Quantum Paradigms of Psychopathology

Supplement

NeuroQuantology 2012;10(2):S1-28

A Long Shadow over the Soul: Molecular and Quantum Approaches to Psychopathology

An Interdisciplinary Dialog with Psychiatrists

Fano – Italy, March 2012

Quantum Paradigms of Psychopathology: Supplement

From 29th to 31st March 2012, will be held in Fano, in the meeting room of the Pastoral Center, Via Roma, 118-Fano, Italy, a major conference on the theme: A Long Shadow over the Soul.

This international meeting at the newest frontiers of Psychiatry provides for participation by leading scientific figures of international renown, including Nobel Prize winner Kary Mullis. The conference aims to address, among other topics, results obtained from the project financed by the Marche Region on Bio-Molecular Markers in Psychiatry, which is now recognized, by the Region, as a Project of Excellence. The data collected have not only generated the possibility of grading bipolar and depressed subjects biochemically for the first time in history; they have also pointed toward a possibility of directing the nutrition of those individuals who suffer from this devastating disease affecting the "person" and constituting a social phenomenon whose massive incidence over the next 20 years is forecast by WHO. The Project of the Marche Region has achieved results that can contribute a diagnostic laboratory tool sharpening the diagnostic precision of psychiatrists and thus drastically reducing the deleterious effects of incorrect therapy. The conference is also an extraordinary opportunity to bring together most of the members of the Quantum Paradigms of Psychopathology (QPP) group. The primary purpose of QPP is to explore the relevance of quantum physics to the most sensitive processes of the abnormal brain.

The concept of mind as a quantum field phenomenon has been under study since the final decades of the last century. Pioneers such as physicists Hiroomi Umezawa, Kunio Yasue, and Giuseppe Vitiello, mathematicians such as Roger Penrose, and biomedical investigators as Stuart Hameroff, Gordon Globus, and Gustav Bernroider have probed the depths of subatomic structure and its amplifications in search of substrates for macroscopic quantum computation and other capabilities that may correspond to the attributes of the human psyche better than conventional models supported by cognitive neuroscience.

The live conference in Fano harbors the potential to generate a productive, face to face synergy, leading eventually to advances in this new area of scientific exploration.

There will also be masterful discussions of the relationships between theology and psychiatry and between philosophy and psychiatry.

Prof. Massimo Cocchi

1. MOOD DISORDERS AND OPTIMIZATION DYNAMICS IN THE BRAIN

Avi Peled
M.D., Sha'ar Menashe Mental Health Center, Hadera, Israel. Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel. Correspondence; Dr. Avi Peled, Sha'ar Menashe Mental Health Center, Mobile Post Hefer, 38814, Israel, Tel: 972522844050
Email:av_peled@netvision.net.il

Abstract
In this paper Mood is reformulated as an emergent property form whole brain organization and dynamics. The brain achieves internal representations in the form of attractor maps, these are dynamic continually matching updated by environmental inputs. Mismatch dynamics de-optimizes these internal configurations causing an emergent property of depressed mood, antidepressant medications re-optimize the system increasing matching dynamics by synaptogenesis.

Development and plasticity induction of internal configurations in the brain
Psychiatrists cannot avoid the psycho-physics problem their patients suffer from psychological maladies. If psychiatrists consider themselves scientists they then acknowledge that these maladies emerge from the brain which is a physical entity. Thus the question that cannot be evaded is, how can a physical system explain a psychological phenomenon?

For a scientist this question can only have one answer, that of "Emergent Properties." Emergent Properties are characteristics of the system as a whole which are not found in its elements. "Mood," "consciousness," "awareness" and "identity" are not found in single neurons or even groups of neurons but they are properties of the brain as a whole. This materialistic explanation is not only critically necessary if we ever plan to treat the brain and cure patients; it also directs us to the prediction that mental disorders will involve the disturbances of large-scale neural networks in the brain (whole-brain disturbances).

The brain is non-linear, in the sense that it does not offer one-on-one relationships. For example, gradually increased input does not lead to linearly correlated increase in output. Threshold and saturation behaviors representing curved sigmoid and U shaped graphs are the law. Transmission between single neurons is non-linear and brain activity is also non-linear It is known that non-linear systems show emergent properties, mathematically parameters of a curved graph are higher compared to a linear one, this difference is the expression of emergent properties. The mathematics of this will not be part of this manuscript.

Emergence of properties requires interacting elements that generate a whole. Per definition a system is a compound whole made of interacting interdependent elements. The brain is composed of multiple levels of elements ranging from single neurons interconnected by axons dendrites and synapses, up to brain regions and neural network ensembles connected by multiple modalities, from direct physical pathways to synchronized functional connectivity.

The networks of such interactivity can evolve in many patterns, they can be centralized, where many units (e.g., neurons or brain regions) of the system are connected to few (or one) main units (Hubs) or they can be distributed with units randomly connected forming no central organization, thus having no Hubs at all. Recently it has been found that the best organization of well-functioning (optimal) systems is in-between the organizations described above; the organization is neither too centralized nor randomly dispersed, it is composed of Hubs receiving many connections from many far-away units that are a part of clusters of 'locally' spread highly connected nearby units. This type of organization is most effective for a well-functioning system; In the case of communication networks it is most effective for information transfer earning the title of "small world network (SWN)" describing effective communication transfer around the globe.

SWN organization entails high clustering and small path length (connections from many far-away units) comparable to random graphs. Thus in addition to small worldliness clustering coefficient, path length and hierarchy are also important measures that can be used to estimate whether a system is optimal and effective. These parameters become critical when one wants to investigate the efficacy of functioning networks and needs

measurable extracted parameters to decide (or detect) whether a system is functioning optimally.

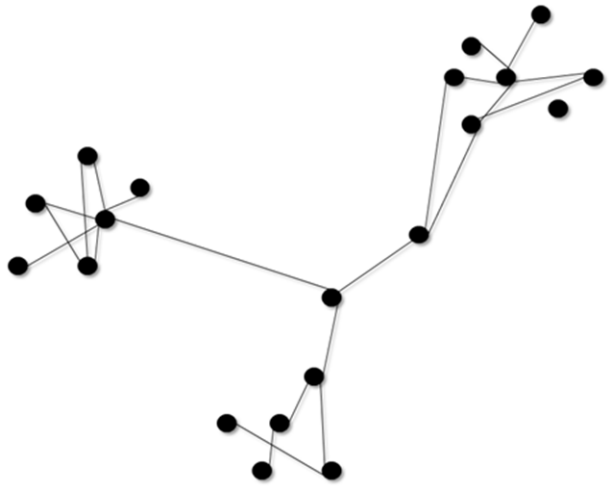

Figure 1. Schematic structure of a small world network organization.

How is network organization relevant to emergent properties? To answer this question we shall consider consciousness as an emergent property of the brain. According to Bernard Baars consciousness emerges from global brain organizations; at each moment in time sets of partial processes integrate to form e global formation of activity. Across time the participating partial processes may change because some partial processes might be "dropped out" and new ones engaged in the global formation. Thus, from instant to instant the global message may change, just as conscious experience is aware of changing contents from moment to moment. Stanislav Dehene showed that the small world network organization is a relevant organization for Baar's formulation. The Hubs of long connections from multiple clusters act as integrators of processes within the clusters, thus partial inter-cluster activity is integrated more globally at the higher level offered by the Hubs. This structure offers a multiple-level hierarchy where even higher-level integrators that have nested lower level networks can integrate even more global cognitive computations.

As early as 1884 Theodor Meynert a Viennese neuropsychiatrist, stated that thoughts are represented by activated neuronal ensembles. When we have a thought, he said, it is represented by a group on acting neurons, when we have another thought it is represented by another group of activated neurons, when we have associations between these two thoughts, connections form between them. Meynert preceded his time, but today, especially with artificial intelligence and neural network models; we can understand how neuronal ensembles actually represent information.

Thus global organizations that support emergence of consciousness can be viewed as hierarchically emergent neuronal ensembles. At this point one can introduce the concept of state-space dynamics to offer a good description of the conscious thought process as a process emerging from physical complex brain systems. In state-space formulation, every neuronal activation at any given instant is a "state" and this state is represented as a point in a "space". The space represents all the other possible states of the system. As conscious experience proceeds from one occurrence to the other, and thoughts progress from one concept to the next, so the point in space "moves" ahead from one point to the next, creating a trajectory. Thus space-state trajectories can represent the dynamics of consciousness as the dynamics of a changing physical brain system.

We know that our thoughts and experiences depend on learning and practice. How is learning and acquisition of experiences accomplished within the physics of the brain? As already mentioned, as early as 1884 Meynert stated that associating information is related to the forming of connections in the brain. Donald Hebb in 1948 stated that if two (or more) neurons fire simultaneously together for certain long periods than the connection between them is strengthened. The opposite is also relevant connections weaken if neuronal activity is not synchronous. More important is the resulting fact that when connections between two (or more) neurons are strengthened, the chance that they will fire together is increased as one activates the other (or others).

Today we know that learning is a process that involves formation and strengthening of connections on a variety of scales from neurotransmitter chemical connections to structural actual synaptic connections. Once the connection within a neural ensemble is strengthened, that ensemble will tend to activate itself because of mutual activations. As such, the ensemble is a state of the system and it is represented by a point on the space

(of all other states) of the system, thus the system will tend to assume that state more than other states, where neuronal connections were not strengthened. In other words the system will tend to be "drawn" to that state, or point in space. These dynamics of becoming drawn to a state are called "attractors" because the system as a whole is attracted to the state that activates it. For purposes of imagination the space of the system can now be viewed as a landscape of basins and peaks where the peaks represent the states, or activations that the system tends to avoid. In contrast the basins represent the states that the systems tend to activate and achieve.

This means that when we learn something new it is embedded in the physical brain in the form of attractor formations. When we recall this information the trajectory of conscious dynamic activity has reached the basin-state and activated it. This also means that in our brains we have a representation, or a "map," if you will, of all of we have learned and experienced from birth until the present, in other words we are equipped with an internal representation of the world (including its psychosocial players) as we have come to know it. We can conclude that internal representations of the world which cognitively and socially guide our actions and enable us to, adapt and function in the environment, are corporal attractor configuration maps of the physical brain.

But why should learned acquired maps match the actual world, and how can such maps be achieved in a continuously changing environment?

A match between environmental occurrences and the internal maps of these occurrences is intuitively explainable. If internal maps guide our reactions and behaviors in the environment, then in order to function in the environment we need to have an accurate representation of it. Because the environment changes continually our internal map of representations must be dynamic to adapt, learn and represent these changes. Building upon thermodynamic physics and biological evolution, Karl Friston (2007) delineated a unifying theory for the brain in which he showed that the brain acts to reduce "Free Energy." In this case Free Energy is a measure of surprise, or in other words the statistical difference between the predictions made by the brain and the results of those predictions. The brain continually generates predictions about its input and acts to validate those predictions in a way that every change in the brain is governed by the free-energy-reduction law. The consequences are that the brain acts to achieve flexibly updated internal representations of its input. It also acts to actively develop organ senses (epithelia) and motor actions that reduce free energy by actively making input-sampling match internal predicted representations. The brain networks achieve free-energy reduction with any change of connectivity strength in order to create a hierarchy that mediates effective free energy reductions.

When the brain achieves optimal reductions of free energy the cost is rooted in the connectivity values of its neural network. Optimization is "to make perfect or as effective as possible" and to find the best compromise among several requirements that are often conflicting. So how does the brain obtain and maintain its flexible dynamics?

It can be concluded that the physical brain that obeys the natural laws of physics reduces entropy (measure of disorder) by reducing free-energy when interacting with its environment. This reduction is achieved by hierarchical network structures and motor-sensory adaptations, ultimately resulting in the formation of dynamic actively-predictive internal-representations that are actuated in the physical, ever-changing state-space configurations activated by plasticity of the physical brain of protoplasmatic neural networks.

Mood in the brain

Connectivity adapts to the environment by obeying the free-energy principle that reduces predicted differences between the environment and the input, thus the developing brain continuously predicts the occurrences in the environment and adapts in order to reduce surprises, and create adaptable matching (surprise-less) internal representational maps of reality. The process of internal synaptic-connectivity changes resulting from interactions with the environment is best described using the term of Experience-Dependent-Plasticity (EDP). Carhart-Harris and Friston (2010) describe the connections between Ego, DMN and free-energy in a detailed all-encompassing review.

Mismatch between environment and an internal representation is hypothesized to emerge as depressed mood. What causes mismatching of internal representations? The answer is rooted in development; the internal representations are formed gradually during childhood / adulthood under the mechanisms of synaptic changes that obey the free-energy laws (see above). If the developmental process is delayed or hampered for some reason then the internal representational maps will be rudimental and not sufficiently complex to represent multifaceted environmental occurrences, and thus result in non-adaptive and inappropriate behaviors. Alternatively the developmental process maybe progressed but adapted to biased conditions which inevitably create biased internal representations and maps. Biased internal representations are also maladaptive and inappropriate.

