Chapter 3

The Molecular and Quantum Approach to Psychopathology and Consciousness — From Theory to Experimental Practice

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Additional information is available at the end of the chapter

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> *With the idol of certainty […] there falls one of the defences of obscurantism […] for the worship of this idol hampers not only the boldness of the questions, but also the rigor and the integrity of our tests. The wrong view of science betrays itself in the craving to be right; for it is not its possession of knowledge […] that makes the man of science, but its persistent and recklessly critical quest for truth.*(K.R.Popper, *The Logic of Scientific Discovery*, engl. tr. Hutchinson, London 1959)

1. Introduction

This decade has clocked the review of the new DSM, the fifth in the series, the instrument considered the "bible" of psychiatry worldwide.

The document, which is accomplished today, appears firmly rooted in traditional conservative psychiatry ignoring the progress made by the biological research field. Clearly, the dichotomy between conservative and progressive psychiatry is not over, despite the efforts of the scientific research in the field of psychiatry, of brain, of neurotransmitters and of quantum computation of the brain and consciousness, i.e., the disciplines that belong to neuroscience. It seems correct, from the point of view of ethics, remember how it is difficult to think of the research in psychiatry as completely independent of influential external factors (kuhnian paradigms).

Recently some major events have allowed a movement of thought not only innovative, but of profound and insistent criticism, mainly at a high intellectual and scientific level, on the

ideological implications of psychiatric diagnosis and of the increasing complexity of the nuances that classify the psychiatric disorder, rather than looking at a window that allows, through biological markers, a reliable diagnosis and appropriate care in the first diagnostic instance by limiting the diagnostic error unaware that psychiatric diagnosis has dragged on for years about the recognition of bipolar disorder from major depressive disorder [1] where there is a diagnostic misinterpretation ranging from 40% [1] to 70% (Tenth World Day for the Prevention of Suicide, Rome, 2012).

The fifth edition has been criticized by a number of authorities, even before it was formally published. The main thrust of criticism has been that changes in the DSM have not kept pace with advances in scientific understanding of psychiatric dysfunction. Another criticism is that the development of DSM-5 was unduly influenced by input from the psychiatric drug industry. A number of scientists have objected that the DSM forces clinicians to make distinctions that are not supported by solid evidence, distinctions that have major treatment implications, including drug prescriptions and the availability of health insurance coverage.

2. Retrospective research on humans and animals

In the first experimental phase two mathematical tools were identified, one complex (the Self-Organizing Map-SOM) and a simple one (the Index B2) which in time will prove valuable not only to define the condition of the Major Depression and Bipolar Disorder, but will provide the possibility of reasonable inferences about the biological significance of the two molecular mood disorders.

The SOM is an artificial neural network that has the ability to put together similar objects and distant different objects using the characteristics of the objects considered.

The index B2 (so named by the authors of the research, (namely, Cocchi and Tonello) is derived from a mathematical operation that relates the characteristics of molecular weight and melting point of the fatty acids isolated and recognized, by the SOM, to have the power of recognizing the two disorders.

Proceeding by grades we will say that the two groups of subjects investigated in the first phase of the research (apparently normal and depressed) were determined by the fatty acids of platelets, having chosen this cell type for the morphological and functional particularities that distinguish these cells, i.e., the presence of receptors for neurotransmitters, particularly serotonin, and because they are also the seat of the molecular events that regulate the hemocoagulation process.

The results obtained experimentally, interpreted by the non-linear mathematical function, the SOM, and the index B2 showed the ability to distinguish "psychiatric" patients from "normal" ones. The problem was that the psychiatric diagnosis we had received was generally expressed as Major Depression, while the arrangement of subjects within the framework resulting from

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the SOM and the index B2 induced us to think that some aspect was unclear about the diagnosis that we had received.

Placement in the SOM and the evaluation indexes B2 (negative and positive) led us to look for an opportunity to relaunch the experiment that, as we thought, might be able to recognize the apparently normal individuals from major depressive and bipolar.

The opportunity came with a grant from the Marche Region, and in two years of intense work, including the contributions of psychiatrists, biochemists, molecular biologists, mathematicians and quantum physicists. A research that has used a combination of biology and nonlinear mathematics was carried out, in order to identify, within the psychiatric chapter of mood disorders, whether it was possible to identify in the platelets, and in particular in their fatty acids, molecular features that could allow a clear and precise classification of subjects with Major Depression (MD) and with Bipolar Disorder (BD). The results were obtained using an Artificial Neural Network, in particular a network called Self-Organizing Map (SOM) [2, 3]. The SOM is an unsupervised competitive-learning network algorithm, which was created by Teuvo Kohonen in 1981–82 [4-6].

