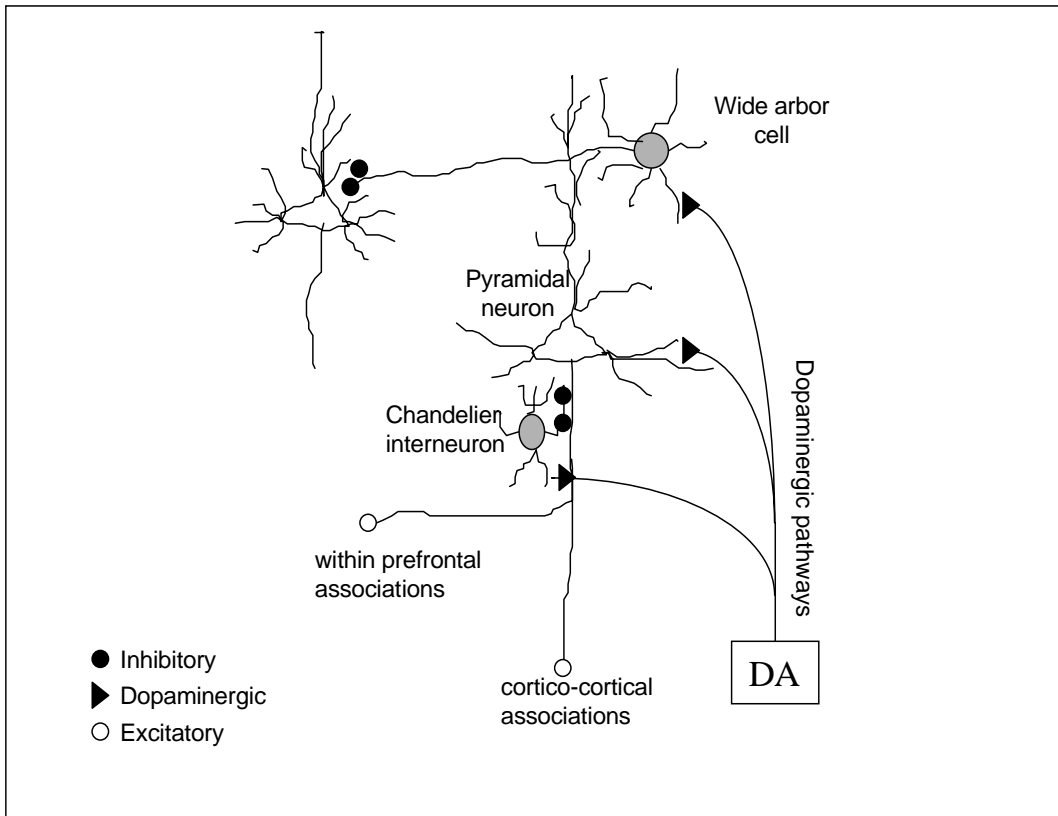
The original dopaminergic hypothesis for schizophrenia proposed that hyperactivity of dopamine transmission is responsible for schizophrenia. This hypothesis was supported by two principal observations: 1) the correlation between the antipsychotic potency of neuroleptics and their potency to block D₂ receptors and 2) the psychotogenic effect of amphetamine and other dopamine enhancing drugs. The dopamine hypothesis formulated more than 30 years ago, still lacks definitive experimental validation and certainly must be modified to account for both the diversity of clinical syndrome and also the complexity of dopamine transmission in cortical and subcortical regions of the brain (Soares & Innis, 1999).

More recently, a dynamic perspective of the dopamine hypothesis proposes that an imbalance between cortical and subcortical dopaminergic activities could have relevance to schizophrenia (Davis *et al*, 1991). Two formulations built upon such imbalance have been proposed. According to the first formulation, negative symptoms of schizophrenia are related to decreased dopaminergic function in the cortex, whereas positive symptoms are associated with increased transmission in subcortical mesolimbic dopaminergic pathways (Davis *et al*, 1991). According to the second formulation, low basal levels of synaptic dopamine predispose to excessive

phasic or burst release of dopamine (Grace, 1991). In both formulations, negative symptoms of schizophrenia are associated with low dopamine function and positive symptoms with excessive dopamine transmission.

Dopaminergic pathways relevant for schizophrenia are predominantly those making synaptic connections with prefrontal and frontal neurons. Prefrontal functions have been repeatedly cited as relevant to schizophrenia (Goldman-Rakic, 1987; Winn, 1994; Goldman-Rakic, 1996; Lewis, 1995; McCarthy *et al*, 1996; Selemon *et al*, 1995; Stanly *et al* 1995). The prefrontal associations play an important integrative function for typical high mental functions such as those tasks requiring delay response and sequencing of goal directed decision making or planning (Mesulam, 1998). An overall view of the dopaminergic interactions with the prefrontal cortex suggests a neuronal circuit for “complexity regulation” relevant to prefrontal integrative function (figure 11).

Figure 11



Cortico cortical connectivity both within the prefrontal cortex and with other cortical regions is sustained by the activity of pyramidal neurons (Fuster, 1995; 1997; Mesulam, 1998; Lewis *et al*, 1999) (figure 11). It has been suggested that reverberating feedback activity in these networks is responsible for holding information online to execute goal-directed delayed-response tasks (Cohen *et al*, 1996; Davis & Lewis, 1995; Frith *et al*, 1991; Goldman-Rakic, 1996; Lewis *et al*, 1999; Williams & Goldman-Rakic, 1995). These reverberating networks are regulated by the combined excitatory and inhibitory influences on the input-output function of the pyramidal neuron. Direct excitatory influences are provided by dopaminergic synapses on the dendrites of the pyramidal cell. At the same time dopaminergic synapses also provide inhibitory effect on the same pyramidal cells via indirect circuitry; the chandelier interneurons (Lewis *et al*, 1999). Thus, the dopaminergic activity is in a unique condition to both increase and decrease the activity of the pyramidal neuron.

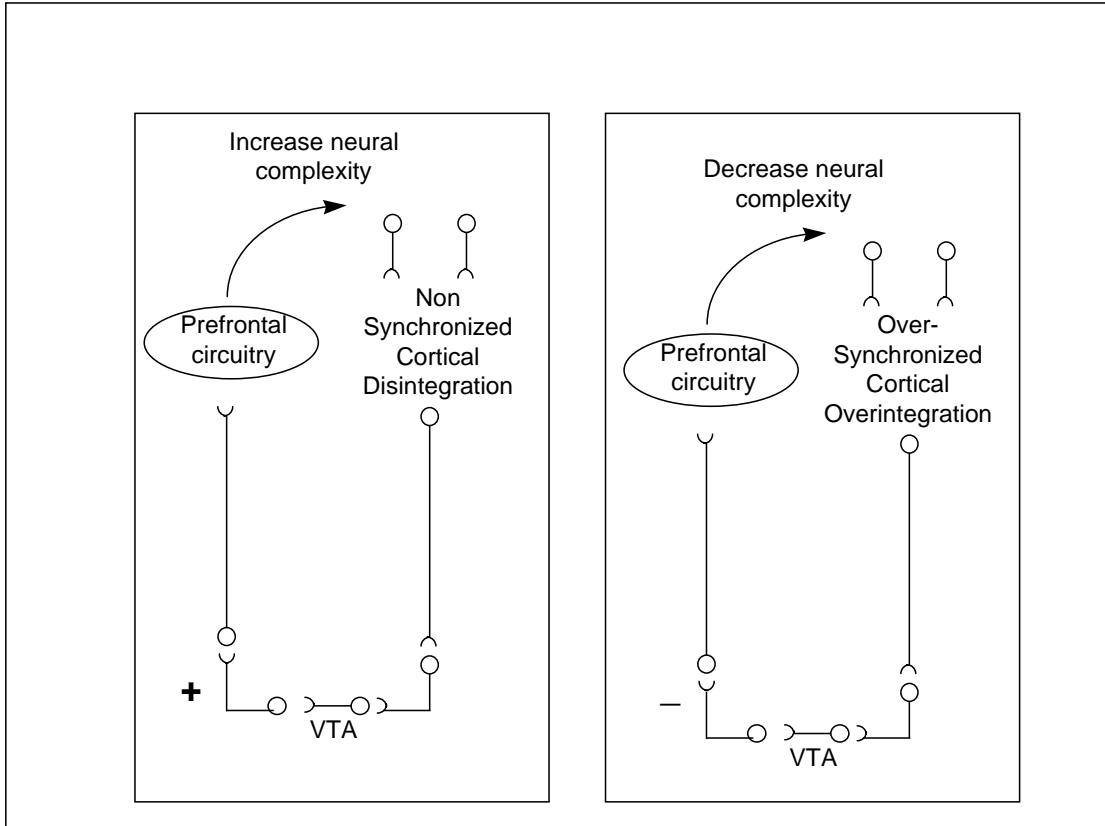
This characteristic of the dopaminergic system puts it in a special situation to promote and maintain neural complexity for integrated cortico-cortical activity of the prefrontal cortex and the overall dopaminergic activity optimizes neural complexity. Whenever inhibitory effects “threaten” to disintegrate (segregate) between the associations sustained via the accommodated activity of pyramidal neurons, the dopaminergic excitatory synapses rebalance the dissociation by increasing the integrative pyramidal activity and *vice versa*, reduced dopaminergic activity will “loosen up” over-integration and over-connectivity. According to this description, the dopaminergic system could function as the “optimizing surveillance” of neural complexity. Such function is necessary in view of possible perturbations to the level of neural complexity that takes place during regular information processing activity.

As mentioned in previous chapters, information processing requires both integration and segregation between neuronal assemblies. The segregation is needed to allow for flexibility and adaptation to new patterns of information whereas integration is needed to represent and preserve the acquired information in relatively stable pattern activation of the relevant neural networks (Tononi *et al*, 1994). The whole system functions best at the border between randomness (i.e., segregation) and orderliness (i.e., integration) (Ditto & Pecora, 1993). The complex information processing in the brain probably involves dynamic oscillations between integration

and segregation during cognitive computations (Paulus *et al*, 1996; 1999). These oscillations risk reducing neural complexity by moving the system to one or the other direction in the graph of figure 5 (see previous chapters).