For the last couple of centuries it has become clear that there is a correlation between neuronal plasticity and mood, in effect neuronal death and reduced plasticity (i.e., reduction of dendrite extensions and spines) has been associated with depression. The notion that such plasticity is central to depression has been supported by findings that antidepressant medications increase plasticity by growing dendrite extensions and new spines. Reduced neuronal plasticity can readily explain the common depression associated with dementia and with alteration of neuro-hormones such as thyroid hormones and others. But how can we explain other types of depression for example reactive (due to stress) depression and the common depression that characterizes those with personality disorders? But even before answering such questions how can we explain the association between the psychological phenomena of mood with the physical observation of reduced plasticity?

The answers are rooted in our conclusions from above, where emergent properties result from whole-brain or at least from massive brain, organizational dynamics. Plasticity is in this case, is a widely distributed process. In fact it is known that the target serotonin receptors are found in 60% of cortical neurons spread in the cortex, supporting the notion of widespread whole brain activity. Second we need to understand the meaning of increased plasticity in terms of physical system dynamics? Plasticity makes the system more dynamic as each of its units (neurons) increases the number of input-output possibilities, and increases the number of possible states (values) that it can accomplish. So as the whole system becomes more plastic it is more amendable and susceptible to change, transformation and adaptation.

But how is increase in changeability related to mood change? Here we need to introduce an assumption which involves 'optimization.' We have seen in above that the brain-system functions by continually matching and optimizing internal representations according to environmental occurrences, thus the brain continuously optimizes internal organization to adapt to demands of occurrences in the real world. We can progress and assume that the brain's optimization dynamics are of two types, 1) toward better optimization, we shall call that simply "optimization dynamics" and 2) toward less optimal match in respect to environmental occurrences, we shall call this type of dynamics "deoptimization dynamics." We shall further assume that the emergent property of optimization dynamics is mood elevation and that of deoptimization dynamics is mood depression. This assumption gives us the correlation needed between plasticity and mood. Whenever plasticity decreases as in dementia and neuronal atrophy, adaptability of the brain to the dynamic environment is reduced, because the brain does not change at the same rate of the changes in the environment., Thus, the direct result is deoptimization dynamics because the internal representations do not 'update' as fast as the changing events in the environment. Administration of antidepressant medication to the depressed patient increases plasticity, thereby offering the brain a better chance for adapting and changing. By increasing changeability internal representations are updated and more accurately match external occurrences, resulting in increased optimization dynamics and the emergent property of elevation of mood, thus explaining the antidepressant effects of the medication.

To conclude; according to this hypothesis, we assume that optimization dynamics underlies mood elevation and de-optimization dynamics underlies depression (as emergent properties).

The model of optimization dynamics for mood changes is also useful to explain reactive depression from stressful events. A stressful event always implies a massive abrupt change in the environment, (*e.g.,* losing a close family member, or being fired from work. These changes in environmental occurrences will inevitably mismatch the internal configurations that represented the pre-stress environmental configurations. These major abrupt changes in the environment cause an abrupt increase of free energy which the brain struggles to avoid (see above). Deoptimization dynamics are triggered as the mismatch between the internal representations and the altered environment increase drastically. The resulting emergent property is depressed mood.

It is now readily explainable why those suffering from personality disorders typically complain of depression. As explained above, personality disorder is re-conceptualized in terms of altered disturbed mal-developed DMN (Default-mode-network) organization, which embeds altered, immature, biased internal representations within its construct i.e., altered internal configuration of state-space attractor-mapping. These biased and immature internal representations, by definition of being biased in that they do not match the occurrences in the real world, are inevitably deoptimized most of the time. Deoptimization is the emergence of depressed mood, and in effect personality disorder patients suffer from prolonged continuous depression they are continuously dysphoric and are diagnosed with DSM- "dysthimia"

It can be concluded that one unique model of 'Optimization Dynamics' can be useful to relate the physical phenomenon of plasticity to the psychological phenomenon of mood. The same model explains depression rising from "endogenic" causes (probably hormonal, metabolic or dementia-related) as well as from stress as "reactive-depression". Furthermore it explains complaints of depression in those suffering from personality disorders, as their internal configurations rarely optimize to enable a good stable mood. The model also explains why in many mental disturbances depressed mood is a concomitant complaint. It is just logical to assume that whenever the organization of brain-systems is massively perturbed, optimization will be hampered and depression will ensue. We shall see this below when massive connectivity disturbances in schizophrenia putatively explain schizoaffective clinical manifestations.

Using similar reasoning anxiety is conceptualized as an emergent property of widespread whole-brain neural network perturbation. Normally during brain computation and organization the neural networks are more or less stable. Such stability can be conceptualized using the idea of "multiple constraint satisfaction." Each unit in the system, in our case each neuron or group of neurons, exerts connectivity constraints on all the other units connected to it. Similarly it receives multiple constraints from all the other neurons connected to it, thus each unit assumes activity values which can be defined as 'multiple-constraint-satisfaction.' As such the entire network follows this law of constraint-satisfaction which is in accord with the free energy principle. Any perturbation to the network will inevitably increase the "values" of constraints dissatisfaction as 'surprises' increased free-energy and spreads in the network. Such destabilization and increases in free-energy is assumed to emerge as a sensation of anxious mood.

Using this hypothesis one can see how most, if not all types of perturbation presumably involve the emergent-property of anxiety. In effect we know from clinical experience that most mental disorders are accompanied with concomitant anxious mood. Patients suffering from personality disorders, depression and psychosis frequently also suffer also from anxiety.

Therapy for mood disorders in the physical brain

Generally speaking, there are three major categories of interventions applied today in the field of treating mental disorders, 1) pharmacotherapy, 2) psychotherapy (*i.e.,* the talking treatments) and 3) neuromodulations (*e.g.,* electroconvulsive therapy, deep-brain-stimulations, transcranial magnetic stimulations and others).

The most effective medications in their category are SSRIs selective serotonin-reuptake inhibitors). These act by blocking the reuptake of serotonin at the synapses, thus triggering a cellular biochemical chain-reaction which terminates with synaptogenesis. After 6 weeks from initiation of treatment neurons grow new dendrites and

these are more enriched with spines than before treatment began.

The antidepressant effect of synaptogenesis is explained in terms of optimization of internal representations. More dendrites and spines offer the needed plasticity for change thus for better optimization of matching dynamics. The future of brain therapy will probably lay heavily on the ability to make the brain more amendable to change, and increased plasticity will probably play a critical role in the induction of change.

References

Carhart-Harris RL, Friston KJ. The default-mode, ego-functions and free-energy: a neurobiological account of Freudian ideas. Brain. 2010 Apr;133(Pt 4):1265-83.

Geva AB and Peled A. Simulation of Cognitive Disturbances by a Dynamic Threshold Neural Network Model. Journal of International Neuropsychology, 2000 Jul; 6(5);608-19.

Friston , K. Klass, E.S. Free-energy and the brain. Sythese 2007;159: 417-458.

Mesulam, M. (1998) From Sensation to Cognition. *Brain* 121, 1013-1052.

Meynert T, Psychiatry; A clinical treaties on diseases of the for-brain. Translated by B. Sachs Ney York and London G.P. Putnam's Sons 1884

Rogers, C.R. Client Centered Therapy, its Current Practice Implications and Theory. Boston: Houghton Mifflin Company Boston, 1965

Tononi, G., Sporns, O., Edelman, G.M. A complexity measure for selective matching of signals by the brain. Proc Natl Acad Sci U S A 1996; 93:3422-3427.

2. FATTY ACIDS AND MOOD DISORDERS

Johanna Assies
Senior investigator biological psychiatry at the Program for Mood Disorders, Department of Psychiatry, Academic Medical Center, University of Amsterdam. Head and founder of the FADDS (Fatty Acids in Diabetes, Depression and Schizophrenia) Study group. Published a variety of articles on the role of fatty acids in: X-linked adrenoleukodystrophy, schizophrenia and major depressive disorder.

Abstract

"The Brain—is wider than the Sky"
Emily Dickinson (1830-1886)

Our research concerns fatty acid alterations in patients with recurrent major depressive disorder (MDD-R). The focus is on the critical role of *oxidative stress* defined as an imbalance in production of reactive oxygen species (ROS) on one side and the antioxidant defence system on the other in:

a) the bilateral association between MDD-R and the metabolic syndrome (MetS) – a cluster of risk factors for the development of cardiovascular disease (CVD). Compared with the general population psychiatric patients, MDD-R included, have at least twice the risk of dying from CVD (Ohaeri, 2011). MetS may be interpreted as an adaptation to the intense oxidative stress caused by the "Western lifestyle" (physical inactivity, wrong diet with saturated instead of unsaturated fats, lack of antioxidants, smoking, alcohol) combined with an inherited as well as acquired dysfunction of the mitochondria, the major sites of ROS production (Manji, 2012).

b) the interaction of fatty acid - and 1-carbon(C) or methyl – cycle. Fatty acids(FAs) may contain: no double bonds (saturated fatty acids, SFA), one (monounsaturated, MUFAs) or more double bonds (polyunsaturated, PUFAs). The major FA series in humans are ω- or n-3, n-6 and n-9 depending on the position of the double bond in the C-chain.

Fatty acids and their (non)-enzymatic oxygenated derivatives: lipid peroxidation products (lpos) are essential components of the (sub)cellular membrane phospholipid bilayers. By their carbon chain length and degree of unsaturation they have important structural (e.g.membrane fluidity) and (patho)physiological functions (e.g. production of pro-and anti-inflammatory eicosanoids and neuroprotective docosanoids) (Van Meer, 2008).

The 1-C-cycle and fatty acid metabolism are closely intertwined in the regulation of oxidative metabolism/stress. Via the *transmethylation* pathway the 1-C-cycle modulates the production of 1) phospholipids and the ratio of phosphatidylcholine (PC) and phosphatidylethanolamine(PE) and 2) the PUFAs ω-6/ω-3 ratio and via *the transsulfuration* pathway the concentration of the major intracellular antioxidant glutathione (see Figure). At the center of these pathways the amino acid homocysteine (tHcy) reflects the oxidative stress the body is exposed to.

In a matched cased-control study of 137 patients with MDD-R and 65 matched, non-depressed controls) we found that in plasma and erythrocytes of the patients the concentrations of most of the SFAs and

MUFAs, and additionally erythrocyte PUFAs, all with a chain length>20C, were significantly lower than in the controls. In contrast, the concentrations of most of the shorter chain members (≤18C) of the SFAs and MUFAs were significantly higher in the patients. In the erythrocytes of the MDD-R patients the sums of ω-3 and ω-6 PUFAs were lowering and the ratios of Σ ω-6/ω-3 were higher than in the controls corresponding with many reported data (Assies, 2010). Plasma tHcy was higher and folic acid lower in the patients. Interestingly similar patterns are observed in many other diseases characterized by increased oxidative stress (e.g. schizophrenia, Alzheimer and Parkinson disease and cystic fibrosis) and also in aging people. We therefore hypothesize that the fatty acid alterations primarily may have an adaptive function as for example the lowering of PUFA content makes membrane less vulnerable to oxygen radicals. Further research combining new analysis techniques (lipidomics) of FA and their (non) enzymatic lpos with parameters of MetS will unravel the nature of the alterations and hopefully lead to better/earlier treatment of the patients.

Finally research of the clinical effects of oxidative stress induced alterations in FAs and their (non) enzymatic lpos on the electrical properties of cell membranes - membrane potential in particular - and vice versa the effects of electrical forces on membrane fatty acid composition may also be helpful (Leonelli, 2011).

References

Ohaeri JU, Akanji AO. Metabolic syndrome in severe mental disorders. Metabolic syndrome and related disorders 2011;9/2: 91-98.

Manji H, Kato T, Di Prospero NA, Ness S, Flint Beal M, Krams M, Chen G. Impaired mitochondrial function in psychiatric disorders. Nature Reviews Neuroscience 2012; 13: 293-307.

Van Meer, Voelker DR, Feigenson GW. Membrane lipids: where they are and how they behave. Nature Reviews Molecular Cell Biology 2008;9: 112 -124.

Assies J, Pouwer F, Lok A, Mocking RJT, Bockting CLH, Visser I, Abeling NGGM, Duran M, Schene AH. Plasma and erythrocyte fatty acid patterns in patients with recurrent depression; a matched case-control study. PLoS ONE 2010; e10635.

Leonelli M, Graciano MFR, Britto LRG. TRP channels, omega-3 fatty acids, and oxidative stress in neurodegeneration: from cell membrane to intracellular cross-links. Braz J Med Res 2011;11: 1088-1096.