With the above combination, using platelet's Palmitic Acid, Linoleic Acid, and Arachidonic Acid together with SOM and a mathematic index (B2), it was possible to obtain the effect of discriminating between MD and BD, for the first time in years. The B2 index was obtained from the summation of the percentages of each fatty acid multiplied by its melting point and divided by its molecular weight, obtaining an indirect expression of membrane viscosity, which induces us to identify it with the neuron membrane viscosity [7]. The B2 index is found to be negative in MD and positive in BD, that is the membranes in MD are, by far, less viscous than in normals, in BD, in psychotics, showing a unique and specific molecular characteristic for subjects with MD [8]. On these bases it was possible to explain the quantitative biomolecular approach to major depression and hypothesize that in mood disorders a biomolecular pathway exists, moving from cell membrane viscosity through G*sα* protein and Tubulin [9]. We got the result so desired and hoped to confirm that the guess was correct, the depressed subjects were distinguished from bipolar, beyond all psychiatric, classificatory and interpretative dialectics. Figures 1, 2, 3, 4, 5 summarize the main steps of the research. In front of the results, we began to reflect on the distribution and on the logic of the numbers that had been so intimately associated with psychiatric conditions, as they represented a fact which did not take into account therapies and nothing that from the outside could be related to subject. All this led us to think that there was something already written in platelets that can simulate the condition of the neuron, at least, as regards the levels of serotonin. On this observation we wrote some articles that related to the uniqueness of the molecular Major Depression, the role of membrane viscosity and molecular reflections on the state of consciousness and the mechanical strength of the membrane.

During the last experiment [10] the psychiatrists have provided us with eight cases of "Suicidal Ideation".

When we have classified them over the SOM, the Figure 6 was obtained.

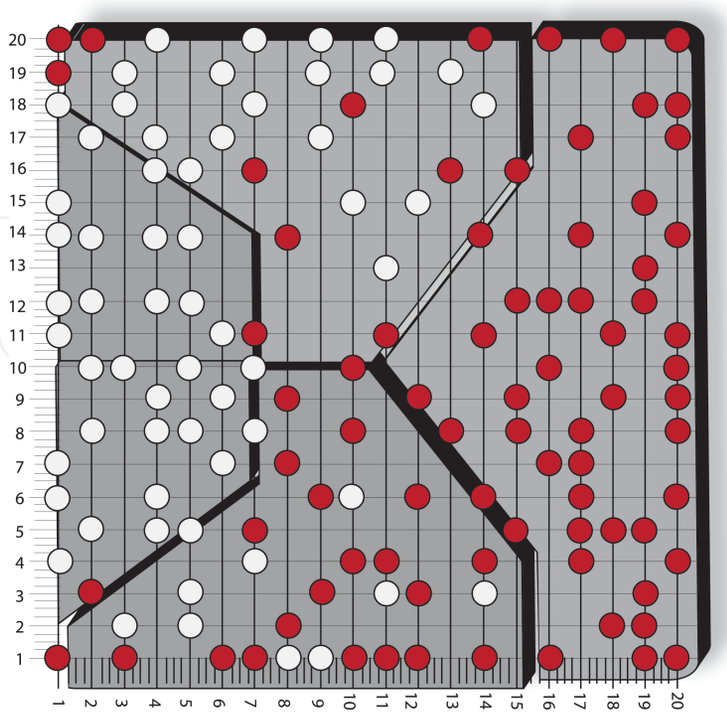

Figure 1. Distribution of all cases [apparently Normal (white) and Pathologic (red) over the SOM obtained by Platelets' Palmitic Acid (PA), Linoleic Acid (LA) and Arachidonic Acid (AA).