If the hypothesis regarding the complexity optimization of the dopaminergic system is correct, descending cortical pathways may be those that convey information about cortical levels of neural complexity to subcortical systems such as the VTA (ventral tegmental area) and midbrain of the dopaminergic system. In other words, descending cortical pathways monitor online neural complexity levels of the cortex. Ascending pathways of the dopaminergic system from VTA and midbrain may complete a feedback system to regulate and maintain cortical neural complexity. Whenever “information processing load” perturbs the level of cortical neural complexity, this perturbation is “picked-up” by descending pathways that reach subcortical “pacemakers” which then induce increased dopaminergic activity to “re-optimize” neural complexity. Figure 12 proposes a schematic representation of the circuitry for maintenance of neural complexity in the brain.

Figure 12



As described above, the expression of reduced neural complexity in schizophrenia could be oscillations between overconnectivity and disconnectivity in the system. Sequential organization strategy in a neuro-cognitive behavioral task performed by schizophrenic patients may support the idea of reduced neural complexity in schizophrenia (Paulus *et al*, 1999). Schizophrenic performance was characterized by oscillating episodes of predictability and unpredictability in a left-right choice task. In this task, subjects had to predict the random appearance of an object on one side of the screen. Intermittence in the task was described by transition between two different states of the system, one in which temporally stable organization governs the system and the other where the system gradually “escapes” organization into random activity. Patients showed marked oscillations between the states indicating oscillations between randomness and orderliness or in other words, probable oscillations between disconnectivity and overconnectivity dynamics (figure 5).

Although connectivity breakdown refers to both disconnectivity and overconnectivity within the disturbed neural complexity, it is intuitively easier to describe it as a disconnection syndrome first. Connectivity may be disturbed between brain regions [e.g., the frontal and temporal regions (Frith *et al*, 1991)], and also within brain systems (e.g., within the neuronal networks of the temporal lobe). Within the temporal lobe, disturbance of connectivity may account for reduced activation in that cortical field even though its correlated frontal activation is maintained (McGuire *et al* 1993). In word-fluency tasks, frontal and temporal regions need to work together to enable the coordination of symbolic word representations with motor speech output. If the constraints between these two regions are not satisfied, each one of these processes may proceed uncoordinated and “regardless” of the other, leading to disordered speech on one hand, and disturbed goal-directed (planned) conceptualization (i.e., thinking) on the other hand.

The left temporal cortex contains the networks that integrate the hearing of words with their higher-level conceptual symbolic representations (Mesulam, 1998). This temporal cortex is also important for associating the heard concepts with all other perceptual occurrences, and thus for forming the sensation of a coherent meaningful experience. A connectivity breakdown, within these systems may account for auditory hallucinations due to disconnections of the auditory perceiving system

from the entire coherent dynamic core spread to other cortical activations (e.g., the frontal networks which continue to be activated). Cortical processes responsible for hearing words continue to function regardless of (or disconnected from) auditory processing systems of speech recognition. Thus, regardless of the fact that sound does not activate the auditory senses, and that visual experience does not identify sound sources, voices can still be experienced (i.e., auditory hallucinations).

Perturbed connectivity dynamics of higher levels of associations such as between and within transmodal regions may set the conditions for the appearance of delusions. Conceptions and beliefs presumably form at the level of distributed associative processes responsible for abstract conceptualization (Fuster, 1997; Mesulam, 1998). These conceptions or beliefs have been typically defined as “schemata” or “context” referring to higher order cognitive structures that underlie all aspects of human knowledge and skill. They are the stored traces of earlier experiences that allow for rapid unconscious processing of redundant information.

False higher-level neural network connections (Hoffman, 1992) may allow for the formation of associations that were impossible (or “wrong”) before regular connectivity constraints were violated. The appearance of such “pathological” associations presumably plays an important role in the formation of false beliefs (i.e., delusions) (Hoffman, 1994).

Usually, sensory evidence (from information of sensory processes traveling up the hierarchy) “corrects” and regulates these faulty associations (delusional belief-schemas) by making them “comply” with (i.e., satisfy the constraints of) the real conditions in the environment. Connectivity breakdown between higher level of the hierarchy and lower levels of sensory evaluation, may curtail the “correction” and thus faulty ideational (i.e., delusional) concepts may persist regardless of information suggesting otherwise (i.e., unshakable beliefs). A shift of connectivity balance toward exaggerated connectivity could play an important role in maintaining pathological “wrong” associations. Overconnectivity could cause the system to “resist” any influence of change to the overly connected delusional pattern, thus reducing adaptability (schemata update) to the environmental condition.

Studies with models of artificial neural networks show that fixed connectivity models (i.e., Hopfield network) (Hopfield, 1982) “push” the system to assume fixed states (i.e., converge into attractor configurations) (Herz & Richard, 1991). The network tends to assume repeatedly the same states over and over again (Hoffman *et*

al, 1986). When applied to semantic networks (Hinton, 1981; Spitzer *et al*, 1993) this activity is representative of repeated activation of concepts that metaphorically resemble perseverative ideation. Perseverative ideation is limited to a few repeating concepts and simulates poverty of thought typical to negative symptoms of schizophrenia. It is suggested that one of the deficiencies relevant to negative schizophrenia is overconnectivity within those networks of speech and thought representations.

Imagine that the breakdown in connectivity engulfs extensive networks both within and between systems of the hierarchy. In this case, mixtures of multiple symptoms may appear. If connectivity breakdown is prominent within multiple systems, the perception of sensations, construction of concepts, and planning of goal-oriented responses will all be affected. Loosening of associations, delusions, hallucinations and disorganized behavior will mix in a grossly disorganized mental condition. In these conditions it may be difficult to assess symptoms such as delusions or hallucinations because they will be “fragmented” by the loosening of associations and “covered” by grossly unorganized behavior (Andreasen, 1982; 1984). This symptomatic profile is in agreement with the description of disorganized schizophrenia (Liddle, 1987).

Reality-distortion, and poverty schizophrenia are two additional entities of schizophrenia classification (Liddle, 1987; Liddle *et al*, 1992). Reality-distortion is typically dominated by hallucinations and delusions. In these cases, multimodal heteromodal and their connections with transmodal networks are presumably affected (i.e., temporo-frontal connections; Mesulam, 1998) causing top-down bottom-up imbalances. A failure to control the contents of consciousness results because input and output processes are not automatically supported by global formations that organize them into larger structures to provide context. Lack of top-down global organization alters the meaning of trivialities. Normally, the experience of significance is dependent on the perception of patterned wholes. When the “Gestalts” are deficient, details attract attention. Because they are experienced as new, they often seem to evoke a sense of significance unrelated to general meaning. Attribution of meanings to unrelated events may emerge just because these events are temporally occurring. Other erroneous reconstructions also occur allowing for endless false recombinations of conscious experiences resulting from the loss of global contextual top-down bottom-up balance.

Poverty symptoms presumably emerge from connectivity failure of the networks located at the highest levels of the hierarchy. These are the networks that connect sensation with action (Mesulam, 1998). Relevant social occurrences or other incidents in the environment fail to activate actions and responses of high-level integration. This leaves the patient behaviorally and emotionally unresponsive to the psychosocial environment; volition is lessened and any socially motivated action is abolished. Hypofrontality, indicating possible failure to activate higher-level associations of sensation with action, has been correlated with poverty symptoms (Andreasen, 1983).

Perturbation to connectivity dynamics could result form a multitude of etiologies that are in agreement with the “stress-diathesis hypothesis” for schizophrenia (Sadok, 1989). Genetic to neurotransmitter alterations can lay the ground for the “diathesis” part of the model. Stressful events, typically of conflicting nature, may constitute the “stress” part of the model. It is relatively easy to imagine how alteration of neurotransmitter activity alters connectivity in the brain, however, it is much more difficult to imagine how external stimuli (e.g., stressful life events) interfere with connectivity in the brain.

One may evoke the analogy of “conflict” to explain the disruptive influences that external stressful stimuli may have on the connectivity of the brain. Environmental external information has a constraining influence on the networks that process incoming information. Imagine that two or more external inputs constrain a network to assume opposing configurations. Units of the network will tend to assume values relevant to one configuration and at the same time these units will also be constrained to assume the values of the other configuration. Since the two configurations are different, necessarily the constraints for each configuration will be different. Those units induced to satisfy constraints of one input will inevitably fail to satisfy the constraints of the other input. The result is a violation of constraint-satisfaction and connectivity breakdown in the network.

Naturally, conflicts are typically resolved one way or the other; in the sense that the network converges to satisfy one set of constraints only. In effect, this is presumably the underlying mechanism of arriving at a mental solution (Rumelhart & McClelland, 1986; Herz *et al*, 1991). However, imagine that the conflict is “strong” in which case the environmental message has either multiple conflicting aspects, or that the conflicting aspects strongly constrain the connectivity. Such conditions have a

threatening potential to “split apart” or “fragment” the pattern of connectivity. Extensive violations of multiple constraint satisfaction could occur and destroy the functional connectivity of the system. In effect, if one examines which are the salient characteristics of environmental stresses, it seems they involve multiple strong alterations in the environment (e.g., in natural disasters or wars), or few single yet highly significant changes for the life of the individual (e.g., death of a spouse or loved one). Such changes introduce “abrupt” new constraints to the networks of information processing that may result in rapid violation of old constraints and danger to the integrity of the connectivity dynamics.

From the developmental point of view, experience-dependent plasticity is important for the organization of the brain. If an individual is reared in an environment that is characterized by inconstancy and confusion this will inevitably influence his brain organization. Continuous conflicting messages during development could damage the development of connectivity within relevant neural systems.

Supporting the developmental idea is a substantial body of research from the 1970s concerning families of schizophrenic patients (Sadok, 1989; Leff, 1987). The idea of “double bind” proposed by Betson indicates conflicting messages at the communication level of the “schizophrenogenic family” (Gross *et al*, 1954). Wayne coined the term “pseudomutuality ” to describe the finding of communication deviances in families of schizophrenic patients (Ariety & Goldstain, 1959). In general, there is substantial evidence that schizophrenic patients have developmental disturbances (Weinbrger, 1987) to the extent that as of recently, a prodrome that predicts psychosis is being formulated (Klosterkutter, 1992).