3. QUANTUM THEORIES OF MIND-BRAIN: WHAT FUTURE?

Eliano Pessa
Department of Psychology, University of Pavia, eliano.pessa@unipv.it, *Pavia, Italy*

Abstract

The attractiveness of quantum theories stems from two main - typically quantum – features: 1) they allow the occurrence of spontaneous (and even large-scale) coherence phenomena without the resort to special design, arrangements, boundary conditions, etc.; 2) in suitable cases (like in quantum field theory) they offer a convenient framework for describing, understanding and forecasting phase transition phenomena. In turn, this implies that quantum theories can support some form of top-down causation, encompassing the pitfalls of the traditional mechanistic and reductionist framework. Therefore, if we assume that all phenomena related to life, brain, cognition, and consciousness are based on some forms of emergent self-organization, quantum theories are the best candidates for an effective theorizing activity in these domains.

It is to be remembered that the expression "quantum theories" can be understood in two different ways: a) denoting a set of known physical theories, like quantum mechanics (QM) or quantum field theory (QFT), in which Planck's constant assumes a specific (and universally prevaling) value; b) denoting a general theoretical framework for describing specific kinds of fluctuating systems (eventually allowing different values of some "effective" Planck's constant). The latter alternative has recently gained in popularity, owing to the fact that some forms of "noisy" field theories have been shown to be mathematically equivalent to QM or QFT, provided we allow the introduction of suitable "effective" Planck's constants (Fogedby and Brandenburg, 2002). Besides, a number of phenomena in psychology and economics, like decision making and concept formation, have been shown to be better described by models equivalent to QM or QFT in which, however, Planck's constant has a value different from the traditional one (Aerts *et al.*, 2010).

So far the main obstacle to exploiting the beautiful possibilities offered by a quantum framework comes from the occurrence of

decoherence phenomena. The latter are due to the interaction of a quantum system with the external environment and can destroy in a very short time the coherence of quantum origin. In this regard a first remark is that decoherence is a crucial problem only for the operation of quantum computers. Namely every biological system needs decoherence in order to avoid becoming like a crystal of sorts. A second remark is that the decoherence is a smaller problem in a number of QFT-like models, owing to the existence of a number of different mechanisms allowing the occurrence of recoherence processes. It is to be remembered that the decoherence game involves a number of different actors, like the nature of the environment, the presence of noise, the influence of dissipation, the occurrence of disorder. On one hand, each actor can be endowed with different kinds of features (for instance the environment can coincide with a simple thermal bath, or with a spin chain, or even with a complex active medium). On the other hand, the different actors can interact in many different – and complex – ways, so as to make the output of the decoherence game strongly dependent on the detailed nature of the specific contexts.

The theoretical studies and the computer simulations so far performed showed that the decoherence game is ruled by a number of general principles that can be shortly listed as follows: i) the destroying influence of environment (for instance, in the case of noise) on a given quantum system can be counteracted by the interaction with another coherent system: different coherent mechanisms can cooperate; ii) linear averaging can hide the quantum nature of coherence: the dynamics of average activations of assemblies of quantum neurons has no longer a quantum nature; iii) higher-order statistical features of quantum systems are the best representatives for detecting quantum effects.

The considerations made above suggest that the quantum theories of brain-mind can have a bright future, provided, however, we introduce models in which all actors of the decoherence game are fully taken into account. In particular, the more recent experimental observations on the activity of neurons *in vivo*, evidencing that the latter are highly sensitive both to the higher-order statistical features and to the global operational features of the neuronal assemblies in which they are embedded (see, e.g., Vlachos *et al.*, 2012), let us think that quantum models of the kind quoted above, could be very useful for the foundation of a quantum psychiatry. Within the latter the quantum models, beyond offering a convenient metaphor, could effectively support the diagnostic and therapeutic activity. In particular, quantum models dealing with complex biological systems, such as the one including the cytoskeleton, the neuronal membrane, the ionic channels, the proteins and their receptors, as well as the intra- and extracellular liquid, could very much help efforts to understand the nature of a number of psychopathological diseases, such as schizophrenia, depression, or autism.

References

Aerts, D., D'Hooge, B., Haven, E. (2010). Int. J. Theor. Phys., 49, 2971-2990.
Fogedby, H.C., Brandenburg, A. (2002). Phys. Rev. E, 66, 016604.
Vlachos, I., Aertsen, A., Kumar, A. (2012). Plos Comput. Biol., 8, e1002311.

4. THE ROLE OF MICROTUBULES IN PSYCHOPATHOLOGY

Massimo Pregnolato
Medicinal Chemistry Professor at the University of Pavia, Italy. Quantumbiolab – Department of Drug Sciences – University of Pavia, Italy. *massimo.pregnolato@unipv.it and maxp@quantumbionet.org*

Abstract
Is it possible that psychopathological diseases such as depression and psychosis involve different states of consciousness through the biological interface called the "cytoskeletal quantum nanowire-network"? Is there any correlation between hallucinations and cellular-molecular interactions or any cause for changes in the conscious state that may be detected by measuring gamma synchrony, which demonstrates a superior correlation with consciousness and which has already provided a variety of responses in different psychopathological conditions and meditation?

In this presentation we try to demonstrate the consistency of the hypothesis that the Schrödinger protein interactome and in particular the cytoskeleton nanowire network comprise the best biological interface

for possible expression of consciousness, being typical and specific for each animal species, and that consciousness is always a potential (1, 2, 3, 4, 5, 6, 7). It is fascinating to contemplate that every animal possesses a primary Schrödinger protein complex (cytoskeleton) and even in the absence of circulating serotonin there is a potential for consciousness that is essential to the behavior of some life forms, while other species such as invertebrates, procaryotes and even archea possess capabilities in their own domain probably mediated by their own Schrödinger protein interactomes. The above-described coherent framework reflects the meaning of the power inherent in a quantitative approach to psychopathology.

References

1. Bandyopadhyay A (2011) Direct experimental evidence for quantum states in microtubules and topological invariance. Abstracts: Toward a Science of Consciousness 2011, Stockholm, Sweden, http://www.consciousness.arizona.edu
2. Cocchi M, Gabrielli F, Tonello L, Pregnolato M: Interactome hypothesis of depression. NeuroQuantology 2010, 8:603-613.
3. Cocchi M, Tonello L, Gabrielli F, Pregnolato M. Consciousness and Hallucinations: Molecular Considerations and Theoretical Questions. NeuroQuantology 2011; 9 (1): 182-189.
4. Roger Penrose, and S. Hameroff. Consciousness in the Universe: Neuroscience, Quantum Space-Time Geometry & Orch OR Theory. Journal of Cosmology Volume 14 Consciousness and the Universe. 2011
5. Pizzi R, Strini G, Fiorentini S, Pappalardo V and Pregnolato.M Evidences Of New Biophysical Properties of Microtubules. Focus on Artificial Neural Networks cap. 9. pag. 191-207. Edited by John A. Flores. Nova Science Publisher Inc. 2011
6. Woolf N, Craddock T, Friesen D, Tuszynski J. Neuropsychiatric illness: a case for impaired neuroplasticity and possible quantum processing derailment in microtubules. NeuroQuantology 2010; 8(1): 13-28.
7. N.J.Woolf, A. Priel, and J.A. Tuszynski. Nanotechnology, nanostructure, and nervous system disorders. In Nanoneuroscience: Structural and Functional Roles of the Neuronal Cytoskeleton in Health and Disease, pages 177–226. Springer, Berlin; Heidelberg; New York, 2010.

5. THE GREEN EPISTEME AND ITS NOT-SO-GREEN PSYCHOPATHOLOGIES

Donald Mender

Donald Mender, M. D., F. A. P. A., is currently a faculty co-sponsor of the Yale Philosophy and Psychiatry Group. He served in the past as an Executive Council member of the Association for the Advancement of Philosophy and Psychiatry (AAPP) and founded the AAPP's New York City Chapter. He has also served as the original organizer of the initiative on Quantum Paradigms of Psychopathology (QPP), as the first corresponding secretary of QPP's Scientific Program Committee, and as the first QPP section editor of the NeuroQuantology Journal. Dr. Mender has published numerous works related to quantum neurodynamics with a recent focus on potential psychiatric applications. His latest publication attempts to reframe elements of thermofield theory and orchestrated reduction in light of the anthropic principle, aiming at a normative consideration of quantum neurodynamical function. Mail: Dmm87@email.med.yale.edu

Abstract

This presentation summarizes content introduced in my paper, entitled "Modes of Dissipation: The Green Episteme and Its Not-So-Green Psychopathologies" NeuroQuantology 2011; 9(3):572-6.

The beginning of the presentation reprises an argument, advanced by the late French post-structuralist Michel Foucault, that normative criteria for mental health and explanations of psychiatric disease have been determined by epistemic frames of reference, each successive framework reflecting the demands of a particular historical era and cultural locus. The presentation then goes on to predict a la Foucault and also, beyond mere value-neutral forecast, to advocate an imminent new global epistemic shift. The coming desired change is to replace the abstract algorithmic orientation of our present information economy with an organic green imperative rooted in a mounting planetary need to reverse humanity's techno-pollution of the biosphere. It is suggested that this larger embedding trend will move psychiatry from the computationally straightjacketed perspective of today's compartmentalizing neuropsychological discourse to more holistic and ecologically informed norms. A likely consequence of the new green epistemic outlook hence will be an integratively enlightened, Gaia-embodied redrawing of our basis for distinguishing between benign and "sick" psychologies. Through normative contrasts with the environmental thermodynamics of affirmative life-enhancement, psychopathological "diagnoses" will come to be understood in terms of dissipatively life-thwarting neurocognitive and behavioral processes.

Theoretical tools empowering this predicted shift will be derived from three scientific sources: 1) insights into the thermofield dynamics of life, pioneered in general outline by Erwin Schrodinger and then applied specifically to the brain's ambient "heat bath" by quantum-neurodynamical theorists such as Giuseppe Vitiello (Vitiello, 2001) and Gordon Globus (Globus, 2010), 2) post-computational takes on neuroscience heralded by Roger Penrose's "gravitonic" physics of consciousness, and 3) anthropic concepts stemming from Hugh Everett's many-worlds interpretation of quantum observation.

Normative notions of the "healthy" sentient brain will be reconfigured in a random distribution across the pluripotential

realities (Cocchi et al, 2011) of multiple universes anthropically linked by that particular subset of observational wavefunction collapses whose end products happen to lie in the "green" (i. e. red-absorbing) frequency band of energy quanta. It may be demonstrated that this pre-defined mode of linkage, in a tautological manner isomorphic with reasoning about Darwinian selection and "fitness," can effectively "endow" phase-coherent quantum order existing before each such wavefunction collapse with a "conscious" ability to enhance classically ordered life preservation in the aftermath of those collapses. Moreover, it can be shown that, in pure systems strictly conforming to the above architecture, toxically disordered thermal byproducts of the above linkage must by statistical necessity be vented unconsciously into dead ensembles of parallel "dumpster" universes.

As a consequence, subtle associated thermofield anomalies, geometrically classifiable in rigorously variegated symmetry-constraining (e. g. metric, affine, diffeomorphic, or homeomorphic) ways, might be used to map "natural kinds" of life-dissipating impurities associated with pathologically "leaky" forms of consciousness. These psychodiagnostic mappings could yield corresponding predictions of deviant symmetry-breaking scalar field "viscosities" with empirically testable import. Broad outlines of implied, radically new therapeutic design possibilities based on differentially constructive and destructive quantum thermofield countercurrents hence may emerge.

References

Cocchi M, Tonello L, Gabrielli F, Pregnolato M. Consciousness and hallucinations: molecular considerations and theoretical questions. NeuroQuantology 2011; 9(1):182-9.

Globus G. Toward a quantum psychiatry: hallucination, thought insertion and DSM. NeuroQuantology 2010; 8(1):1-12.

Vitiello G. My double unveiled: the dissipative quantum model of the brain. Amsterdam: John Benjamins, 2001.

6. QUANTITATIVE PSYCHIATRY: ROLE OF COMPARTMENTALIZED G PROTEIN SIGNALING IN DIAGNOSTICS AND THERAPEUTICS FOR DEPRESSION

Mark M. Rasenick

Distinguished University Professor. Physiology & Biophysics and Psychiatry U. Illinois Chicago, Chicago IL 60612, Jesse Brown VA Medical Center, Chicago. 60612
http://www.uic.edu/depts/mcpb/pages/rasenick/rasenick.htm

Abstract

Lipid rafts are specialized membrane domains, rich in cholesterol and intimately associated with cytoskeletal components. G protein signaling is influenced by these domains, but, depending upon the receptor, G protein and effector enzyme, they either act to facilitate or attenuate signaling. We demonstrate that, for Gs and Gs-coupled receptors (β adrenergic, VPAC and 5HT 4, 6, 7), lipid rafts attenuate signaling by separating Gsα from adenylyl cyclase (Allen et.al, 2007). Data obtained in cells treated with cholesterol chelating agents or in which the lipid-raft protein caveolin is knocked down demonstrate this. Furthermore, caveolin knockout mice show a similar effect (Allen et.al, 2009). Activated Gsα is internalized in lipid raft vesicles, but release of Gsα from those vesicles increases microtubule dynamics and this leads to increased neurite outgrowth and increased formation of dendritic spines in primary neurons (Yu and Rasenick, 2009; Dave et. al. 2011)

Several lines of investigations from several laboratories suggest a post-synaptic effect of chronic antidepressants and a possible postsynaptic target for these drugs. Data from rats, cultured neural and glial cells and tissue from brain of depressed subjects all suggest the localization of the G protein, Gsα, in lipid rafts is modified by chronic treatment with a number of antidepressant compounds (SSRI, MAOI and tricyclic) Donati et.al, 2007; Zhang and Rasenick, 2010). In this study, we sought to establish whether platelet localization of Gsα could prove diagnostic for depression and whether clinical response might be prognosticated as a result of a rapid, antidepressant-induced shift in the lipid raft localization of Gsα. Blood was drawn from normal volunteers or patients at the Dept. of Mental Health (ASUR Fano, Italy). Raft association of Gsα was determined by detergent extraction and cell fractionation as was the case with post-mortem tissue, the association of Gsa with lipid rafts in platelets from depressed subjects was clearly differentiated from both control and bipolar subjects. Most of those treated with

antidepressants did not respond, and the Gsα distribution was consistent with these subjects remaining depressed.