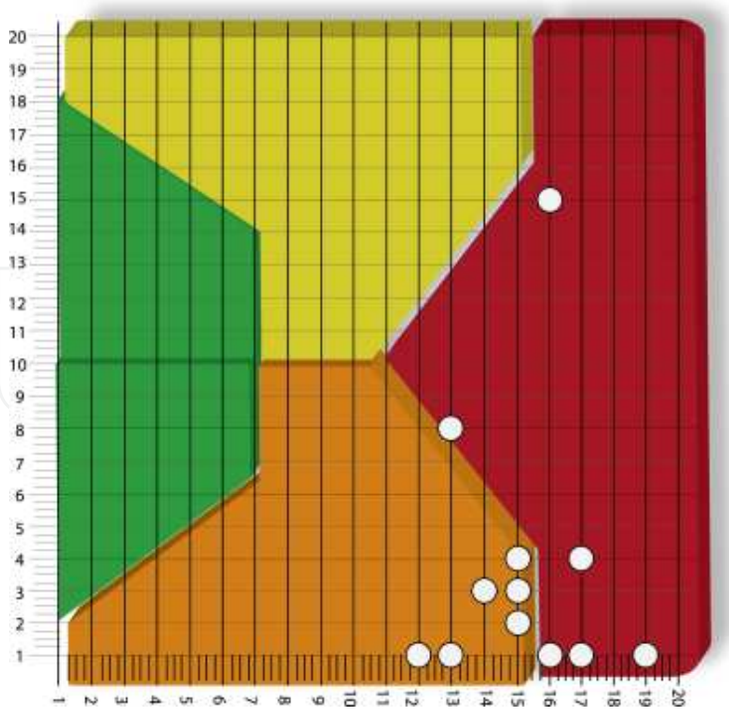

Figure 2. shows the pathologic subjects Major Depression and Bipolar Disorder) all together.

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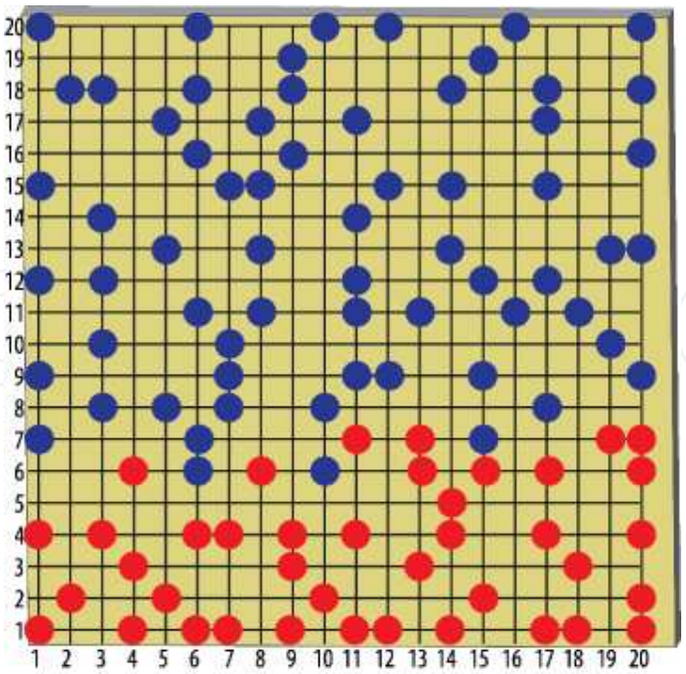

Figure 3. (a new SOM has been realized) shows, clearly, that it was possible to distinguish the subjects with Major Depression (red) from those one with Bipolar Disorder (blue).

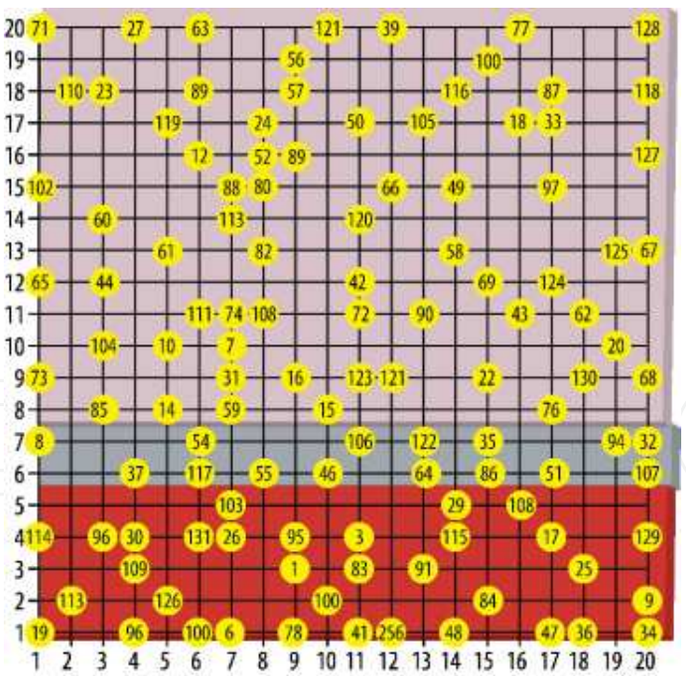

Figure 4. shows the same picture of figure 3 pointing out an intermediate area which collects both cases (Major Depression and Bipolar Disorder). For each subject we have calculated an Index called B2, We have obtained the B2 Index by the sum of the percentages of each fatty acids (AA, LA and PA), multiplied for the melting point and divided for the molecular weight. B2 is negative for subjects with Major Depression, positive for subjects with Bipolar Disorder. In this way it is possible to recognize also the cases that are within a very close range as showed in Figure 5.