Systems approach to brain organization may also provide for a developmental model that explains why schizophrenia emerges between ages 18 to 25. Consider an interactive process between the brain system and the environment system. Specifically, bear in mind an organizational function between the brain system and the environment system. Let us assume that an organizational parameter and an organizational influence are relevant to the interaction between the developing brain and the environmental organization. An infant brain is not organized and is developing to higher levels of organization partly by experience-dependent plasticity, or in other words, the organizational capacity operated on him by his environment. The environment in this case is the family system and the organizing influences are

embodied within parental upbringing and education. One can assume that at this stage the organizational influences from the environment to the infant brain are predominant while infant organizational influences on his environment are practically zero.

As the infant matures to an adult, the direction of predominant organizational influence is reversed. Leaving the comfort of a supporting family environment the individual is left at the mercy of an unorganized and unfamiliar environment. Since the adult brain has acquired the organizational capacity to act effectively on his environment, he organizes his environment by instituting a family of his own. He acts to order his environment having a regular job, a constant family social setting and a daily routine. Thus, the interaction of the adult with his environment is characterized by a “vector” of organizational influence directed to the environment as opposed to the infant, which can only receive organizational influence from the environment.

This dynamic interaction of organizational influences reveals why early adulthood is such a vulnerable period to brain development. Early adulthood is the time when the person leaves the comfort support of home to the unordered unfamiliar life on his own. The person at that stage has not yet achieved any organizing effect on his environment. This is a period where both brain organizations as well as environmental organization are at their lowest level. Having barely achieved adult brain organization as well as having to deal with the disordered environmental challenges put the individual in a low threshold level of organization at in both systems; his own as well as that of his environment. At this phase, organizational influences are balanced. The vector of organizational power from the brain system toward the environment system is balanced by the inverse influences from the environmental system toward the brain system. It is a critical phase-transition that will eventually determine if the person will achieve the level of brain organization that will enable him to organize his life as a mature adult.

If for some reason the brain system does not achieve the threshold organization level to make the phase-transition, it will result in a collapse of organization levels due to the overwhelming disorganization influences of the environmental system. This threshold dynamic of phase-transition may explain the multiple factors that are considered to cause schizophrenia, for example, the idea of the “stress diathesis” model. If some developmental impairment, including haphazard upbringing due to a malfunctioning family, impairs brain organizational development,

then the threshold for organization capacity will not be achieved. On the other hand, normal development but an overly irregular environment that acts to disorganize the brain will also impair the threshold surpass.

These bi-directional interactive organizational influences between environment and brain organization serve to exemplify new modes of explanation to etiological theories of schizophrenia such as the “stress diathesis” model. Such novel explanations may serve to bring our theories closer to brain functions. The concept of matching complexity (see previous chapters) may one day serve as a mathematical formulation to start thinking about possible quantitative measurements of brain-environmental interdependencies and influences. These types of theories are also in agreement with the biopsychosocial medical thinking.

3.3. Instability of Representational Dynamics and Mood Disorders

In the previous section (chapter 2) mood was assumed to emerge (see emergent properties in chapter 1) as a property that accompanies optimizations of internal representations. Elevated mood accompanies optimization dynamics while depressed mood is correlated to deoptimization dynamics.

In general, three conditions can perturb the regular balance of optimization dynamics, 1) alterations in the neural substrate, 2) influences of environmental inputs such as various stressors and 3) internal configurations “shaped by” experience-dependent processes. It is known that certain “organic” factors may cause depressed mood, for example hypothyroidism and certain tumors. Presumably in these cases of “organic” contributors, the deoptimization shift in the system is triggered by the alterations of the neural substrate itself (i.e., neurohormonal and neurotransmitter activity). Probably the hormone or neurotransmitter alter directly 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 the 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 actually 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” i.e., 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. Widespread deoptimization of many internal representations could shift the dynamics of the system toward deoptimization and trigger the emergence of depressed mood.

Internal representations of events are incorporated via interactions with the environment. Hebbian-like learning will represent information of various complex degrees, starting from simple representations of objects to the more complex such as representations of interpersonal events and relationships. If an event incorporated was experienced with frustration of constraints, the dynamics of that constraint frustration can also be embedded in the network by Hebbian-like learning. Thus, future activation of the network would activate these frustrations of constraint and so activating an imbalanced network that can perturb the brain organization. This might explain learned phobias; the remembrance of the phobic stimulus is accompanied by the sensation of fear emerging from the perturbed unstable network associated with that information.

Personality traits play an important role in the interplay between internal configurations and their optimization dynamics by external events. A mismatch between the internal configuration and the statistical structure of an input set that is

coming from a psychosocial event in the environment can deoptimize the relevant set of internal configurations (see previous chapter). Thus, an individual reared to appreciate hygiene and perfectionism will deoptimize these representations when presented with a situation carrying the information of disarray and filth. It is proposed that the combination of certain internal configurations (or in other words, sensitivities of personality traits) with certain specifically significant situations (or stimuli) may create deoptimization shifts that could trigger a depressive reaction. In effect, certain types of depression (e.g., dysthymia, mix anxiety and depression) have been typically related to personality disorders in clinical experience (Sadok, 1989).

In effect, any of the factors mentioned above, (i.e., organic biological, environment stressors or personality configurations,) individually, or in combinations, can trigger the deoptimization shift responsible for a clinical picture of depression. Once triggered, counteraction of optimization balance may “attempt” to compensate the deoptimization shift. This may push the system into an oscillatory dynamics of optimizations and deoptimizations. In this case, a bipolar disorder can emerge. The law of instability states that a system subject to oscillations among few conflicting forces is at risk of rupture and breakdown. In effect, both depression and manic disorders could develop psychosis (psychotic depression and psychosis of mania), indicating that the optimization dynamics perturbed the system enough to cause connectivity breakdown and fragmentation of the dynamic core.

However, before connectivity is disturbed, constraint among distributed networks acts to “absorb” the agitation spread in the system. In the previous chapters, anxiety was presumed to emerge from distributed frustration of constraints that accompany any disturbance of neural network organizations within the dynamic core. For example, destabilization of the higher-level transmodal brain systems relevant to conscious awareness could be reflected by the sensation of losing control, which is typical to anxiety disorders. In an attempt to “absorb” the instabilities (see above) the perturbations typically disseminate to the rest of the nervous system including the peripheral nervous system, creating instabilities in the activities of cardiac, gastric and other peripheral systems. Such instabilities in the activity of peripheral organs of the body are responsible for the peripheral symptoms of anxiety (e.g., palpitations, diarrhea and other symptoms). Thus, the variability of symptomatic manifestation of anxiety is probably correlated with the extent and distribution of destabilization within the nervous system.

Destabilization and constraint frustration in the neural networks of the brain could arise from metabolic and toxic agents acting directly on the neural substrate, or could evolve from conflicting psychosocial events which mismatch internal configurations (see above). Thus, anxiety has been tied to “organic” factors such as hormonal metabolic and toxic influences, as well as to personality traits and environmental stresses (Sadok, 1989). Interestingly, most psychiatric disorders involve anxiety as a common accompanying symptom. Assuming that both optimization dynamics (i.e., mood disorders) as well as fragmentation of the dynamic core (i.e., psychosis) are accompanied by frustration of constraints, it is conceivable why anxiety is typically an accompanying symptom of most psychiatric disorders.

3.4. Neuro-system Analysis and Personality Disorders

According to the previous sections of this manuscript, personality assessment equals the assessment of internal representations. Unfolding the subjective experience of the patient and his perception of the world, especially of interpersonal experiences, allows for reconstructing his internal map of organismic evaluation (see previous chapters). Once reconstructed this internal map of representations is a powerful predictor of the modes of reactions and interactions that the patient will actualize. One could easily predict what the patient with internal optimizations of orderliness and hygiene will experience when confronted with filth and dirt conditions.

In addition to features and content of internal representations, the levels of their development also warrant assessment. Rudimental maps allow for partial and opposing representations to “split” experiences. Partial development of internal representations induces all-or-non experiences (black and white attitudes) impeding complex experiences (varieties of gray attitudes). In short, the assessment of internal representations follows two dimensions in parallel, 1) the development levels and the content features.

As commonly described, lower organization levels of internal representations result in psychological attitudes and complaints, which have been titled “borderline personality disorders.” Higher organization levels of internal representations show representational content-relevant attitudes and complaints. In between diverse levels of organization and relevant representational patterns may provide for a spectrum of personality disturbances.

Frequently, individuals seek psychotherapeutic treatment out of distress that originates from interpersonal relationships. Initially the relations with the therapist will repeat the same patterns of interpersonal relations that caused the distress. The skilled therapist identifies these malfunctioning interpersonal patterns and acts during therapy in a way that gradually changes the attitudes of the client to similar situations in the future. This therapeutic intervention was termed “correcting experience.” Better coping in psychosocial situations reduces suffering and enables the relief from symptoms. Psychodynamic therapy involves overcoming resistance, offering appropriate interpretations and increasing insight to relevant aspects of interpersonal relations (Freud, 1953; Michael, 1986).

According to the approach of constraint-organization in the brain, the psychotherapeutic process can be described as a physical change that takes place in the brain of the client. Initially, the relations between the internal map of reference of the individual (i.e., internal representations) and some aspects of the psychosocial situations he encounters are incongruous (see mismatch mentioned above). This incompatibility reaches the extent where perception and reaction to those psychosocial situations are distorted and interfere with the psychosocial functioning of the individual. The psychosocial dysfunction is generally accompanied by distress, which is typically expressed by symptoms of anxiety and depression.

The goal of the therapy is to reshape the internal representations to include the appropriate internal configurations to cope with the psychosocial situations at hand. Initially, the client perceives the therapist as a person from his past (i.e., transference). This is because the client activates the attractor systems, which represent the person from the past. Since the therapist is not the same as the activated representation, a distorted perception of the therapist emerges. Due to this distortion an inappropriate behavioral reaction to the therapist (transference) occurs. Most probably, this distortion occurs with other interpersonal situations outside the therapeutic sessions. This indicates that there is substantial mismatch between the internal representation and the psychosocial reality.

The therapist acts to enlarge the repertoire of representations of the individual to match many more different psychosocial situations. In other words, the psychotherapeutic process increases the neural complexity (C_N) in the brain of the client (see above). When the therapist reacts to the client in new ways that were never perceived by him before, Hebbian mechanisms of plasticity will gradually create the

new attractor systems needed for the additional internal representations. In this manner, the therapist “shapes” the space-state topology of the brain to form new internal representations. The process probably involves actual changes in the functional connectivity of the neural systems involved, as such, it is a physical process in the brain.