Thus, it appears that the decreased Gsα/cAMP signaling seen in depression is due, at least in part, to sequestration of Gsα in lipid rafts. This may provide a simple biomarker for depression.

References

Allen, JA, Yu, J-Z., Dave, R.H., Bhatnagar, J., Roth, B.L. and Rasenick, M.M. "Caveolin-1 and lipid microdomains regulate Gs trafficking and attenuate Gs/adenylyl cyclase signaling" Mol. Pharmacol 2009 76:1082-93

Allen JA, Halverson-Tamboli RA, Rasenick MM: Lipid raft microdomains and neurotransmitter signaling. Nature Rev Neurosci 2007, 8:128-140.

Dave, RH, Saengsawang,W., Lopus, M., Dave,S., Wilson,L. and Rasenick, M.M.. A molecular and structural mechanism for G-protein mediated microtubule destabilization. 2011 J. Biol. Chem 286:4319-28

Donati RJ, Dwivedi Y, Roberts RC, Conley RR, Pandey GN, Rasenick MM: Postmortem brain tissue of depressed suicides reveals increased Gs localization in lipid raft domains where it is less likely to activate adenylyl cyclase. J Neurosci 2008, 28:3042-3050.

Yu, J-Z, Dave, R.H., Allen, J.A., Sarma, T. and Rasenick, M.M. "Cytosolic Gαs acts as an intracellular messenger to increase microtubule dynamics and promote neurite outgrowth." J. Biol. Chem.2009 284:10462-72.

Zhang L and Rasenick M.M., Chronic treatment with escitalopram but not R-citalopram translocates Galpha s from lipid raft domains and potentiates adenylyl cyclase: a 5-hydroxytryptamine transporter-independent action of this antidepressant compound. J Pharmacol Exp Ther.

7. THE DISEASE AFFECTING ITALIAN POETRY, FROM DANTE UNTIL PRESENT DAYS

Vincenzo Guarracino,
Poet, essayist and translator

Abstract

"*Si Deus est, unde malum? Et si non est, unde bonum*?" "If god exists, where does evil come from? And if God doesn't exist, where does good come from? : This question of Boethius' *De consolatione philosophiae*, is still something that make us think.

"Evil" does exist. It exists and persists in our lives, and we feel it. It imposes on us its presence through sufferings and unhappiness, disharmony and chaos: an unwanted guest in our flesh, our thoughts, our emotions, against a backdrop of a troubled daily life and in the relationship with the world. But it manifests itself even more urgently and sharply through our consciousness, our perception of life, when everyone must confront essential and absolute questions.

Evil can be divided into three levels:

1. Metaphysical level, considered as deprivation and absence, lack of God;
2. Physical level, seen as lack of balance and havoc, embedded in the destiny of body frailty and human nature;
3. Psychic level, understood as lack of self-esteem, loss of meaning in life, black hole sucking in and destroying any will to act and react.

In particular, if we consider psychic evil, "pain of living", which names does it take? Why does it appear? And how can some forms of artistic expression- especially poetry- have positive effects on it? The search for an answer to this question could start from Eugenio Montale's poetic reflection on the "pain of living", in order to draw a sort of illustrative map of Italian poetry, from Dante up to present days, as an expression of the frailty of life.

8. THE SCHISIS OF SCHIZOPHRENIA: A QUANTUM BRAIN VIEW

Gordon Globus
Professor Emeritus of Psychiatry and Philosophy at the University of California Irvine. Dr. Globus is a Distinguished Life Fellow of the American Psychiatric Association. He has been publishing in the area of quantum neurophilosophy from a Continental rather than Anglo-American perspective since 1995. His most recent books are: *Quantum Closures and Disclosures*. Thinking together postphenomenology and quantum brain dynamics (John Benjamins 2003) and *The Transparent Becoming of World* . A crossing between process philosophy and quantum neurophilosophy (John Benjamins 2009). His most recent paper is "Consciousness v. Disclosure: A Deconstruction of Consciousness Studies" (J. of Consciousness Studies, in press). He has published on quantum psychiatry in *NeuroQuantology* (2010) and on quantum neurology in *Medical Hypotheses* (2010). ggglobus@aol.com

Abstract

The bizarre clinical phenomenon of schisis, which is characteristic of schizophrenic dis-integration, is perhaps the deepest puzzle in clinical psychiatry. Current explanations in terms of disconnection between brain systems or neural network theory are not convincing, since they do not account for the unity of consciousness despite the schisis. Vitiello's thermofield brain dynamics is applied to this problematic. It is proposed that schisis is a consequence of a "discoherence" in the self-

tuning component of the matching process with other-tuning (from the environment) and past-tuning (memory traces). It is the match in the "between-two" that splits—the between of two thermofield theoretical modes—and so there are two contents within the unity of consciousness. A general scheme for psychiatric nosology is proposed along these lines.

9. PSYCHIATRY AND REALITY – PERCEPTION OF MATTER OR MATTER OF PERCEPTION?

Ursula Werneke
Associate Professor, Dep of Psychiatry, Umeå University and Sunderby Hospital, Luleå, Sweden, E-mail: uwerneke@gmail.com. Dr Werneke trained at the Maudsley Hospital in London, UK, after which she was Consultant Psychiatrist at East London and Honorary Consultant at the Royal London Homeopathic Hospital. She is now working at Sunderby Hospital Luelå and Umeå University in Northern Sweden. Dr Werneke's main interests are lifestyle and complementary medicine, and her work in these areas has gained broad international attention. Dr Werneke is a biographee of Marquis Who's Who in the World.

Abstract
Current concepts of delusion largely rely on the assumption that one single objective external reality exists as a benchmark for our internal experiences. With the advent of quantum theory holding that reality within the atom is probabilistic and observer-dependent this assumption has become untenable. Accepting the Copenhagen interpretation of quantum theory that there is no reality beyond what is revealed by the act of measurement or observation ultimately implies that there is no objective reality. But this deduction that reality, in general, is thus informational rather than material in nature seems absurd and incompatible with our daily experience. Defining macroscopic reality is not easy though. Scientific realism claims that objects of scientific knowledge exist in an objective world. Antirealism challenges this notion of an objective reality. One alternative interpretation of quantum theory is the "many worlds" interpretation which finds its philosophical correlate in the "plurality of worlds" theory. This holds the idea of all possible worlds being not just possible but real.

Accepting reality as a probabilistic - a cloud- rather than a deterministic concept - a clock- would be compatible with the uncertainty commonly experienced in medical research and practice. In most branches of medicine we would have no difficulties in accepting that the recognition and interpretation of clinical signs and symptoms is inevitably prone to measurement error, random or not. We understand that a true value may lie within a range of possible values depending on a predefined probability level. But what is an acceptable balance between false positives and false negatives? Diagnosis of psychosis based on positive symptoms alone remains difficult where views on reality clash. The problem partly stems from the tendency of our current diagnostic classification systems to be instrumentalist; that is essentially concerned with reliability and prediction. However, most criticism of psychiatry is concerned with validity and explanation, hence strictly constructivist. The constructivist would consider psychotic symptoms social constructs, man-made and prone to abuse in settings intolerant to minority views. With the advent of the information revolution, setting a gold standard for truth and reality will most likely become more, not less difficult. Psychiatrists when explicitly asked seem to agree. But the implicit acceptance of reality in largely deterministic and instrumentalist terms has instilled today's generation of mental health professionals and policy makers with a false sense of security that the diagnosis of delusion and psychosis is straightforward. Highlighting uncertainty as one important principle in psychiatry may be useful, particularly if we accept that life events may be much more prone to random effects than commonly purported.

Even if we believed in one single objective external reality as a benchmark for our internal experience we would still never experience this reality directly. Our experience of reality is essentially one of virtual reality as generated by our brain. This virtual reality may be due to pathological cognitive processes but this does not invalidate the experience. Thus, it will finally become necessary to rethink our currently accepted concept of psychosis. This will become inevitable by the time we master technologies to create sophisticated virtual reality environments individualizing human experience. However, until we have moved to a better understanding

of reality, meticulous history taking coupled with accurate clinical observation and professional empathy remains the best way to account for its uncertain nature. Currently, it remains the only way to explore whether a belief or conviction can ultimately be understood or not.

10. THEOLOGY AND PSYCHIATRY

Don Michele Aramini
Professor of Moral Theology, Catholic University, Milan, Italy. Don Michael Aramini deals, in his college courses, the key issues of bioethics, the new discipline that is interested in the ethical problems posed by advanced medicine. In particular it deals with: The concept of the human person, the concept of nature, the relationship between ethics and science, the relationship between ethics and law, human embryo, abortion and artificial insemination, euthanasia, living wills, aggressive therapy, meaning of human procreation and genetic engineering.

Abstract
The brain is not even thinkable as a material reality, to be observed in its neurochemical components. The brain cannot be studied as a divisible object under the influence of scientific discoveries.

The human person is a "unitarian organism" and when we use the term “person” we do not refer to a hardware brain but we want to include all aspects of life that finds a place in the concrete life of consciousness. Theology has opened itself in recent years in comparison with the human sciences, and this has led it to deal with new issues. The debate with the various theories of neurophysiology of the mind is placed on this background the theologian has to measure the profound changes taking place in the image of the world and man.

Theology has nothing to tell us about the brain and how it works but this does not mean that it doesn’t have its own perspective about the person and his intelligent consciousness and freedom.

Two are the main points of the theological vision: the first is inherited from the Greek world and is the conviction that the human person has a center which regulates the structural links with the entire part.

The second element of the theological tradition stems from the biblical presentation. It indicates the center of the person - often referred to *leb*-heart or *ruah*-spirit - as something deeply intimate and dynamic including particularly the relationship to God who knows "what comes into your mind.”

On this basis, the Christian tradition has conceived of the *ratio* in terms of process: it is in relation to the truth in whose service it is.

In short, the mind is not something complete in itself and almost separable from the rest, but - to use this language - it is a "right", a faculty of the soul toward God, supreme truth and supreme good.

Such a perspective doesn’t allow considering the mind and, even less, the brain as something unrelated: they refer beyond themselves, to a totality of meaning, to truth.

The brain is not thinkable - theologically - as a definite and close reality, as the instrument of a totalitarian reason, independent of God and master of the meaning of life and things.

The person is more than his brain and that, while important for the spiritual dynamics, is not sufficient to explain all aspects. In the same way, the evidence of the truth cannot be reduced to an “experimental evidence”, like the positivists think. The person, in short, comprises a plurality of dimensions that cannot be forgotten or marginalized, without impoverishing the person himself.

11. TREATMENT RESISTANT DEPRESSION: AN UP-TO-DATE

Cesario Bellantuono
Director of Psychiatric Unit, United Hospital and University Politecnica of Marche, Ancona

Abstract
Treatment-resistant depression (TRD) affects a significant number (about 40%) of depressed patients. Many randomized clinical trials as well as the STAR-D study, have well documented that initial treatment with an effective antidepressant drug (AD) is often not sufficient to achieve a full remission of an episode of major depression. The aim of this presentation is an update of the psychopharmacological options so far available in the management of patients with

TRD. Among the potential well documented therapeutic strategies in TRD, such as switch to another AD, combination with another AD and augmentation with non-AD drugs, the association of a Second Generation Antipsychotics (SGA) with a Serotoninergic AD (SSRI) is nowadays considered an effective, safe and well documented therapeutic option. Among the marketed SGA, *Quetiapin* (150-300 mg/day) is the only drug so far approved in Italy as augmentation strategy in patients with major depression who do not respond adequately to an antidepressant treatment.