The process is actually much more complex than the above description suggests. For example, due to a lack of representational systems, many times the interpretations offered by the therapist are denied and do not gain access to the global formations (see denial above). These interpretations will never reach conscious levels (resistance in psychoanalytic terminology). The set of inputs from the interpretation of the therapist simply does not satisfy the constraints of the global configuration thus conflicting with the message in the global workspace. It has been wisely indicated that for an interpretation to succeed it must be delivered at the right time (i.e., when the individual is ready for it) (Michael, 1986). There must be a certain constellation of the global organization, which is favorable for including the new patterns of information proposed by the interpretation. The therapist first prepares the patient by repeated clarifications, confrontations and other interpretations. This process changes the global formation, “moving it slightly” toward the pattern that will be favorable in accepting the critical interpretation (i.e., the one that will induce the change).

Freud indicated the importance of overcoming resistance in psychotherapy (Freud, 1953). By gradually changing the global formation to a favorable configuration, the therapy enables the incorporation of an interpretation and the therapist overcomes the resistance to that interpretation. Repeating this process over and over again will eventually “reshape” the state-space of the brain to increase the complexity of internal representations and thus the psychological repertoire of the individual. These changes transpire and are maintained by the experience-dependent plastic processes of the brain. It is probably the increase in neural complexity that improves psychosocial adaptability. In turn, psychosocial adaptability reduces the suffering that originates from conflicts of interpersonal relations. In other words, the outcome of psychotherapy is relief of distress in interpersonal situations. It is achieved via the reduction of specific sensitivities of personality traits and the increase of flexibility adaptability to changing psychosocial situations.

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Psychiatric Brain Profiling A New Psychiatric Diagnosis

Reality is merely an illusion, albeit a very persistent one.

Albert Einstein (1879 - 1955)

4.1. Psychiatric Brain Profiling Outline

Some of the names for mental disturbances early on in the history of psychiatry were based upon etiologic theoretical assumptions, for example “melancholia” proposed that depression resulted from an excess of black bile and “hysteria” proposed that the uterus wanders in the body causing somatic pain and discomfort in hysteric women. Later, the name “schizophrenia” was proposed to describe the splitting of mental functions (“schizo” meaning splitting). Other nomenclatures of mental disorders were descriptive, for example “dementia praecox” an earlier name for schizophrenia that was related to the clinical description of the patient having dementia earlier than usual at early adulthood. Terms like depression and anxiety are purely descriptive relating only to clinical symptoms and signs.

Psychology introduced concepts such as “weakness of ego” and “defense mechanisms” to psychiatry. These were etiologically oriented terms originating from psychoanalytic theory. The multitude of diagnostic terms and the mixture between descriptive and etiological nomenclature created a great deal of confusion and markedly reduced validity and reliability of psychiatric diagnosis (Willson, 1993; Van-Praag, 1997; Toker, 1998).

In the beginning of the 1980s, the DSM (diagnostic statistical manual) was developed from the RDC (research diagnostic criteria) providing a checklist of signs and symptoms to each diagnostic entity in psychiatry. The DSM uses exclusive and inclusive criteria in an attempt to form independent distinct reliable diagnostic entities of mental disorders. The DSM was somewhat successful in achieving the goal of increased reliability and validity for psychiatric diagnosis, but not without cost. The set of exclusively descriptive symptomatic checklists was criticized for “narrowing the gaze of psychiatry” and the creation of distinct “disease” entities was not achieved as demonstrated by the overlap of symptoms, for example, in schizoaffective disorder (Willson, 1993; Van-Praag, 1997).

In the reality of clinical practice, the understanding of the patient’s problems requires a complex integration of multiple considerations. It is not enough to categorize the symptoms. The patient’s past and his brain (psychological)

development cannot be ignored. Existing approaches have difficulty achieving an integrative comprehensive evaluation of the patient. This is due to different conceptualizations, or as mentioned in the introduction, because of the development of different languages each unrelated to the brain.

At this point, it is important to go back to Freud's initial quest in his project to furnish a psychology, or in this case a psychiatry, that shall be a natural science, i.e., neuroscience. The new diagnostic system is termed psychiatric brain profiling (PBP) to emphasize psychiatric evaluation as a functional brain assessment. It is based on the theoretical considerations detailed in this manuscript.

The PBP is a diagnosis of the perturbations caused to normal brain organization. As such, it uses an input-output model (figure 13) where the input to the system relates to possible perturbators and the clinical manifestations reflect the different perturbations caused to the system. The conditions of the system are also evaluated as they are critical to the behavior of the system within input and output occurrences. In sum, the PBP considers the causes, the symptoms and the brain system all in a unified context. Being a communicating language between mental disorders and their relevant assumed brain disturbances, the PBP emphasizes "neuroscience orientation" attempting to relate mental disorders to hypothetical brain disorganizations as mentioned so far in this manuscript.

Figure 13

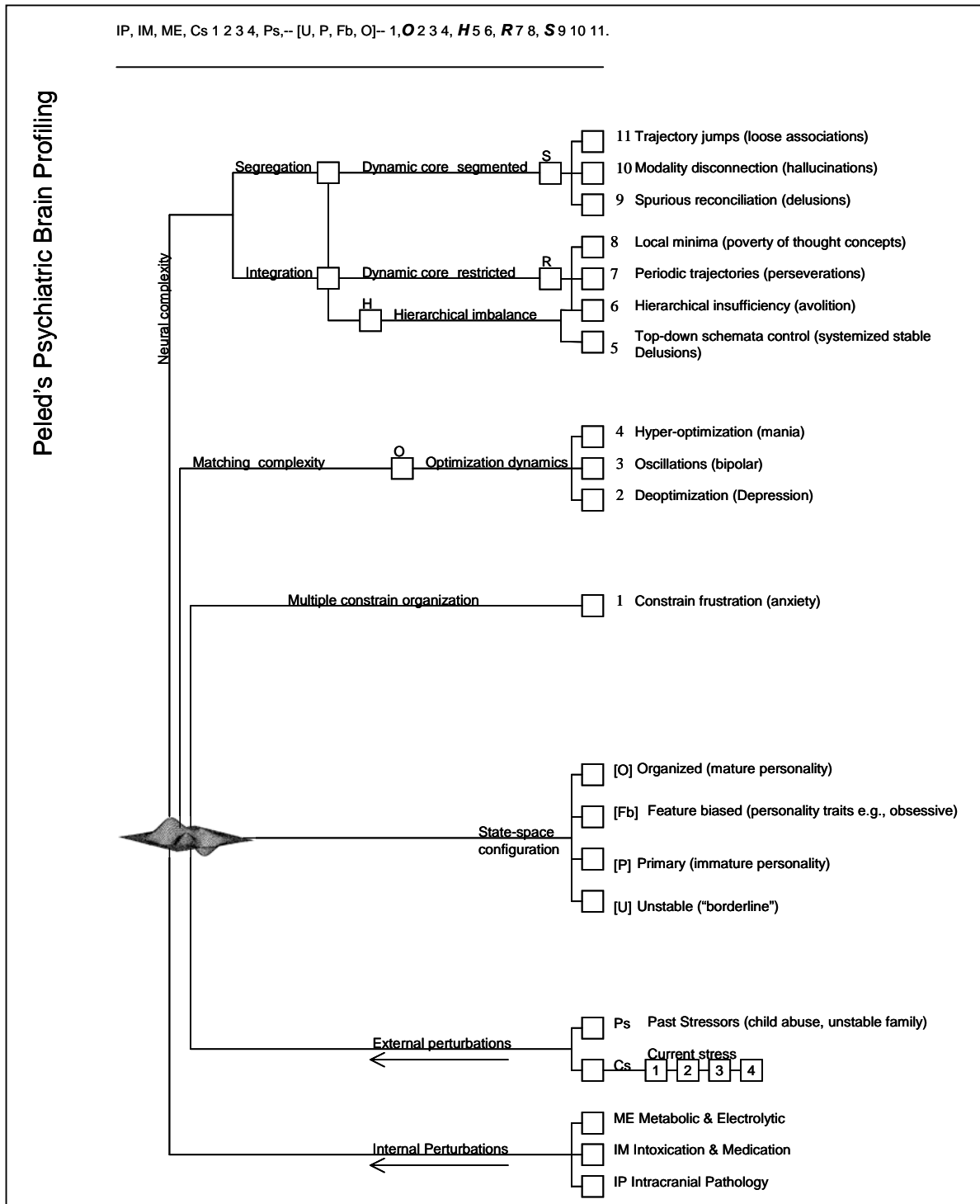


Figure 13 schematizes the input, the system and the outputs from the bottom up. At the bottom “external and internal perturbators” input the system, a state space configuration sign symbolizes the system and perturbations are listed by severity going from top to bottom on the upper part of the figure. Check boxes are inserted to enable the clinician a proper registration of his evaluation.

Four aspects of brain theory are utilized in PBP, 1) state space configuration and organization levels of the system, (i.e., the brain), 2) connectivity dynamics as reflected by neural complexity, 3) matching complexity optimization dynamics, and 4) constraint satisfaction between neural processes and neuronal ensembles. Even though state space configuration and organization levels of the brain system are most important for PBP, in the clinical assessment they are harder to diagnose and less evident on first clinical evaluation. Typically, in the first evaluations symptoms are more evident. These are the symptoms that reflect disturbances of connectivity and optimization dynamics. I choose to proceed in the clinical approach and start with the diagnostic schematization of these disturbances first. Thus, the clinician starts by identifying or ruling-out the most severe perturbations, going down the list to evaluate the less evident but more important aspects of brain organizations.

If the patient’s speech is disordered, words are unrelated to each other and sentences are confused and incomprehensible, then it is assumed that the trajectory of concept activations in the state space of his brain conceptual network is characterized by “jumps” which disconnect associations forming the thought process (also termed loosening of associations). Sometimes, the loosening of associations manifests in a milder form, where words within sentences make sense and sentences are logically connected, however, topics of speech content are unrelated and discussion is derailed without course and direction. All these findings in a patient qualify checking the box numbered 11 in figure 13.

When patients hear, see, feel or smell what is not there, or in other words experience perception without stimulus then the brain system is acting disconnected from external input as well as from other modalities. For example, visual perception is normally connected to its auditory co-stimulus, seeing someone speak is perceived by hearing his voice speak. When schizophrenic patients have auditory hallucination, they not only perceive a stimulus that is not there but they also activate auditory

processes disconnected from other modalities such as visual processes. Findings of hallucinations in a patient qualify him with a score in position 10 of figure 13.