12. NEURAL CORRELATES OF HIGHER LEVEL BRAIN FUNCTIONS

Gustav Bernroider
Ph D, Assoc. Prof. Neurobiology, Department of Organismic Biology, Neurosignaling Unit, University of Salzburg, Austria. Gustav Bernroider is leading a research unit for Neurosignaling and Neurodynamics in the Department for Organismic Biology, University of Salzburg, Austria. His research focuses on neural correlates of higher level brain functions, such as conscious perceptive states, cognition and emotions. His work integrates theoretical, physical, model-oriented, and empirical research within the field of behavioral and comparative neurobiology and comparative cognition. Gustav Bernroider has organized several international conferences and workshops related to consciousness research and the mind-brain interface (e.g. Quantum-Mind 2007, Salzburg) . His main working hypothesis assumes that consciousness is a purely perceptual property that is based on multiscaled transition dynamics ranging from atomic to classical states, hosted by membrane channel proteins and organized along the sensory-motory segregation pattern in the brain. His more recent behavioural work is summarized in Neuroscience and Biobehavioral Reviews, 35, 2009-2016 (2011). e-mail: Gustav.Bernroider@sbg.ac.at

Abstract
How can the phenomena behind conscious experience become integrated with a physical description in brain science? Although once controversial, it is becoming increasingly accepted that essential progress in cognitive neuroscience cannot avoid the central question on how the phenomenology of subjective experience is connected with the physical analysis of brain processes. In this presentation I first outline the three routes that need to be combined when addressing fine grained correlates of brain states that can possibly qualify as unique signatures for the subjective states of an agent. First, we have the functional anatomy of brains ranging from cellular to molecular, sub-molecular and quantum-chemical levels of neural organizations. The 'neuronal specificity' behind this aspect can quite generally be found within the '*synaptomics*' of neuronal connections. Particular features behind the complexity of synaptomics can now be successfully attributed to various dissociations of the states of consciousness. For example, the intact presence of top-down recurrent connections in higher order associative cortex has recently been shown to be indispensible for the presence of conscious perception (e.g. *Boly, et al., Science, 332, 2011*). The second aspect involves the electrical signaling pattern of the brain. Here again several unique properties can dissociate conscious states (e.g. large scaled synchronizations of potentials and small scaled, de-correlations during awake states, e.g. *Ecker et al., Science, 327, 2010,* or reproducibility of activation patterns in response to sensory stimuli, *Schurger et al., Science 327, 2010* and cyclic recurring brain events, *Madl et al., Plos ONE, 6,4,2011*). Finally, we can discern a distinctive class of behaviors and motor expressions in men and animals that clearly point to the presence of conscious perceptive states and propositional learning behaviors (e.g. reviewed by *Bernroider & Panksepp, Neuroscience and Biobehavioral Reviews, 35, 2009-2016 (2011)).*

Despite this progress in identifying brain characteristics that can discriminate different states of experience ranging from vegetative states to minimally and fully conscious states and despite of the picture that emerges from these studies, one essential question remains unanswered: what precisely is the mechanism that is different in states of experience that either come along with 'how it feels to have this experience' or are not associated with any phenomenal and purely subjective quality? Can we 'fine-grain' the list of necessary properties for the presence of conscious experience to the extent that we may finally agree on a sufficient explanation and extend this explanation to the challenging world of individual variations and psychopathology?

'Experience' goes beyond data processing. I therefore advocate the view that a sufficient explanation for the phenomena of experience, if purely framed within the corset of objectivism and strict physicalism, cannot really be expected. Physics deals with the

states of systems. It is rather blind to the *transitions* between these states. *Transitions* are only inferential in physics (assumed causal connectivities between states). My own conjecture, based on an extensive list of necessary properties behind multiple scaled 'brain-states' is, that there is a particular *class of transitions* between these states, setting out from the quantum scale and organized over a large range of physical dimensions, that carries the phenomenal quality of experience. Adopting a more 'constructivistic view' in neurobiology may eventually allow us to discern this class of (physical) state successions with transients that shift the preconscious and subliminal domain of experience into the states of consciously 'being like something'.

13. BRAIN FOOD

Alessandra Bordoni
Department of Food Sciences – University of Bologna. Alessandra Bordoni, MD and PhD in Biochemistry and in Nutrition Science and Dietetic, is working as researcher at the University of Bologna (Italy) and is professor of "Human Nutrition" and "Applied Nutrition" in the degree courses of "Food Technologies" at Faculty of Agricultural Sciences, University of Bologna (Italy). She is the coordinator of the Human Nutrition Unit at the Food Science Campus of the Faculty of Agricultural Sciences, University of Bologna (Italy). She is working on several topics of nutrition and nutritional biochemistry, and published about 120 full papers in national and international journals. Dr. Bordoni participates to different EU project, and is the coordinator of the project PATHWAY, recently funded by the EU Commission. She was member of the Board of the Italian Society of Human Nutrition (SINU) in the years 2004-2009.

Abstract
The brain, as well as other organs, has specific nutritional requirements related to both energetic and structural needs, that are important for proper physiological function.

Since glucose is an obligatory metabolic fuel for the brain, hypoglycemia always represents an emergency that signals the inability of the brain to meet its energy needs. When left untreated, hypoglycemia can result in permanent brain damage and ultimately, death. The major goal of maintaining glycemia at normal level is to ensure a sufficient flux of glucose to the brain. In turn, in the brain glucose-excited or glucose-inhibited neurons located at different anatomical sites, mainly in the brainstem and the hypothalamus, are master regulators of glucose homeostasis. Lower brain glucose metabolism has been reported to precede and therefore contribute to the neuropathologic cascade leading to cognitive decline in AD.

Brain needs for fatty acids is not simply related to ketone bodies, which are released by the liver into the circulation and provide energy to tissues that are not able to oxidize fatty acids such as brain when glucose is not available. Polyunsaturated fatty acids, particularly n-3 ones, have a structural role that is tightly related to brain function, and are considered dietary factors able to prevent cognitive decline.

14. HOW MATHEMATICS CAN INFORM THE DIAGNOSIS OF MOOD DISORDERS

Massimo Cocchi
Lucio Tonello
Massimo Cocchi and Lucio Tonello are professors at L.U.de.S. University. *Lucio Tonello:* Major scientific research has always been connected with study, teaching and application of aspects of brain and brain mathematical models, as well as the following topics: Algorithms, Methods and Systems within the Science of Complexity; Meta-Heuristic Algorithms (Genetic Algorithms, Simulated Annealing); Swarm Intelligence and Artificial Life Systems (Ant Colony Optimization); Fuzzy Logic Systems; Chaos Theory; Complexity (Self Organizing Criticality, Fractals); Games Theory (Conflict Analysis); Statisitical Learning (Support Vector Machine); Artificial Intelligence; Membrane computing; Quantum computation. *Massimo Cocchi:* Major scientific research has always been connected with study, teaching and application of: Ethanol and lipid; Studies concerning unusual fatty acids; Dietary lipids and tissue lipids; Studies about Essential Fatty Acids (EFA); Fatty Acids of the n-6 and n-3 series; Cellular nutrition; Lipid metabolism during development and growth; Molecular aspects in quantitative psychiatry; Molecular aspects of ischemic heart disease.

Abstract
At present. psychiatric diagnosis in most cases is performed without using any objectively biological diagnostic tool. Psychiatry seems to be one of the few areas of medicine, perhaps the only one, which does not regularly employ any technological instrumentation and often diagnosis and treatment are entrusted to the psychiatrist's experience.

There have been countless attempts and proposed solutions to this problem but there

are no known simple and economical methods for practical clinical use. However, the literature has suggested considering platelets as a key area of promise.

In this regard, the initial idea, conceived in 2005, was to find a means of looking at platelets in their entirety in order to search for an approach that will capture the sum of their characteristics, their essence. The result was the idea of analyzing the fatty acid content of the membrane. The complexity of membrane dynamics has also suggested the potential utility of investigation by means of advanced non-linear analytical tools. In particular, it seemed appropriate to enlist a type of artificial neural networks: the SOM (*Self Organizing Map – Kohonen Network*). This particular algorithm allows a graphical view of the empirical data, building a two-dimensional map which sorts subjects along a continuous domain, the range not necessarily turning out in to be dichotomous.

This approach has been used to assess membrane platelet fatty acids of a population of subjects with a clinical diagnosis of Major Depression versus a population without the disease. The values of fatty acids of the 2 populations were fed into the SOM, mixing healthy and pathological individuals and withholding information regarding their psychopathological condition. The output of the SOM was able to map the two populations using 3 specific fatty acids, recognizing as similar those belonging to the same psychiatrically defined population and segregating as disparate those belonging to different psychodiagnostic categories.

The above method "photographs" the two psychodiagnostic populations in their empirically delineated behavioral states and tries to find biological commonalities and differences. Thereafter, appropriate sample choices beyond age, sex, therapy may be considered. It was the precise intent of the two researchers to construct a method with a strong discriminating capacity for studying major depression and also possibly for detecting under-classifications that might misleadingly limit the scope of results.

The main goal of the method is not to find the biomarkers of a disease. Rather, it is to find differences between two populations "as they are" and to build an instrument with discriminating capacity, with a logic whenever possible that is not dichotomous, with the aim of creating a technological tool really capable of doing clinical psychiatric diagnosis. The direct task of finding bio-markers, according to the rules given by *Evidence Based Medicine* (EBM), requires elimination of selection bias but may lead to distortion of population selectivity away from clinical realism. Now, however, using the above method, it has been possible to distinguish clinically bipolar subjects from depressed subjects.

In conclusion, the work outlined in this abstract brings to light a highly innovative method that offers revolutionary enhancements in the study of Major Depression and Bipolar Disorder, for which currently there are not enough reliable technological instruments available for clinical application.

15. IS THERE A RATIONALE FOR DESIGNING NEW PSYCHIATRIC DRUGS?

Jack A. Tuszynski
Department of Physics, University of Alberta Edmonton, AB, T6G 2J1, Canada and Division of Experimental Oncology, Cross Cancer Institute, 11560 University Avenue Edmonton, AB T6G 1Z2, Canada. As the Allard Research Chair in Oncology, Jack Tuszynski is the head of an interdisciplinary team that is focused on building "designer drugs" able to kill tumors and eventually lead to improved cancer cures. Through his work in computational biophysics Prof. Tuszynski is attempting to create optimized drugs that would target cancerous cells while reducing side effects to the healthy cells. In collaboration with researchers from Texas he has already developed a new generation of chemotherapy drugs that are derivatives of colchicine; the new class of these drugs preferentially affects cancerous cells. To achieve success in the promising field of biological modeling, he draws upon his physics background to create computer software that scans molecular targets against all available drug entities to find the optimal match. Prof. Tuszynski works in a cancer clinic environment with the sole objective of offering hope to patients who have exhausted their conventional options. Prof. Tuszynski is also a full time senior faculty member of the University of Alberta and is on the editorial board of the Journal of Biological Physics, Journal of Biophysics and Structural Biology (JBSB), Quantum Biosystems, Research Letters in Physics, Water: a Multidisciplinary Research Journal and Interdisciplinary Sciences-Computational Life Sciences. He is an Associate Editor of The Frontiers Collection, Springer-Verlag, Heidelberg.

Abstract
Our ultimate objective is to provide an integrated view of the molecular phenomena taking place at the level of brain microtubules in a bottom-up scheme, demonstrating that

subtle physical interactions impact neuronal functions including the computational and memory storage capabilities of the brain. As consequences of the model proposed we discuss how information processing takes place inside a neuron and how memory can be encoded and erased within the cytoskeleton, and we will show how molecular dynamical simulations reveal the action of anesthetics. Direct connections to neurological disorders, especially Alzheimer's disease, will be presented. The talk will end with a proposal for specific drug design strategy.

Acknowledgements
This work has been done in collaboration with T. Craddock (Univ. of Alberta), S.R. Hameroff (Univ. of Arizona), N. Woolf (UCLA), R. Tanzi (Harvard Univ.) and A. Priel (Israel Inst. of Advanced Studies). This research was supported by NSERC (Canada)

16. PHILOSOPHY AND PSYCHIATRY: "THE VIOLATED BODY IN THE ERA OF THE INVISIBLE MAN"

Fabio Gabrielli
Dean of the Faculty of Human Sciences and Professor of Anthropological Philosophy, L.U.de.S. University, Lugano – Switzerland. Fabio Gabrielli publications include a variety of essays and specialized Reviews in the fields of anthropology, biology, medicine and consciousness studies. At present, his research is focused on the biological and anthropological-cultural bases of depression, quantum and philosophical approaches to mental phenomena, and the existential dynamics of the disease processes and treatment. He is member of the Advisory Board of the initiative on Quantum Paradigms of Psychopathology (QPP) and of the Scientific Committee of the "Paolo Sotgiu" Research Institute for Psychiatry and Quantum and Evolutionary Cardiology.

Abstract
To the extent that our temporality is characterized by what Bauman (1) calls *pointillist time*, a time with no cohesion, direction, or *telos*, a time wrapped up in itself and capable of expressing only immediate satisfaction in the eternity of the instant, we cannot any longer organize our existence into a long-term project but rather must operate within the framework of the *hurried* culture, of voracious consumption, according to Bertman (2).

And so Eriksen's (3) tyranny of the moment takes shape: "*The consequences of this terrible haste are devastating; the past and the future seen as mental categories are threatened by the tyranny of the moment [...]. In fact, the threat even concerns "here and now", since the following moment comes so quickly that living the present becomes difficult*".