Concepts are activated in the state space of the brain system in an experience-dependent orderly manner allowing for a reality-oriented adaptive environment-dependent reconciliation. When spurious reconciliation of these concepts emerges due to disconnections of neuronal ensembles then false ideations biased from real occurrences emerge. These are the delusions characterized as unshakeable false beliefs. They are false because they are biased from the real events and they are unshakable because they are dominating the dynamic core and as such, they are the conscious content of the individual as real experiences are. Since these delusions emerge within disconnected segregated brain systems, they are frequently unstable and can change over time. If the patient experiences such delusions, he qualifies for coding position 9 in figure 13.

As described in previous chapters, the constriction of the dynamics of state space due to over-connectivity results in “local minima” restricting the number of possible conceptual activations and thus resulting in poverty of thought and consequently, also of speech (position 8 in figure 13). These cases also result in a less extreme form, that of “periodic attractors” which are reflected by perseverations and repeated ideations (position 7 in figure 13).

Since the dynamic core reflects the highest integration of the brain system, that of elevated consciousness activity (see previous chapters) then if constricted to serious degrees, the upper hierarchical organization could stop functioning abolishing the transmodal integrative levels. As mentioned in Masulam’s work (see previous chapters) such reduction of the highest hierarchical levels of the brain system may result in disconnection between sensation and cognition, which probably reduces response of active ideation to the sensations coming from experience. This is further translated to “activity disinterest” to whatever transpires in the patient’s life. Avolition is the term reserved for these cases in the clinical literature. Scoring position 6 in figure 13 is reserved to those patients suffering from avolition such as that of post-psychotic schizophrenic patients with negative signs schizophrenia.

Another type of hierarchical disturbance mentioned in previous chapters is that of higher-level rigid schemata that achieve top-down imbalanced control over incoming bottom-up processes of environmental experiences. Stable systemized delusions that gradually grow to engulf each new experience result from biasing

incoming bottom-up experiences by top-down rigid over-control. Patients suffering from systemized stable delusions qualify scoring on the top-down schemata control of position 5 in figure 13.

Disturbances of matching complexity optimizations are the next serious disturbances after neural complexity disturbances. As explained in previous chapters optimization dynamics of internal representations is accompanied by the emergent property of mood sensation. Hyper-optimization (position 4) is reserved for patients having a manic episode. Deoptimization (position 2) is reserved for depressed patients and oscillations (position 3) is reserved for bipolar patients. If a patient is bipolar and is currently depressed, he will score positions 2 and 3 together. Similarly, if he is bipolar and currently manic his score will include both positions 3 and 4 (see figure 13). Having no other current brain measurement for optimization disorders other than DSM signs and symptoms these will temporarily be used in the PBP to score positions 2 to 4.

As mentioned in the chapters about constraint frustration among neuronal ensembles, most perturbations of brain organization also result in constraint frustration. Fear sensation and anxiety score position 1 in figure 13. If the patient also scored position 9, 10 or 11 he may then qualify for an old description of psychotic panic, or in any case, such scoring describes these psychotic patients that are also highly anxious. If the patient also scores position 2 for deoptimization of matching complexity, then the clinical picture of mixed anxiety and depression is described.

If the patient has repeated ideations, thus scoring periodic trajectories in position 7, together with anxious feelings (score in position 1), then the clinical picture is that of obsessive-compulsive disorder currently used to describe certain psychiatric cases. If position 1 is scored together with positions “Ps” (past stressors) and “Cs” (current stressors) it can account for certain phobias. With additional scorings, position 1 can account for currently nominated posttraumatic stress disordered patients, and even eating disordered patients (these will be described later in this chapter).

In the previous chapters, extensive parts were dedicated to show how Freud’s psychological concepts and those of his followers the object relations psychologists, were relevant to brain organization and the development of state-space configuration. The maturity of brain organization and state-space configuration cannot be measured directly. In the meantime, such evaluation would require the investigation of

psychological performance similar to that described by Kerenberg for personality organization levels.

The development of state-space configuration can roughly have four levels, 1) “organized” as the most mature level, 2) “feature biased” when slightly immature aspects cause biases of representations, 3) “primary” when immature personality is the case and 4) “unstable” when organization was never achieved correctly.

Scoring organized state-space configuration “O” is both exclusive, when there are no findings suggesting otherwise regarding state-space configuration levels, as well as inclusive, when there is evidence of flexible adaptable compatible behaviors in front of difficult stressing situations. Feature biased “Fb” is scored for personalities that develop signs and symptoms due to specific “sensitivities” for example, the anxiety of the obsessive confronted with the untidy room.

Immature personality is characterized by childish attitudes and behaviors. Typically a child is egocentric, has a low frustration threshold and is dependent. These characteristics when found to be responsible for perturbations in adults score “primary state-space configuration, i.e., P.” Egocentricity is expressed by an attitude that puts the individual at the center of entitlement. It is an individual that can not experience the fact that he has to adapt to the environment and is astonished that everyone does not act to accommodate his needs. This can be exemplified when going to work in a demanding system or being drafted to the army. These individuals cannot adapt to demands where they are not primarily accommodated for their needs. Another aspect of egocentricity is that of lack of empathy. Just as the child snatching a toy from another child looks at him with disregard as he swipes, so is the egocentric adult unable to put himself in the mental situation of another to experience what he might be feeling. It is a lack of developing internal representations that enable experiencing what other may experience thus developing the ability for empathy.

Low frustration threshold in the child is typically expressed with “temper tantrums”. In the adult, this would be transformed to violent outbursts or attacks of anxiety or depressions or both. With no motor outlet in the adult, perturbations probably frustrate constraints and deoptimize the system. Immature personalities depend on others consultation and approval for their guidance and self-esteem, thus like children they are dependent. For those familiar with the terminology of psychotherapy, these patients have also narcissistic traits (see previous chapters).

The score of “unstable state space configuration, U” is reserved for those patients that are currently titled “borderline personality organization”. These are cases where the state-space configuration is unstable thus subjecting the patient to repeated perturbations of neural complexity (i.e., psychosis). Additionally, the configuration space in these patients is rudimental and representations are partial and incomplete. This allows for splitting, (i.e., “all or none”) attitudes and other distortions typical to these patients (see previous chapters).

According to the PBP, external and internal perturbators effect the system development and organization. External perturbators are both past stressors “Ps” as well as current stressors “Cs.” Child abuse and markedly unstable family history qualify scores on “Ps” code. “Cs” is scored according to the Holmes-Rahe Social Adjustment Scale (Sadok, 1989). Table 1 explains how to score “Cs” “1” to “4” positions according to the Holmes-Rahe Social Adjustment Scale.

Table 1

Cs1	1] Minor violations of the law 2] Christmas 3] Vacation 4] Change in no. of family get-togethers 5] Change in sleeping/eating habits 6] Small mortgage or loan 7] Change in social activities 8] Change in residence/schools/recreation 9] Change in work hours or conditions 10] Trouble with boss
Cs2	11] Revision of personal habits 12] Change in living conditions 13] Begin or end school 14] Partner begins or stops work 15] Outstanding personal achievement 16] Trouble with in-laws 17] Son or daughter leaving home 18] Change in responsibilities at work 19] Foreclosure of mortgage or loan 20] Major mortgage
Cs3	21] Change in no. of arguments with spouse 22] Change to different line of work 23] Death of close friend 24] Change in financial state 25] Business readjustment 26] Gain of new family member 27] Sex difficulties 28] Pregnancy 29] Change in health of family member 30] Retirement
Cs4	31] Marital reconciliation 32] Dismissal from work 33] Marriage 34] Personal injury or illness 35] Death of a close family member 36] Jail term 37] Marital separation 38] Divorce 39] Death of spouse

Any biological effect on neuronal function may interfere with brain organization thus metabolic, infective, malignancies or any other pathology whether intracranial (position IP) or extracranial (positions ME and IM) needs to be coded. Table 2 explains medical findings qualifying scores on “ME” “IM” and “IP” positions.

Table 2

34	Metabolic electrolytes imbalances and infections that might influence neuronal activity
35	Medications intoxication effects, alcohol and street drugs that influence neuronal activity
36	Inter-cranial pathology, tumors, CVA, Alzheimer, Parkinson, seizures, brain infections.

Compared to the DSM the PBP summarized in figure 13 is less categorical and has more degrees of freedom. Being very categorical, the DSM tends to “constrain” clinical profiles to certain predetermined checklists. For example, clinical pictures of psychotic patients with concomitant high levels of anxiety and even panic attacks find less expression in the nomenclature of the DSM. Another example has to do with the lately found higher than initially thought co-occurrences of OCD (obsessive-compulsive disorder) symptoms and Schizophrenia. A profile of coded positions 11, 10, 9 and 1 would describe the first example, while a profile of coded positions 7, and 1 together with 11, 10, and 9, could provide for the diagnosis of the second example.

Contrary to the DSM, other clinical conceptualizations such as psychoanalytic conceptualizations have unlimited degrees of freedom allowing for all concepts to describe all occurrences thus are operationally meaningless. Even though the PBP diagnostic system is non-categorical and flexible, it is still constrained to certain profiles and cannot be blamed for having limitless degrees of freedom. The constraints of the PBP are neuroscience oriented reflecting the hypothesized brain organization of the patient and their perturbations that exert the constraints on the diagnostic profiling.

The DSM, like other traditional diagnostic systems provides a numerical code for each diagnostic entity. Medical provider institutes such as medical insurance typically require such a code. In advantage over other coding systems that assign

some routine meaningless code to mental disorders, the PBP diagnostic system provides a clinically meaningful code that actually reflects in-depth both the clinical picture of the patient as well as the hypothetical neuro-scientific disorder of the patient's brain (Figure 13 top left). Going from left to right, the code describes perturbators, system condition and perturbations. The code can include only the findings leaving out unscored items, or it can be translated into a vector of ones and zeroes, coding 1 for findings and 0 for unscored items. Such vectors, carrying the clinical neuro-scientific information about individual patients can be used for statistical analysis of large follow-up and epidemiological investigations, thus opening new research insights toward brain pathology in mental disorders.