In other words, we have gotten used to a non-genuine restlessness, completely different from the Augustinian or Pascalian one, linked to the original desire to fulfil our human contingency, fed only by a forced, spasmodic tendency to consume every product frantically, almost as a vampire might, in order not to be excluded from the market, that is to say from the supreme ruler which establishes who belongs to the community and who doesn't.

This kind of restlessness is similar to the one depicted in this clear passage by Maria Zambrano (4): It is a "*...restlessness that is not that of the past, when life was full of adventures, since it is a restlessness we endure, that makes us feel like prisoners. It is a restlessness that comes from the outside, not a liberating activity that originates from the inside. The most degrading thing for a human being consists of being carried away, swept along as if he had hardly any option or it was hardly possible to choose, as if he couldn't ...[make] any decision because someone else, without even asking, is deciding in his place. This passivity manifests itself in the form of the worst loneliness. Not only [do] we feel anxious, but we also feel subdued to an "unceasing loneliness". But loneliness is just like restlessness: loneliness is part of daily life; it is in the background of human life. And yet, the loneliness in a period of crisis is very different from the loneliness experienced by a bright man, since it is not caused by an increased lucidity and it can even imply an increased confusion. It is a loneliness caused by the restlessness, for we can't be sure of anything. We find ourselves alone because we are restless and confused.*"

The man of this crisis, devoted to productivity, efficiency, functionality and the market, is restless, since the existential field of his "technological" possibilities is so wide that it generates powerlessness and dismay.

Obviously, one cannot renounce anything if one wants to stay in the fictitious community created by the Market. At the same time, one feels anxious because on the one hand it is structurally impossible to choose, the choice being denied in the name of all or nothing, and on the other hand the search for "something more", compared with

the certainty of what you possess, is risky and therefore could unhinge that very same certainty, in a wicked, vicious circle.

Anyway, a sort of *turboconsumerism* is prevalent, and it has produced a progressive and radical oblivion for limits, temperance or sobriety, in other words for that anthropologic dimension in which one can see existence as the recognition of his own and other people's finitude; an existence expressing economic frugality (5), existential patience and the necessary sedimentation of experiences, projects and love.

A new man originates from the turboconsumerist restlessness, as Aubert (6) says; a man who is *always busy, always in a hurry*, characterized by an auto-referential, hyper-familial, rocky existence, impenetrable from the outside and impermeable against any emotional intrusion, focused on poor and mere biographic realities or stuck in emotional indifference, in which the individual is left behind and feelings are approached in a mean and managerial way.

The new *transcendental* characteristics of existence, namely efficiency, effectiveness, productivity, and consumption, are embodied by Technique, seen in its radical metaphysical expression as disguised nihilism (7), and these characteristics are socially manifested by unlimited work performance and eternal individual consumption.

Those who cannot keep up are excluded, and the exclusion implies a self-denuding, a violation of the body, a social invisibility, which in turn cause the shame that leads to depression There is not enough space here to contextualize and dialectically interrogate the ostensible "neutrality" of Technique and ask whether, on one hand, man is to blame for lusting after the power of excess efficiency or, on the other hand, it is Technique that establishes not only the means but also the ends of our actions, influencing modes of living, choices, ethical behaviours, and the deeper meanings of history. Concerning this issue we would like to recommend two essays: Galimberti's exposition (8) on the non-neutrality of Technique, which influences our mode of existence in the world, and Nacci's work (9) dealing with the innocence of Technique, seen as incorporated with the human being and not as a separate entity.

In a world in which the extent of what one can produce and consume tells how much one is worth, questions fail to thrive, meaningful alternatives to hyper-technological life are not explored, and ethical and existential provocations are not disseminated, because, once the original interrogatives that normally harbour the human soul are eradicated, everything morphs into standardization and indifference.

Hence, we can easily understand that a context in which the person is assessed on the basis of the goals he meets, the things he displays, and the products he voraciously consumes in the moment represents a fertile breeding ground for depression, since its genetic predisposition is amplified due to the fact that disposition and emotion, nature and culture, biology and the study of the soul have always been closely intertwined.

References

1. Bauman Z. (2007). Consuming life, Polity Press, Cambridge.
2. Bertman S. (1998). Hyperculture. The Human Cost of Speed, Praeger, Westport (CO)-London.
3. Eriksen Th. (2003). Tempo tiranno. Velocità e lentezza nell'era informatica, it. tr. Elèuthera, Milano.
4. Zambrano M. (1996). Verso un sapere dell'anima, it. tr. R. Cortina, Milano.
5. Bouckaert L. et al. (2008). Frugality. Rebalancing material and spiritual values in economic life, Peter Lang Publishing, Oxford.
6. Aubert N. (2003). Le culte de l'urgence. La société malade du temps, Flammarion, Paris.
7. Gabrielli F. (2005²). L'oro della sapienza. Sull'anima: laboratorio filosofico per l'uomo tecnologico, Dialogolibri, Como.
8. Galimberti U. (1999). Psiche e techne. L'uomo nell'età della tecnica, Feltrinelli, Milano.
9. Nacci M. (2000). Pensare la tecnica. Un secolo di incomprensioni, Laterza, Ro

17. PARADIGM SHIFTS IN MENTAL HEALTH

Mansoor Malik
Associate Professor of Psychiatry, Howard University Medical School, Washington, DC, USA. Dr. Malik currently serves as corresponding secretary for the QPP initiative. He has published widely in the area of quantum neurodynamics. mamalik@howard.edu

Abstract
Psychiatry as a discipline has relied historically on many other fields of inquiry for its insights and methods of investigation. These other fields range from purely philosophical domains, such as phenomenology, to purely mathematical disciplines, such as statistics.

The inferential process for psychiatry has traditionally conformed, at least by way of analogy, to pre-quantum Newtonian physics. Thus Freud based his theories of instinct on a hydraulic model essentially drawn from classical fluid dynamics. The operative assumptions on which the DSM psychodiagnostic taxonomy rests and through which algorithmic approaches are incorporated into various treatment and psychotherapy models are ideally formalized by Boolean logic. The resulting framework is deterministic, presupposing prediction of a later state if all the coordinates of a previous state in the system are known. There is an implicit expectation of the capacity to predict complex human behavior such as violence. This becomes ever more difficult as we try to fit complicated phenomena such as psychotic states into simplistic cause-and-effect models, in part to fulfill certain societal expectations and in part to follow a deterministic medical model.

With the prevalent so called "biological model", it is assumed that classical brain mechanisms will ultimately suffice to explain all psychologically described phenomena. This assumption originates from the idea that the brain is made up entirely of material particles and electromagnetic fields. It is further assumed that all causal mechanisms relevant to neuroscience can therefore be formulated solely in terms of properties of these components. Thus, experiential content (subjective feelings, free will, knowing, etc.) are not included as primary causal factors.

However, this world view in psychiatry (and in the neurosciences generally) is based on an outdated paradigm in physics. Contemporary understanding of quantum physics fundamentally differs from classical physics with reference to the role of a conscious observer entering into the structure of empirical phenomena. Such new principles directly contradict the deterministic idea that local mechanical processes alone can account for all observed empirical phenomena.

This talk highlights a need for today's field of psychiatry to adopt a "quantum paradigm" and will attempt to provide support (both theoretical and empirical) for that assertion. It will be shown that allowing for the quantum phenomenon at the neuronal level provides an alternative conceptual framework for describing neural processes. The new theoretical framework, unlike its classical predecessor, rests directly upon and is compatible with currently prevailing principles of physics.

References

Schwartz, J. M. Stapp, H.P, and Beauregard, M, Quantum physics in neuroscience and psychology: a neurophysical model of mind–brain interaction, Phil. Trans. R. Soc. B (2005) 360, 1309–1327

Bohm, D A new theory of the relationship of mind and matter, Journal of the American Society for Physical Research,(1986) 80:13-35

Bohr N, Atomic theory and the description of nature, Cambridge University Press 1961,96

Bohr, N Atomic Physics and Human Knowledge, Wiley 1958Crick, F and Koch, C, Towards a

Kuhn, T, S, Black body Theory and Quantum Discontinuity, 1814-1912, Oxford, Eng, Clarendon, 1978

Libet B, The neural time factor in perception volition and free will, Revue de Metaphysique et de Morale, (1992), 2: 255-72

Porter T, Dotson L, Beatty J, Kruggler L The empire of chance, how probability changed science and everyday life, Cambridge University Press 1989

18. DESCRIBING THE PSYCHO-PHYSICAL DYNAMICS OF PERCEPTION USING QUANTUM FORMALISM

Efstratios Manousakis

Donald Robson Professor of Physics, and Distinguished Research Professor, Florida State University. Dr. Manousakis received his Ph. D. in Theoretical Physics in July 1985 from the University of Illinois at Urbana-Champaign (First Ross J. Martin Award for his thesis). After a Post-Doctoral Research position at the Center for Theoretical Physics at the Massachusetts Institute of Technology (1985-1987) and at the Supercomputer Computational Research Institute (1987-88) he joined the Physics Department of FSU. Presently, Dr. Manousakis is the Donald Robson Professor of Physics and holds the title of Distinguished Research Professor. In 2008, Prof. Manousakis was named Fellow of the Institute of Physics. In 2002, he was named Fellow of The American Physical Society. He also received the PAI Award for Excellence in Teaching and Research (1998) and the Developing Scholar Award (1990) from Florida State University. Prof. Manousakis' research is in the area of theoretical condensed matter physics and includes a number of subfields, such as, quantum many-body theory, strongly correlated electrons, the quantum Hall effect, superconductivity, and superfluidity. In addition, he has recently done work on the interpretation of quantum mechanics and in particular mathematical description of the operation of consciousness. Manousakis has published over 100 articles in the most prestigious journals in his field and his work has been widely cited.

Abstract

A mathematical formalism is sought to describe the subjective (first-person experience) or abstract/mental process of perception by examining the general character and operation of the process of perception. This formalism should describe the psycho-physical dynamics of the subjective or cognitive experience as communicated to us by the subject. By making some simple observations of the nature of awareness as we all experience it we derive a formalism to describe basic aspects of the first-person experience of perception, which exactly parallels the structure of quantum mechanics.

Namely, we find that the formalism of orthodox quantum theory of measurement, where the observer plays a key role, may be a broader mathematical foundation, which can be adopted to describe the dynamics of the subjective experience.

Subsequently, the formalism is used to describe simple perceptual processes and, in particular, to describe the probability distribution of dominance duration (PDDD) obtained from the testimony of subjects experiencing binocular rivalry. Using this theory and parameters based on known values of neuronal oscillation frequencies and firing rates, the calculated PDDD of rival states in binocular rivalry under various conditions is found to be in good agreement with available experimental data. Motivated by this theory, we carried out binocular rivalry experiments with a large number of subjects to obtain high quality statistics on PDDD for the case in which the rival stimulus is periodically removed to test detailed counter-intuitive predictions of this theory. The data and the theoretical predictions are in very good agreement using no adjustable parameters.

The audience is not required to have any prior knowledge of these phenomena as they will be illustrated during the talk.

References

1) E. Manousakis, Found. Phys. 36 (6), 795 (2006).
2) E. Manousakis, BioSystems 98, 57 (2009).
3) E. Manousakis, http://arxiv.org/abs/1009.3656

18. MOLECULAR CHANGES IN MOOD DISORDERS RESULTS OF THE MARCHE REGION SPECIAL PROJECT

[1]Benedetti S., [6]Bucciarelli S., [1]Canestrari F., [1]Catalani S., [5] Cocchi M., [3]Colomba M. S., [3]Gregorini A. [4]Mandolini S., [2]Marconi V., [2]Mastrogiacomo A. R., [6]Rasenick M., [4]Silvestri R., [1]Tagliamonte M. C., [5] Tonello L., [4]Venanzini R.

[1]Department of Biomolecular Sciences, Section of Clinical Biochemistry , University of Urbino "Carlo Bo", Italy. [2]Chemistry Laboratory - Biotechnology Section-Department of Biomolecular Sciences i, University of Urbino "Carlo Bo", Italy. [3]DiSTeVA, University of Urbino "Carlo Bo", Italy. [4]Department of Mental Health, ASUR Fano, Italy. [5] "Paolo Sotgiu" Institute for research in Quantitative & Quantum Psychiatry & Cardiology, L.U.de.S. University, Lugano, Switzerland. [6]University of Illinois Chicago College of Medicine, USA.

Introduction

The need for a deep, radical turning point in the world of psychiatry is rapidly growing. Present diagnostic methods cannot continue to be considered acceptable because they are almost completely based on the psychiatrist's opinion, which does not depend on any objective diagnostic technology and thus has a very high error rate.

A debate is essential between the advocates of traditional diagnostic and therapeutic methods and advocates of emerging methods resulting from new discoveries.

Major depressive disorder and other related and unrelated psychiatric conditions are still characterized and defined by descriptive and non-biological criteria, but it is hoped that we can adequately characterize this and other psychiatric disorders with the addition of new quantitative approaches.

Purpose of the research

The aim of this study was to evaluate molecular changes in blood occurring in Mood Disorders.

To achieve this goal we investigated 105 subjects:

- 71 f (68%) mean age 50
  34 m (32%) mean age 50
- Depressed (MD) n°40 of which:
  28 f (70%) mean age 49
  12 m (30%) mean age 54
- Bipolar (BD) n° 65 of which:

43 f (66%) mean age 51

22 m (34%) mean age 49

Patients were subjected to a thorough clinical diagnosis and a blood sample was collected and fractionated in order to obtain plasma, platelets and lymphocytes.

Inclusion criteria

All subjects had been diagnosed with Bipolar Affective Disorder (BD) or Major Depression (MD). Diagnosis is reached through a survey clinical - anamnestic time to ascertain the presence of the criteria specified by DSM-IV-TR.

All patients underwent psychodiagnostic investigation in the following ways: HRSD-21, HRSA, CGI, SCL-90, HCL-32. The subjects were recruited without regard to sex, age, food intake pattersn, or pharmacological therapies. To carry out the experimental work authorization was requested from the Local Ethics Committee. The study was double-blind.

Exclusion criteria

Subjects who did not give consent, patients with a diagnosis other than an affective disorder, and persons in their first clinical episode were excluded.

Blood chemistry analyses

Platelet fatty acids, Gsα protein, soluble plasma antioxidants, plasma markers of oxidative damage, plasma indices of inflammation, platelet serotonin and plasma, lynphocyte gene expression.

Results

Platelet membrane markers

Experimental tests demonstrated the presence of a significant correlation between the alteration of the concentration of certain fatty acids present on the platelet membrane, which determines its fluidity, and mood disorders as well as other pathological entities, including cardiac and neurodegenerative diseases.

In particular we saw that major depression and ischemic heart disease are associated with a specific composition and viscosity of the platelet membrane.

The results obtained showed that the percentage composition of the platelet membrane fatty acids is less variable than that of the plasma and red cell membrane.

The index of membrane fluidity, obtained from analysis of platelet fatty acids (Palmitic Acid, Linoleic Acid, Arachidonic Acid), was shown to be capable of discriminating the cases diagnosed as MD from those diagnosed as BD.

The index of membrane fluidity is stable in the same subject over time. A condition of greater or lesser clinical compensation corresponds to variations which are not substantial and never register transition from a positive value to a negative or vice versa. Clinical improvement appears to correspond to an increase in the indices of the membrane, ie at a lower fluidity.

Oxidative stress

Patients with MD and BD presented a reduction of plasma antioxidant defenses as well as an accumulation of inflammatory markers. Subjects with MD also had increased levels of oxLDL and Hcy (homocysteine) which are associated with increased cardiovascular risk. In this context, integration with antioxidant supplements might be useful as a support for drug therapy (generically possessing pro-oxidant effects) in the containment of oxidative and inflammatory phenomena characterizing psychiatric disorders.

Platelet serotonin

Subjects with MD and BD, under treatment with antidepressants, demonstrated a significant reduction of platelet serotonin in comparison to corresponding untreated subjects.

Gsα protein

Mean (+SEM) ratios of Gsα in non-raft vs raft platelet membrane fractions as measured by sequential extraction with the detergents TX-100 and TX-114 in subjects with Major Depressive Disorder (MDD) and Bipolar Disorder (BPD) were evaluated.

Results from a one-way ANOVA test followed by a Bonferroni's Multiple Comparison Test showed a significant difference between Control (1.444 ± 0.17 N=5), MD (0.5080 ± 0.047 N=25), and BD (0.7815 ± 0.065 N=40) groups.

Gene Expression

Patients with MD *versus* controls: twenty-three genes involved in the catabolism of arachidonic acid appeared overexpressed by a factor of at least two with reference to controls. In particular, a subset of genes was upregulated by a factor of four (ALOX12B, HPGDS) to (ALOX15) with respect to healthy subjects. Among these, ALOX15B (lipoxygenase 15B) was the most significant from a statistical point of view (fold: 4.88; $p<0.05$).

Patients with bipolar disorder *versus* controls: six genes were overexpressed by a factor greater than two compared to controls. Of these, five were upregulated in patients with major depression as well; however, although higher than in controls, expressed values of these genes as assessed in bipolar disorder patients were only a half (ALOX12B, PLA2G2D) or a third (GPX5, PLA2G2C and PLA2G12B) of those detected in patients affected by major depression. Interestingly, ELOVL7 (elongase 7) appeared to be overexpressed only in patients with bipolar disorders.

Major depression versus bipolar disorder: nine genes were overexpressed by a factor of two to three in subjects affected by major depression; among them LTA4H (leukotriene A4 hydrolase) ($p <0.05$) may be considered a good candidate.

Overall, several promising candidate genes (most of them related to pathways leading to the inflammatory response) potentially associated with major depression or bipolar disorder were detected. They will require further validation by a more extensive study entailing a larger number of subjects.

19. INCOHERENT QUANTUM METALANGUAGE AND SCHIZOPHRENIA

Paola Zizzi

"Paolo Sotgiu" Institute for research in Quantitative & Quantum Psychiatry & Cardiology, L.U.de.S. of Lugano, Switzerland. Paola Zizzi is a theoretical physicist and has a PhD in Mathematics from the University of Padova. She is scientific researcher at the Institute di Ricerca "Paolo Sotgiu" in Psichiatria e Cardiologia Quantitativa ed Evoluzionistica, Università L.U.de.S. in Lugano, Switzerland. For four years, she also collaborated with the Department of Psychology of the University of Pavia. She has been working on quantum computing, quantum gravity, and quantum logic. She has also investigated the logic of quantum robots. Recently, she became interested in the quantum-metalogical description of selected mental disorders including autism and schizophrenia. paola.zizzi@uniludes.ch paola.zizzi@unipv.it

Abstract

Human thought processes can be formalized by means of a quantum metalanguage [1] leading to a quantum logic of human information processing.

A healthy mind is capable of abstract thought, which is coherent and logical, as well as of creative, unpredictable thought which is incoherent, but still logical, although the logic is different. At the metalogical level, these requirements imply the existence of two different quantum metalanguages, the coherent quantum metalanguage and the incoherent one. The corresponding assertions are (quantum) coherent assertions and (quantum) incoherent ones respectively [2].

The physical interpretation of such quantum coherent (incoherent) assertions is that of coherent (incoherent) quantum field states in the context of a Dissipative Quantum Field Theory of the brain. [3]. The decay rate of coherence due to dissipation is the same in both domains. Hence, the healthy mind comes easily to the classical state of consciousness, through decoherence, from both domains. In this case, the coherent and incoherent domains form a whole system, and the "double" [4], is just the environment absorbing the energy loss.

For schizophrenia, in contrast, the domain of quantum incoherent assertions plays the role of the double. This fact makes the incoherent domain very strong against decoherence and the mind is trapped in the quantum unconscious [5] and cannot reach the classical state of consciousness. We believe that hallucinations are driven by the "incoherent double".

References

[1] P. Zizzi, From Quantum Metalanguage to the Logic of Qubits. PhD Thesis, arXiv:1003.5976 (2010).
[2] P. Zizzi, The Uncertainty Relation for Quantum Propositions, arXiv:1112.2923v1 (2012)..
[3] G. Vitiello, Dissipation and memory capacity in the quantum brain model, *Int. J. Mod. Phys.* B 9, 973 (1995). quant-ph/9502006.
[4] G. Vitiello, *My Double Unveiled*. Amsterdam: John Benjamins, 2001.
[5] P. Zizzi, When Humans Do Compute Quantum, in: A Computable Universe, Hector Zenil (Ed), Word Scientific Publishing. Forthcoming.

20. CLINICAL BRAIN PROFILING; A FUTURE DIAGNOSTIC SYSTEM FOR PSYCHIATRY

Avi Peled
Sha'ar Menashe Mental Health Center, Hadera, Israel. Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel. Correspondence; Dr. Avi Peled. Sha'ar Menashe Mental Health Center, Mobile Post Hefer, 38814, Israel, Tel: 972522844050, Email: av_peled@netvision.net.il

Abstract
Even though everyone talks about the importance of neuroscience to psychiatry, in reality the common psychiatric clinical work is unrelated to neuroscience. The diagnostic taxonomy used by psychiatrists (the DSM) is not related to the brain, and none of the advanced insights gained from neuroscience has reached all the way to everyday clinical work of the psychiatrist.

Clinical Brain Profiling (CBP) is a novel and unique approach for conceptualizing mental disorders designed to overcome this problem. Using integrated knowledge from complex-system-theories, neural-computation, neuroscience, psychology, neurology and psychiatry, it is possible to generate a testable-prediction conceptual framework that re-conceptualizes mental disorders as brain disorders.

In my talk I will explained the theoretical background for a novel diagnostic approach to mental disorders, and will show how it is relevant to the clinician at the forefront of the clinical setting, http://neuroanalysis.org.il/

21. HOW FAR IS MATTER FROM THE SOUL?

Andrea Peracino
Vice President of the Giovanni Lorenzini Medical Science Foundation, *Milan-I, Houston-TX,* andrea.peracino@lorenzinifoundation.org

Abstract
The interdisciplinary attributes attached to the dialogue in this conference seem to be an invitation to scholars who have spent their lives within the realm of palpable matter to have the courage to participate in a meeting among researchers on the soul, including psychopathologists, theologians, and innovators from the initiative on the Quantum Paradigms of Psychopathology.

The pathologist examining a corpse and the physician investigating a diseased patient, do not ask where the soul is but instead are interested in the impact of the disease on the soul and how much the soul helped in reducing the affliction generated by the pain. Beyond the effectiveness of more advanced innovations in diagnosis, treatment, and prevention of the most severe pathologies, a decisive role in the outcome of the disease is played by the synergistic commitment of the patient together with his or her physician, a role where the souls of both partners are essential.

Before raising questions about the distance between matter and the soul, a short survey of chronic non-communicable diseases (NCD), e. g. cardiovascular disease, diabetes, cancer, chronic respiratory disease, rheumatic diseases, and tumours, might be of help. Currently a proposal is being entertained to expand NCD to include central nervous system disorders (CND).

NCD are responsible for more than 35 million deaths per year globally, 80% of which occur in low middle income countries (LMIC). The economic burden of cardio-cerebrovascular diseases in the EU is € 200 billion in direct and indirect costs, and CNSD require than € 300 billion to cover annually their direct and indirect costs.

The value of the pharmaceutical market relevant to the treatment of eleven CNSD, including Alzheimer's disease, multiple sclerosis, Parkinson's disease, diabetic neuropathy, major depressive disorder, bipolar disorder, schizophrenia, insomnia, epilepsy, attention deficit hyperactivity disorder, and migraine, totaled $53.1 billion in 2010, having grown from $36.8 billion in 2002.

With the imperative "Stop the global epidemic of noncommunicable disease," the WHO launched its strategic 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Non-Communicable Diseases, drawn up by the Secretariat as requested by the Health Assembly in resolution WHA60.23. During last September's session of the UN general assembly in New York, the WHO, in accordance with the General Assembly's unanimous decision was congratulated by the

World Heart Federation, International Diabetes Federation, International Union Against Cancer, and the International Union Against Tuberculosis and Lung Disease; other international scientific institutions joined the alliance afterwards. An NCD Summit raised the profile of NCDs on the global stage, mobilized the international community to take action, secured the commitment of heads of state to lead the intergovernmental effort necessary to reverse the epidemic, and sent a clear message to donors and funders. Extensive consultations will be required to define the key tasks of the NCD community and ensure that the meeting produces concrete outcomes. Further research will be required in order to estimate the costs of national interventions needed to successfully address NCDs in LMCs. It will also be critical to ensure that NCD interventions contribute to the strengthening of health systems within the context of a horizontal rather than a vertical funding approach.

Questions: How much participation of the experts on psychopathology was there in the abovementioned alliances? How much of the probable but not yet finalized budget will be allocated to support studies on ways of combining matter and soul as an approach to the huge number of people suffering from NCD?

Are ongoing proposals to treat NCD moving away froma silo approach toward a common effort by allied stakeholders? Countries should combine efforts to fight NCD as an undivided global epidemic, and comparable efforts should be solicited toward better understanding pathogenetic mechanisms common to the abovementioned diseases and toward developing efficient approaches to their diagnosis, treatment and prevention. As time goes on, scientists are realizing that these diseases have many pathogenetic mechanisms in common, and their common genetic and environmental antecedents suggest that they spring from a "common soil." *(Diabetes 1995; 44 (4):369-74 – Pathophysiol Haemost Thromb 2003; 33 (Suppl 2): 1-Thrombosis Research 2010; 125 (Suppl 2): S92-S95)*

Questions: how much is known about metabolic dysfunction in CNS disorders such as Alzheimer's disease (AD) and vascular dementia or Depression?