Finally, the PBP diagnosis is less stigmatizing than old terminology. While old terminology considers a mental illness of the patient, the new approach considers a brain disorder for the patient. A brain disorder is more comparable to other disorders in medicine, which have to do with deficiencies of internal organs (i.e., the brain) rather than deficiencies of the patient himself.

4.2. Case Reports and their Formulations of Brain-System Analysis

Case 1.

Mr. A is a 22-year-old male admitted to hospital for the second time because of restlessness and aggressive violent reactions. His parents complain that his behavior gradually changed over a period of the last three days becoming bizarre and inappropriate. He became withdrawn and non-responsive to others. He began speaking to himself and performing rituals that did not have any meaning. He would move objects around, and position himself in unnatural postures. In addition, he stopped sleeping at night and reacted with aggression when approached.

On the day of admission to the psychiatric department he smashed the TV. That was when the decision about hospitalization prevailed and his parents decided to bring him in for examination at the emergency room. On admission, he seemed disconnected. When asked about his problem he responded about other topics. His arguments were fragmented and sentences were unrelated and disconnected from each other to the extent that did not enable a comprehensive understanding of what he was saying. Frequently he would glance to the corners of the room or fixate his gaze on

the phone in the examination room. When questioned about his glances he briefly reported about voices talking to him, and devices controlling his actions. During the examination he often stood and started for the door only to be brought back by his parents.

This type of behavior also occurred two years ago and required hospitalization. It also happened again one year ago but to a lesser extent and did not reach hospitalization. Family history reveals that his mother suffers from recurrent episodes of mixed anxiety and depressions and that her attitude towards Mr. A always alternated between neglect and rejection (during her depressions) and overprotective attachment during anxious behavior. Typically, she would be ambivalent in her attitude toward her son. History of his psychological development reveals marked immaturity expressed by egocentricity, low frustration threshold, impulsive reactivity and emotional liability even to minor stresses. After hospitalization, Mr. A was able to perform only simple jobs. He lost interest in hobbies and social activity and complained that nothing motivated him anymore.

Neural complexity breakdown would be the diagnostic hypothesis for Mr. A's condition during examination on admission. It seems that the clinical picture results from a disintegration of transmodal levels of organization in the brain, causing Mr. A's incongruent behavior, disturbed perception and his disorganized and delusional thinking.

Mr. A's history of interpersonal relations with his primary caregiver at an early age proposes lower level configuration, which contributes to his disorder. It seems that at infancy, when Mr. A's brain was highly plastic and its prime organization took place, he experienced conflicting (double bind) and inconsistent attitudes. These could have disturbed first constraint organization causing and maintaining developmental weakness to the optimal connectivity of the brain. At the time of the first hospitalization, the period of young adulthood when brain organization is required to deal with the increasing demands of life, the optimal neural complexity of Mr. A collapsed creating the first episode of psychosis. As a result of this disturbance to the transmodal organization level of Mr. A's brain, a compensatory over-integration shift probably occurred (see previous chapters). Over-integration is evident by reduction in functioning and volition.

According to PBP described in this manuscript Mr A's diagnostic profile is Ps, [P] S- 9, 10, 11. The coding of 9, 10, and 11 positions reflects his neural complexity

breakdown of disintegration with jumps, disconnected processes and spurious reconciliation of neural network ensembles. History of marked immaturity expressed by egocentricity, low frustration threshold, impulsive reactivity and emotional lability even to minor stresses qualifies Mr. A for a score at the [P] position. The evidence of conflicting attitudes during childhood and biased interpersonal relationships at those periods qualifies Mr. A for a score at the “Ps” position.

Case 2.

Miss F, a 25 year old female complains of mild ongoing anxiety and depressive symptoms. She complains of depressed mood part of the day at least once a week and hypersomnia. She feels frequently insecure with low self-esteem. Her appetite and sleep are mildly disturbed. On examination, these symptoms emerge within problematic interpersonal relations. Specifically, in relations where Miss F feels that she does not get the attention and the esteem she is entitled to. Even in front of mild criticism, Miss F reacts with deep feelings of worthlessness and depression. Sometimes Miss F can pull herself together and the depression never takes a long lasting course. However, depression and anxiety do appear frequently and accompanies Miss F for most of her adult life.

Conventional psychiatric evaluation would define Miss F as suffering from “mixed anxiety and depression” or “dysthymia.” She would also have the additional diagnosis of a personality disorder of the narcissistic type. According to the BPP, the diagnosis of Mrs. F codes as Ps, Cs -1, [P] 1, O-2.

Miss. F’s history and background reveals overprotective parenting typically providing immediate satisfaction and practically no or little frustration. The lack of significantly frustrating situations during infancy and adulthood left Miss F without any experience with such situations and thus without the so-called “psychological tools” to deal with them.

According to the formulations regarding topological and configurational representations by neural systems (see above), her psychiatrist concludes that experience-dependent internal representations in the configuration space of Miss F induce specific sensitivity to signals of rejection and disapproval within interpersonal constellations. Having experienced only appreciation and admiration, Miss F never developed the internal representation to perceive and “deal” with frustration. Her “map” of internal configuration is limited only to presentations created by

experiencing admiration and approval. This rational leads to scores in positions Ps, and [P].

Frustrating messages of rejection and disapproval deoptimize those internal representations of heightened self-esteem and endorsement creating an extensive deoptimization shift in the space-state of the organization of transmodal systems in Miss. F brain. The psychiatrist concludes his diagnosis stating that Miss F suffers from recurrent deoptimization shifts of the transmodal levels (position *O* -2 figure 13). The deoptimization is accompanied by constraint frustration, coding position 1 in figure 13. These shifts originate from specific interactions between the configuration of her internal map of representations (one that incorporates sensitivity to, and inability to cope with, rejection and specific messages of rejection within interpersonal settings (Cs - 1).

Case 3.

Mr. D is a 40 year old male working as a salesman in a big firm. He was admitted to hospitalization due to marked behavioral changes. He stopped going to work, withdrew to his room and slept all day closing all the windows. His family admitted him against his will after he stopped eating and reduced in weight up to 6 Kg over a period of 4 weeks. On admission, he refused to cooperate and did not answer questions. In addition, he seemed suspicious and hostile toward the examiner psychiatrist. He was motionless and demonstrated considerable psychomotor retardation.

Collateral information given by his family reveals that Mr. D suffers from a delusional disorder; over the years, he has gradually developed a firm conviction that his boss, together with the administration at the company, workout a scheme to persecute him, incriminate him and cause him to lose his job. His suspicious attitude did not change even when he obtained a prize for excellency in the workplace. He interpreted it as another phase in the general plan to fire him. When a new event occurred at work, for example, a new employee being hired, his delusion would worsen and he would become depressed.

Recently, his depressions became worse and his general practitioner diagnosed lower levels of thyroid hormone suggesting that this could be the source of depressive symptoms. Mr. D views this diagnosis as another attempt to fire him on the basis of incompetence due to medical conditions. An in-depth investigation about the

beginning of the delusion reveals that early on when Mr. D started working at that company, there really was a criminal affair of conspiracies in the administration and two managers were convicted for criminal acts and sent to jail. Since that affair there was nothing that could suggest improper management performances.

It is obvious that Mr. D developed a system of false convictions that has crystallized around an initial interpretation of a real event, but that has since built-up to a systemized delusion incorporating into it any new event. His system is delusional because it is unshakable even in front of contradicting evidence in promotion and prizing. As such, Mr. D scores 5th position in the PBP indicating a certain reduction of neural complexity by over-integration and a consequent brain hierarchical imbalance.

Mr. D's false set of convictions built into his representational configurations continuously deoptimizes the system causing depressive symptoms that qualify him with additional score on position *O-2* of the BPP.

The findings about hormonal imbalance of the thyroid hormone probably perturbs the optimization dynamics of the brain by interfering with the normal neurohormonal functions in the nervous system designating Mr. D with a score on the "ME" position of the PBP. Concluding the above diagnosis, the PBP of Mr D is as follows; ME, *O-2*, *H-5*.

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Psychiatry Science: The Next Generation

*Imagination is more important than
knowledge... Albert Einstein*

5.1. Testable Predictions

In light of the ideas formulated in this manuscript, psychiatry approaches an exciting era; an era of phase transition from an approximated tentative discipline to real science, a brain science. Before progress in research and therapy can be obtained in psychiatry, some general approaches to the study of mental disorders should be reemphasized. It is common in medicine to think in linear terms about causation of disease. The degree of infection is in linear relations to the effects of bacteria (or virus), the degree of ischemia is linearly related to artery constriction, and so on. Powerful therapeutic interventions were achieved in medicine in cases where this kind of relations was found. It was enough to intervene by reducing the causative factor in order to achieve a linearly related reduction of the effect, (i.e., the diseased process). This success induced doctors to think in linear cause and effect relations. Less success was achieved when less obvious, (i.e., linear) relations existed between the diseased process and its causation. It is evident that the linear cause and effect relations are predominant in relatively simple systems. The more complex the system the less trivial is the relations between its components. For example the hormonal systems with its multiple components, is more complex than bone structure and dynamics. Accordingly, orthopedic medicine is relatively more successful in correcting malfunctions than endocrinological medicine.

Because the linear cause-effect relationships are so successful in medicine psychiatrists naturally follow this approach. However, the brain is not a simple linear system, if other body systems can be “linearized” to a certain extent, and thus successfully treated by linear interventions, the brain is exceptionally complex and its behavior is far removed from any linear relationships. It is thus of critical importance that psychiatrists should abandon their medical-borne simple linear conceptualizations and adapt a more relevant higher-level non-linear view of their profession’s science.

Non-linear conception is not only relevant for research of mental disorders it is significantly helpful in everyday clinical work. For example, psychiatrists typically become frustrated to find that frequently there are no dose-related, or even drug-related effects to the psychiatric medications. Increasing the dosage of the drug is not always accompanied with related clinical improvement. A small change in medication dosage can result in a massive alteration of clinical condition and vice versa, big changes of medication dosage may not affect the clinical conditions.

The idea of a “biological marker” in psychiatric research reflects the simplistic search of linear cause-effect relationships. A “biological marker” is a physiological or biochemical factor that presumably correlates to a mental disorder and thus has a causative relevance to it. In this manuscript, it has been shown why the search for a “biological marker” is an erroneous direction to follow. Research in psychiatry must consider non-linear relationships between cause and effect and must involve the intermediate link of perturbed dynamically disordered system effects.