There is an increasing number of studies focused on the relationship between dementia and metabolic disturbances like diabetes, obesity, hypertension and dyslipidemia. Careful attention to measurement and characterization of the insulin resistance syndrome is expected provide better answers to questions about pathogenetic mechanisms entailed by those disorders in midlife and to improve diagnostic and clinical approaches to the Alzheimer's and vascular disease patients *(Arch Neurol 2009; 66 (33): 300-305)*. Diet-induced metabolic disturbances independent of diabetes are associated with decreased expression of genes involved in oxidative phosphorylation and decreased expression of genes involved in mitochondrial biogenesis (*Circ Res 2007; 100: 795-806)*. Other studies report reduced mitochondrial biogenesis in response to a high fat diet and also during diabetes with pronounced effects on mitochondrial functions essential to brain homeostasis. Consequently questions have been raised concerning deleterious changes induced by improper diet in mitochondrial homeostasis within the again brain or during age-related neurodegeneration *(Clin Interv Aging 2007; 2: 347-359)*. The fact that in the pre-diabetic state the effects of a western diet are partially or even fully reversible increase the necessity for better understanding the role of diet and daily food choice in the genesis of brain disease *(Biochim Biophys Acta 2009; 1792 (5): 417-422)*. Several lines of evidence show that mitochondria-derived reactive oxygen species (ROS) result in enhanced amyloidogenic-amyloid precursor protein processing, and that ß amyloid (Aß) itself leads to mitochondrial dysfunction and increased ROS levels (*Antioxid Redox Signal 2012 Jun 15;16(12):1421-33. Epub 2012 Feb 28.)*.

Oxidative stress and Aß worsen the imbalance between fission and fusion dynamics in mitochondria within vulnerable neurons, enhancing ROS production, redistributing mitochondria in the cell body, and decreasing the number of mitochondria in such remote areas as axons and dendrites. This could cause mitochondrial dysfunction, neuronal dysfunction, synaptic dysfunction, and eventually neurodegeneration (*J Neurochem. 2009 May; 109(Suppl 1): 153–159*). In Alzheimer disease, Parkinson's disease and forms of motor neuron disease,

autophagic machinery and signaling pathways that regulate induction of autophagy are modified. The possibility of metabolic manipulation for the therapeutic benefit of patients with neurodegenerative disorders is considered. (*Nat Rev Neurol. 2011 Dec 20;8(2):108-17)*

Regarding depression, identification of associated metabolic disorders or links with inflammation will require more studies. Improved knowledge about inflammation and the complex relations between action and reaction within naive and mature immune systems is also needed with reference to mental disorders. Depression seems to be more robustly related to inflammation in hostile individuals, and there is a stronger correlation among women than among men *(Psychosom Med 2010; 72: 333–339)*.

Questions: what about metabolic reactions and exposomes?

The risks for developing chronic diseases are attributed to both genetic and environmental factors *(NEJM 2000; 343: 78-85; Proc Natl Acad Sci USA 2009; 106: 9362-5; Science 2002; 296: 695-8)*. Attention to the genome is increasing, and a more comprehensive and quantitative examination of environmental exposure is needed to better determine the major causes of chronic diseases. To understand toxic deleterious effects of the environment, it is advisable to study the actions of chemicals in altering critical molecules, cells, and physiological processes within the body. Thus, it would be apt to consider as the "environment" the body's internal chemical milieu and as "exposures" the concentrations of biologically active chemicals in this internal environment *(Science 2010; 330:460-461)*. Exposures are not just chemicals entering ithe body from air, water, or food but also include chemicals degenerated by metabolic reactions to external influences by way of inflammation, oxidative stress, lipid peroxidation, infections, changes in gut flora, etc. *(Clin Chem 2006; 52: 601-23; Chem Res Toxicol 2008; 21: 117-28. Science 2010; 330: 1768-73)*. The term *exposome* subsumes the internal and external environments plus exposures. The *exposome* is continually modulated during the course of a lifetime, because of internal and external changes and influences such *as* aging, life style, nutrition, physical exercise, jobs, stress, psychosocial factors, indoor and outdoor pollution, and pre-existing diseases *(Science 2010; 330:460-461)*. To investigate diseases, exposomewide *association studies (EWAS)* are desirable alongside the recently established approach known as *genomewide association studies (GWAS) (Science 2010; 330: 1768-73)*.

Summary

It should not be surprising to observe a central role for metabolic processes and the integration of metabolic pathways with many diverse signal transduction pathways in NCD. It also should not to be surprising to uncover common mechanisms and common soil in the development of diseases that at first may seem clinically to be mutually independent. A better understanding of the metabolic pathways shared by the abovementioned diseases might enhance support for a global approach to their prevention and treatment.

Questions: how much can combined studies on matter and the soul help to better manage NCD patients? How much can psychopathologists can help somatic physicians reduce afflictions of the soul?

22. QUANTITATIVE PSYCHIATRY: ROLE OF COMPARTMENTALIZED G PROTEIN SIGNALING IN DIAGNOSTICS AND THERAPEUTICS FOR DEPRESSION

Mark M. Rasenick
Distinguished UIC Professor of Physiology & Biophysics and Psychiatry, Director, Biomedical Neuroscience Training Program, U. Illinois Chicago College of Medicine. Dr. Rasenick's responsibilities have been primarily to conduct research on G protein signaling and the cytoskeleton and to probe their relationship to neurodegenerative disorders, mood disorders and the normal function of the human brain. He has been continually funded by the National Institute of Mental Health since his arrival at UIC and has also been funded by the National Institute on Aging, the Air Force Office of Scientific Research, and various corporate and philanthropic sources.

[1]Andrew Czysz, [1]Jeffery Schappi, [1]Alexander Jackson, [1]Sabina Buciarelli, [2]Raimondo Venanzini, [2]Raffaella Silvestri, [3]Anna Rita Mastrogiacomo, [4]Franco Canestrari, [5]Lucio Tonello, [5]Massimo Cocchi and [1]Mark M. Rasenick

[1]Dept. of Physiology & Biophysics, Dept of Psychiatry U. Illinois Chicago, Chicago IL 60612, Jesse Brown VA Medical Center, Chicago. [2]D.S.M. ASUR Fano. [3]Centro di Biotecnologie, Università degli Studi di Urbino "Carlo Bo", Sede di Fano (Italy). [4]Dipartimento di Scienze Biomolecolari, Università degli Studi di Urbino "Carlo Bo". [5]"Paolo Sotgiu" Institute for research in Quantitative & Quantum Psychiatry & Cardiology, L.U.de.S. University, Lugano, Switzerland.

Abstract

Lipid rafts are specialized membrane domains, rich in cholesterol and intimately associated with cytoskeletal components. G protein signaling is influenced by these domains, but, depending upon the receptor, G protein and effector enzyme, they act either to facilitate or to attenuate signaling. We demonstrate that, for Gs and Gs-coupled receptors (β adrenergic, VPAC and 5HT 4, 6, 7), lipid rafts attenuate signaling by separating Gsα from adenylyl cyclase. Data obtained in cells treated with cholesterol chelating agents or in which the lipid-raft protein caveolin is knocked down demonstrate this. Furthermore, caveolin knockout mice show a similar effect. Activated Gsα is internalized in lipid raft vesicles, but release of Gsα from those vesicles increases microtubule dynamics and this leads to increased neurite outgrowth and increased formation of dendritic spines in primary neurons.

Several lines of investigations from several laboratories suggest a post-synaptic effect of chronic antidepressants and a possible postsynaptic target for these drugs. Data from rats, cultured neural and glial cells and tissue from brain of depressed subjects all suggest the localization of the G protein, Gsα, in lipid rafts is modified by chronic treatment with a number of antidepressant compounds (SSRI, MAOI and tricyclic). In this study, we sought to establish whether platelet localization of Gsα could prove diagnostic for depression and whether clinical response might be prognosticated as a result of a rapid, antidepressant-induced shift in the lipid raft localization of Gsα. Blood was drawn from normal volunteers or patients at the Dept. of Mental Health (ASUR Fano, Italy). Raft association of Gsα was determined by detergent extraction and cell fractionation as was the case with post-mortem tissue; the association of Gsa with lipid rafts in platelets from depressed subjects was clearly differentiated from both control and bipolar subjects. Most of those treated with antidepressants did not respond, and the Gsα distribution was consistent with these subjects remaining depressed.

Thus, it appears that the decreased Gsα/cAMP signaling seen in depression is due, at least in part, to sequestration of Gsα in lipid rafts. This may provide a simple biomarker.

23. THE DISSIPATIVE QUANTUM MODEL OF BRAIN

Giuseppe Vitiello

Dipartimento di Fisica "E.R.Caianiello", Universita' di Salerno, 84100 Salerno, Italia. Giuseppe Vitiello is Professor of Theoretical Physics at the University of Salerno, Department of Physics and Istituto Nazionale di Fisica Nucleare (INFN). His research activity is focused on elementary particle physics and the physics of living matter and the brain. He is the author of about 140 research papers, of many reports to International Conferences, and of the following books: *Quantum Mechanics*, co-authored with H. Umezawa (Bibliopolis, Napoli 1985 and, translated in Japanese, Nippon Hyoron Sha. Co.Ltd., Tokyo, Japan 2005); *My Double Unveiled* (John Benjamins Publ. Co., Amsterdam 2001); and *Quantum Field Theory and Its Macroscopic Manifestations,* co-authored with Massimo Blasone and Petr Jizba (Imperial College Press, London 2011). Together with Gordon Globus and Karl Pribram, he is editor of the book *Brain and Being. At the Boundary Between Science, Philosophy, Language and Arts.* (John Benjamins Publ. Co., Amsterdam, 2004).
vitiello@sa.infn.it

Abstract

Imaging of scalp potentials and cortical surface potentials of animals and humans from high-density electrode arrays has demonstrated the dynamical formation of patterns of synchronized neocortical oscillations in the beta and gamma ranges. They re-synchronize in frames at frame rates in the theta and alpha ranges and extend over spatial domains covering much of the hemisphere in rabbits and cats and over linear size domains of about 19 cm in human cortex with near zero phase dispersion [1].

By resorting to the dissipative quantum model of brain [2,3], I describe [4] the field of activity of an immense number of synaptically interactive cortical neurons as the

phenomenological manifestation of underlying dissipative many-body dynamics such as the one responsible for the formation of ordered patterns and phase transitions in condensed matter physics in quantum field theory. I stress that neurons and other brain cells are by no means considered quantum objects in our analysis.

The dissipative model explains two main features of the electroencephalographic data: the textured patterns correlated with categories of conditioned stimuli, *i.e.,* the coexistence of physically distinct synchronized patterns, and their remarkably rapid progression into irreversible sequences resembling cinematographic frames. Each spatial pattern is deemed to result from spontaneous breakdown of symmetry triggered by an external stimulus and is associated with one of the unitarily inequivalent ground states. Their sequencing is associated with non-unitary time evolution in the dissipative model. The dissipative model also explains the change of scale from microscopic quantum dynamics to the macroscopic order parameter field and the classical character of trajectories in the brain state space. Moreover, by drawing upon recent results relating fractal self-similarity with coherent state structure, the dissipative model also accounts [5] for the self-similarity and scale-free dynamical properties of brains observed in the laboratory [1,6,7].

The dissipative quantum model enables an orderly description that includes all levels of the microscopic, mesoscopic, and macroscopic organization of the cerebral patterns. By repeated trial and error each brain constructs within itself an understanding of its surroundings, the knowledge of its own world that we describe as its *double* [3]. The relations that the self and its surroundings construct through their interactions constitute the *meanings* of flows of information exchanged during the interactions. I comment on the perception-action arc in light of the dissipative model and Merleau-Ponty's phenomenology of perception.

References

[1] W. J. Freeman, Origin, structure, and role of background EEG activity. Part 1 & 2, *Clin. Neurophysiol.* Vol. 115, 2077 & 2089 (2004); Part 3 Vol. 116, 1118 (2005) ; Part 4. Vol.117, 572 (2006).
[2] G. Vitiello, Dissipation and memory capacity in the quantum brain model, *Int. J. Mod. Phys.* B 9, 973 (1995). quant-ph/9502006.
[3] G. Vitiello, *My Double Unveiled.* Amsterdam: John Benjamins, 2001.
[4] W. J. Freeman and G. Vitiello, Nonlinear brain dynamics as macroscopic manifestation of underlying many-body dynamics, *Phys. of Life Reviews* 3, 93 (2006), q-bio.OT/0511037.
W. J. Freeman and G. Vitiello, Brain dynamics, dissipation and spontaneous breakdown of symmetry, J.Phys. A: Math. Theor. 41, 304042 (2008), q-bio.NC/0701053v1
[5] G. Vitiello, Coherent states, Fractals and brain waves, New Mathematics and Natural Computation 5, 245-264 (2009)
[6] W. J. Freeman and J. Zhai, Cogn. Neurodyn. 3 (1), 97 (2009).
[7] E. D. Gireesh and D. Plenz, PNAS 105, 7576 (2008).