Instead of a simple direct two-factor model of cause and effect, a three level model is proposed; a lower level of multiple biological factors, an intermediate level of system organization and finally, the higher level of system functions and emergent properties. Any study about the etiology of mental disorders should “trace” or “map” biological alterations onto system perturbation up to mental disturbances. Mental disorders are thus conceived as emergent properties from disturbed patterns of brain organization, which in turn reflect malfunctions of lower-level biological components.

As mentioned a few times before, the PBP is a hypothesized schematic outline of a futuristic diagnostic approach. This approach would depend on the ability to detect and monitor all those perturbations outlined above. Meanwhile, the PBP is being advanced using regular traditional assessments.

It is of prime importance to develop the means to detect and define perturbations of brain organization. Sampling of brain activity typically uses electrophysiological assessments and magnetic resonance signals from functional imaging devices such as MRI. The source of the biological signal and its sampling techniques pose many problems that are beyond the scope of this text. Regardless of the source of the signal, interpreting the neural organization reflected by a signal is a tremendous problem (Hoffman *et al*, 1996). One measurement widely used in signal analysis is that of coherence in terms of correlation-coefficients. This measurement proposes that regions in the brain influence one another if the signals emitted from these regions have the same waveform (i.e., frequency and amplitude) (Morrison-Stewart *et al* 1991; Norman *et al*, 1997; Peled *et al*, 2000). If two regions have the same waveform but the signals are shifted in time (as expected, considering time delays in activity transfer), the correlation coefficient will be reduced and the time shifts need to be taken into consideration (Gevins & Remond, 1987).

Principle component analysis (PCA) can provide a rough estimation of the dimensionality of a biological signal (Koukkou *et al*, 1993). Dimensionality can be

interpreted as the number of components that contribute to the signal. Increased dimensionality indicates that more sources are contributing to the signal. Independent component analysis (ICA) is designed to identify how many components contribute to the signal (Cardoso & Laheld, 1996; Makeig *et al*, 1996). For example in schizophrenia if one expects a disconnection syndrome, then one would expect an increase in the number of independent components in the signals from schizophrenic patients compared to those of normal controls (Friston, 1996).

Most recently, mutual information (MI) measurements used for assessing neural complexity C_N (see above), are being applied to brain signals (Tononi *et al*, 1994; 1996). They hold the promise of detecting the degree of neural integration in the brain (explained above). The degree of cortical integration in the brain will probably provide some insight into the degree to which neural systems are organized via functional connections. However, this is only a rough indication of the actual dynamic organization taking place in the brain. Future research will have to rely on more sophisticated signal analysis in order to decode the precise patterns of interrelations among neural systems in the brain.

Even though signal analysis and modern sampling technology would carry ~~the~~ most of the burden of future PBP. In the meantime, other methods can be developed to augment the accuracy of PBP. For example, the recorded assessment of patients speech (association and quantity charts) can help score positions 11, 8 and 7 by applying cut-off points using research from large samples of patients. Motor activity can be assessed using actigraph such as those used by sleep researchers. Galvanic skin response and other physiological monitoring such as heart rate and respiration could be concomitantly studied to score position 1 in the PBP. Certain cognitive and psychological tests such as those of “theory of mind” could be adjusted to score positions [P] or [U].

The formulations raised in this manuscript have value only if they can provide testable predictions for future research in psychiatry. Their value can also be in pointing to future directions in psychiatric treatments. Being futuristic, these ideas about research and therapy are inevitably highly speculative. The reader is asked to hold this in mind while reading this chapter.

According to this manuscript, any future therapy in psychiatry would involve control over brain organization. Two major directions can be formulated when control over brain organization is targeted 1) direct and internal, and 2) indirect and external.

Internal control involves all those direct interventions on the activity of neurons in the brain. These could be biochemical vectors such as drugs or electrophysiological applications such as ECT (electro convulsive therapy), TMS (trans-cranial magnetic stimulation) or DBS (deep brain stimulation). External indirect control involves all those interventions in the experience of the patient for example, behavioral therapy, psychotherapy, and group therapy. The scientific support for external control comes from the evidence about experience dependent plasticity in the brain (see previous chapters).

Brain plasticity is a crucial factor in the dynamics of brain organization. It is known that after a certain age this plasticity is reduced thus having the potential of “fixating” undeveloped malformed and disorganized brains, thus resisting any therapeutic change in mental disorders. Since any relevant change of brain organization for the treatment of mental disorders will require neuronal plasticity, it is of major importance to be able to induce neural plasticity in the brains of patients.

Based on the assumptions forwarded so far, three future directions will be outlined in this chapter: 1) Synaptogenic connectionist control, 2) Direct Brain-Pacemaker control and 3) Experience control. In the psychiatry of the future all three modes of intervention together or in various combinations, would probably achieve the needed optimization of brain organization that will cure mental disorders.

Synaptogenic Control

As stated above, any relevant change to brain organization would require some control over brain plasticity at the level of synaptogenesis. Recently, the long-held view that neurogenesis in the human brain ceases after birth has been broken. It is known today that new cells are born (i.e., stem cells) in the periventricular zones and migrate to cortical and hippocampal regions making regional and even more distanced functional cortical connections (Berry, 1986; Kukekov, 1999). This growth is increased when injury occurs and also with intensive training within rich stimuli environments.

Certain neurohormones and growth factors generate new cells in the brain for example, fibroblast growth factor (FGF) injected subcutaneously in rats successfully passes the blood brain barrier (BBB) and increases cell and synaptic growth (Xian and Gottlieb, 2001). However, evidence suggests that in humans FGF might induce brain tumors (Berking *et al*, 2001) making this factor inadequate for treatment.

A better candidate for inducing neurogenesis in the human brain could involve neurotransmitter agonists and antagonists. The activity of serotonin and norepinephrine has been found to participate in cell growth. Chronic antidepressant treatment has been found to increase neurogenesis of hippocampal granule cells via postreceptor increase of AMP (Thompson *et al*, 2000). Agonists of serotonin for 5HT1A and other receptor, have also been mentioned as important neurogenetic factors (Lotto *et al* 1999). In effect, serotonin depletion during synaptogenesis leads to decreased synaptic density and learning deficits in the adult rat (Mazer *et al*, 1997). Tianeptine a 5HT1A agonist blocks stress-induced atrophy of CA3 pyramidal neurons (Magarines *et al*, 1999). Intrathecal treatment with quipazine (another serotonin agonist) has improved locomotion deficit induced by ventral and ventrolateral spinal neural injury (T13) in two cats. Both cats recovered quadrupedal voluntary locomotion and maintained regular stepping with this treatment (Brustein and Rossignol 1999). Sumatriptan (CPP) is a 5HT agonist (5HT2C, 5HT1D and 5HT1A agonist) typically used in treatment of migraine headaches, chronic administration of sumatriptan has been found to slightly improve OCD patients (Hwang and Dun 1999). Additional findings relevant to neurogenesis involve electroconvulsive seizures (ECS), chronic ECS administration induced sprouting of granule cells in the hippocampus (Kondratyev *et al*, 2001; Lamont *et al*, 2001). This effect is dependent on repeated ECS treatment and is long lasting (observed up to at least 6 months after the last ECS treatment). Excitotoxin and kindling-induced sprouting are thought to be, at least in part, adaptation in response to the death of target neurons. In contrast, there is no evidence of cell loss or dying neurons in response to chronic ECS (Gombos *et al*, 1999).

Synaptogenic interventions alone would probably have no therapeutic effect. Synaptogenic interventions would serve as promoters, enhancers or basic requirements for the other internal and external interventions (see below).

Direct Pacemaker Control

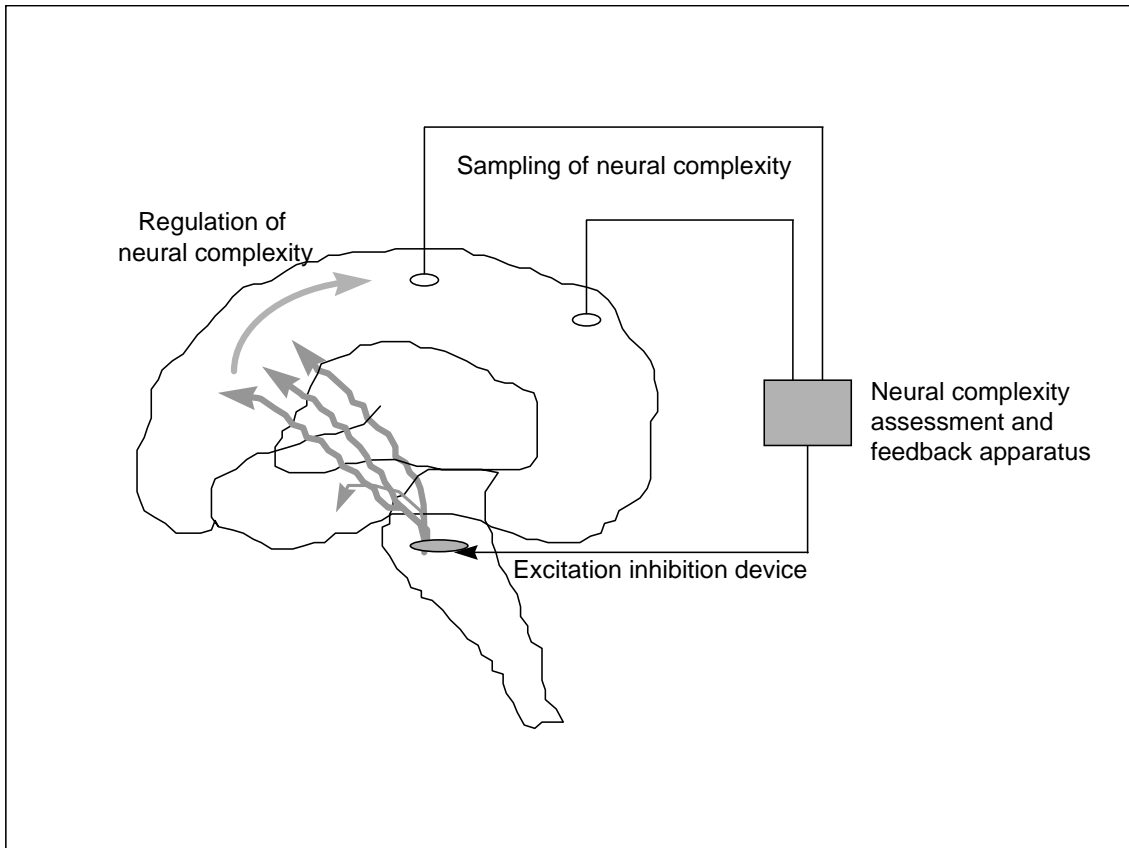
Brain pacemaker control is a term reserved for manipulations directed to the neural tissue in the brain intended to enhance task-dependent neuronal integration and differentiation. Speculating on current technology, two main directions can be formulated, transcranial magnetic stimulation (TMS) pacemaker and electrode transplant DBS.

TMS is a technique introduced in 1985 (Barker *et al*, 1985) that uses the principle of inductance to activate nerve cells in the cerebral cortex (Hallett, 2000). Current psychiatric research with TMS is conducted with the purpose of substituting electroconvulsive therapy (ECT) with magnetic stimulation in the treatment of mental disorders such as depression (Klein *et al*, 1999, Pridmor *et al*, 1999). ECT is an established way of “resetting” brain activity, without much scientific basis, but with empirical success (Fogg-Waberski).

In a recent work, Klimesch and colleagues (2003) showed that rapid transcranial magnetic stimulation (TMS) induced task-related alpha desynchronization in human individuals caused enhanced task performance. Hoffman and colleagues (2003) showed that TMS of <1Hz administered to the left temporoparietal cortex in drug resistant hallucinating schizophrenics could significantly reduce the hallucinations. Since EEG, together with other imaging techniques, are beginning to reveal possible disturbances of brain organization, then coupling of TMS with EEG offers new potential directions to start controlling brain functions directly by feedback EEG-dependent TMS delivery. A future potential “brain pacemaker” would probably involve a multiple-coil TMS device coupled with an EEG dependent feedback mechanism, similar to a cardiac pacemaker set to act according to the ECG arrhythmias.

Deep brain stimulation (DBS) could be an additional direct method of brain organization control. It has been successful in patients with severe Parkinson’s disease. Electrical stimulation of basal ganglia structures has been found crucially beneficial for these patients. Based on the assumption (mentioned previously) about midbrain structures as cortical complexity pacemakers a scientific rationale for direct measurement and control of their activity in the schizophrenic patient is present. If the algorithm of catecholaminergic neuronal activity responsible for optimizing integration as well as differentiation within brain activity is found, then a futuristic brain complexity pacemaker could be designed as a cortical complexity feedback to a DBS device (figure 14).

Figure 14



Experience Control

Experience control should include emerging computer technology of virtual reality (VR) that provide for interactive control over the important senses and enables the creation of controlled environments as well as interpersonal situations. VR is a set of computer technologies which when combined, provide an interactive interface to a computer-generated world. Virtual reality technology (VRT) combines real-time computer graphics, body tracking devices, visual displays, and other sensory input devices to immerse a participant in a computer-generated virtual environment. He then can see, hear and navigate in a dynamically changing scenario in which he participates as an active player modifying the environment according to his interventions. This technology provides such a convincing interface that the user believes he is actually in the three-dimensional computer-generated environment. The term “presence” was coined by the experts of VRT to describe this conviction.

The field in which VRT is currently most intensively investigated in psychiatry is that of exposure therapy for treating anxiety disorders such as phobias and PTSD (Glantz *et al*, 1997; Walderol and Tailor, 2000; Vincelli *et al*, 2001; Pertaub *et al*, 2001; Jo *et al*, 2001; Rothbaum *et al*, 2000). In traditional exposure-therapy, the subject is exposed to anxiety producing stimuli while allowing the anxiety to attenuate with the aid of various relaxation techniques. VRT enables low cost (flight phobia treatment without really flying), time saving (from therapist's office) and controlled (the phobic stimulus can be designed and controlled) virtual phobic environmental exposures.

VRT has staggering potential both for neuropsychological assessment as well as for cognitive rehabilitation. There are already a few research groups experimenting with VRT for cognitive rehabilitation (Gaurly *et al*, 2000; Christiansen *et al*, 1998). Traditional neuropsychological testing methods are limited to measurements of specific theoretically predetermined functions such as short-term memory or spatial orientation. Given the need to administer these tests in controlled environments, they are often highly contrived and lack ecological validity, or any direct translation to everyday functioning (Rizzo and Buckwalter, 1997).

VR technology enables subjects to be immersed in complex environments that simulate real world events that challenge mental functions more ecologically. While existing neuropsychological tests obviously measure some brain mediated behavior

related to the ability to perform in an “everyday” functional environment, VR could enable cognition to be tested in situations that are ecologically valid. While quantification of results in traditional testing is restricted to predetermined cognitive dimensions, with VR technology, many more aspects of the subjects’ responses could be quantified. Information on latency, solution strategy, visual field preferences, etc. could be quantified. VR can immerse subjects in situations where complex responses are required and the responses can then be measured (Rizzo, 1997).

These capabilities can serve to challenge diagnosable specific brain cognitive deficiencies. For example, performing within virtual environments that require intensive activation of working memory would enhance the integration of higher-level contextual systems. If additional multimodal integration is required to perform within that environment then additional multimodal integration will be enhanced.

Virtual environments could also target delusional ideation attempting to correct them by providing opposing or “correctional” occurrences tailored to counteract the specific false ideation. The correctional situations provide additional possible interpretations of the situation thus increasing the number of possible interpretations increasing differentiation in the representational contextual system. Performance within complex social situations that require theory-of-mind capabilities would enhance the more higher-level brain integration needed to represent and perform within socially cued situations.

In sum, the VRT in diagnosis and rehabilitation of mental disorders could have a significant role both for increasing integration as well as differentiation by exposing the patient to complex challenging specially designed interactive virtual environments.

Based on the directions described so far a series of future research designs can be outlined in general terms. First, experiments designed to detect alter and disturb brain organization should try and ‘map” imaging EEG and MRI correlates of mental disorders. The big picture of altered brain organization in mental disorders has been outlined in this manuscript and could serve as guidance for this research. For example, in psychosis and schizophrenia neural complexity should be assessed. In depression and anxiety optimization dynamics should somehow be measured.

Second, experiments coupling EEG and TMS such as cognitive enhancement by alpha synchronization should be executed with and without synaptogenic enhancers. Experience-dependent training and rehabilitation with virtual

environments combined with synaptogenic medications could make the difference between low efficacies of rehabilitation and real change of cognitive ability. Two major factors are considered for planning a therapeutic virtual environment that would correspond with the specific therapeutic needs, say, of the schizophrenic patient; 1) the clinical symptomatic manifestation of the disorder, and 2) the presumably associative, or connectionist, disturbance that causes the disorder. Furthermore, one should keep in mind that since schizophrenia is a disorder of the more complex (higher) functions, then also the associative manipulations should be performed between complex virtual situations. For example, in patients who suffer from repeated auditory hallucinations of voices conversing, the assumption being that neuronal systems for perceiving vocal language become dissociated from the rest of experience (e.g., visual and other constellations), then the virtual therapeutic experience should be designed to re-associate the detached perceptions. The disturbance described here will require planning a virtual encounter where the specific hallucinatory voices are attached to virtual behaving figures. These figures should act the conversation theme and react to the patient according to the hallucinations. Although virtual, this kind of experience re-associates the voices which the patient hears with their experiential visual and situational counterparts.

Drawing upon the theory of experience-dependent plasticity, it is presumed that many sessions with the pre-designed virtual experience will eventually “reconnect” and re-associate the neuronal network circuitry required to re-establish consistent and coherent everyday experience for the patient. Thus, with no speaking figures in the immediate experience, also their voices should disappear. It is predicted that once experience control sessions are stopped and the speaking figures disappear also the voices will vanish. The newly formed consistency in the system will inhibit the activation of voices without their counterparts of experience (i.e., will not enable inconsistencies of experience). The end result abolishes the hallucinations providing symptomatic relief for the patient.

Delusions could be treated by repeated sets of virtual experiences where the delusional thinking contrasts the virtual events. For example, the patient who is convinced of being persecuted by the FBI might be virtually introduced to the FBI headquarters where he experiences warm and caring acceptance, with no evidence of persecution. Gradually, such repeated “corrective-experience” might alter his delusion, reducing its threatening content. One may argue that delusions are

unshakable beliefs and thus could never be altered. Nevertheless, clinical experience shows us that beliefs may come in various degrees from normal superstition and overvalued ideas to real delusions. Intensive and repeated virtual experiences delivered in an “aggressive” and “focused” manner to the specific delusional system of the patient may turn delusions to overvalued ideas or even to normal thinking.

5.2. Fantastic Therapies

The psychiatrist of the future will be a neuroscientist. He will have to master the vast knowledge of multiple interdisciplinary scientific fields that are relevant to brain functions, especially those of neural-computation and imaging signal analysis. The first discipline will provide knowledge about possible brain organizational disturbances underlying mental disorders. The latter will serve to document and diagnose those disturbances. Biochemistry, molecular biology, electrophysiology and computer sciences would also make up part of the knowledge of a future psychiatrist. Such disciplines will serve for planning and executing therapeutic interventions, be it synaptogenesis, planning and delivering disorder-specific magnetic stimulations or shaping and controlling the experience of the patient via virtual reality technology.

The psychiatric patient of next generations would encounter a psychiatrist better equipped to deal with his mental problems, accordingly relief from symptoms and improvement in functions will be greater. After a regular psychiatric interview, the psychiatrist will have a first-step orientation about the brain disturbance of the patient. For example, psychosis will direct the psychiatrist to the diagnostic hypothesis of disturbed neural complexity in the patient’s brain. The next step would involve some imaging analysis to determine the extent and specific algorithm of breakdown of the patient’s neuronal organization.

Once these first steps are concluded the psychiatrist will then start to plan his therapeutic strategy tailored specifically to his patient’s disturbance. Using a variety of methods, from EEG coupled with TMS feedback devices to experience control induced experience plasticity with VRT, the delicate process of optimizing brain organization, will be planned and executed. Gradually, using repeated assessment from the first two steps (above), the artwork of brain optimization will take place. The psychiatrist will be taking a delicate path of gradual optimization of brain

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organization gently balancing brain functions setting them to their proper equilibrium of normal function. This therapeutic process would terminate after the patient resumes his well-being as well as his functional skills from prior to the beginning of his mental disorder.

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