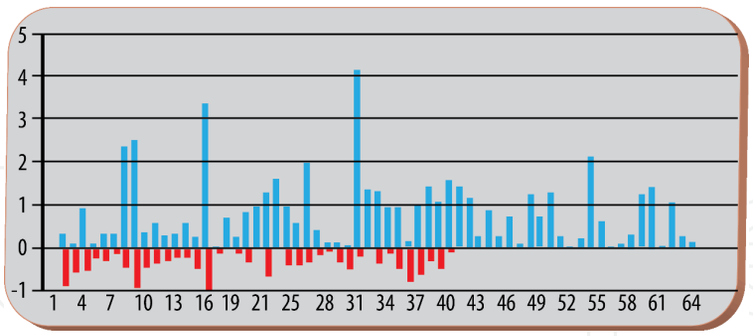

Figure 5. In Figure 5 is represented the classification of the subjects with Major Depression (B2 negative-red) and Bipolar Disorder (B2 positive-blue). As can be seen, the cases, also within a very close range, are clearly distinguishable. The combination of the SOM and of the B2 index is able to perform the right diagnosis [10].

The cases were collected where the SOM recognizes the minimum of Linoleic Acid. In particular seven cases were Bipolar and one with Major Depression, confirming that both can have suicidal ideation and can attempt suicide [10]. The subject, in position 15:4, was uncertain at the psychiatric evaluation; in effect his position is a little bit out from the critical area of the minimum of Linoleic Acid. In the same way, other areas has been found within the SOM (fig. 7): Obsessive Compulsive Disorder (OCD) area, Major Depression area, Bipolar area (the largest), Psychotic area etc.

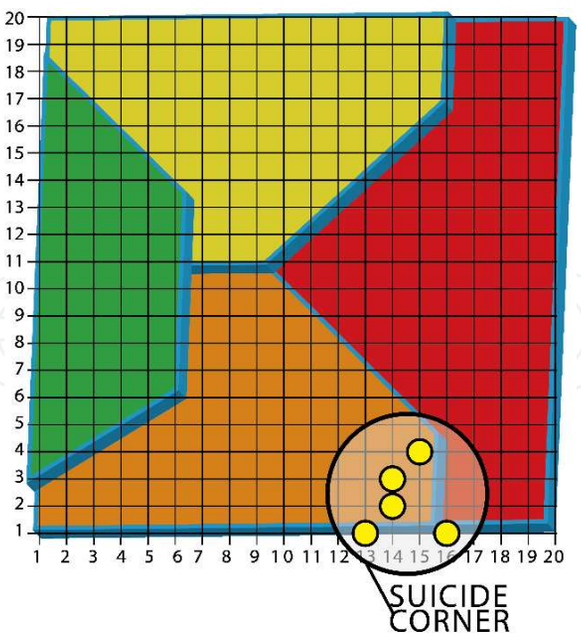

Figure 6. Distribution of the "suicidal" cases over the SOM.

All the experimental findings in humans and animals are resumed in Figures 7 and 8.

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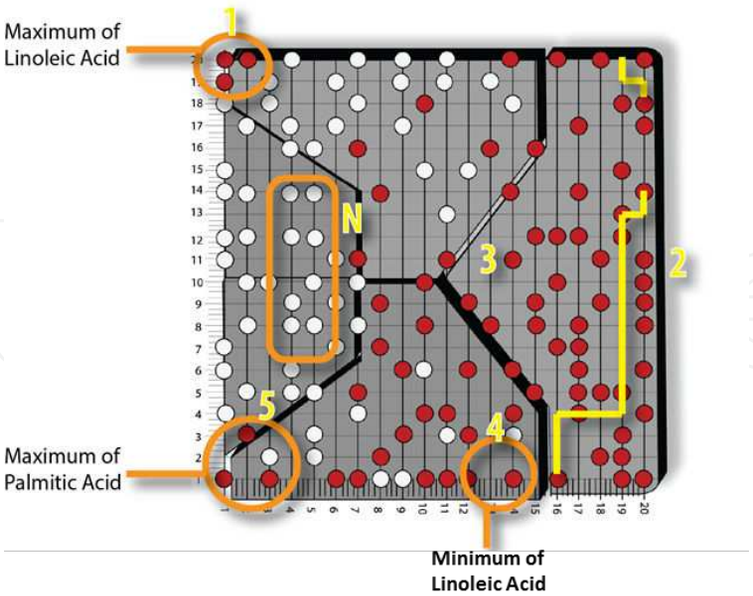

Figure 7. Distribution over the SOM of human subjects and animals. According to the psychiatric diagnosis (when definitive) we can recognize: 1= OCD area, 2= Major Depression area, 3= Bipolar area (the largest), 4= Suicide area, 5= Psychotic area, N= apparently normal area. N area collects about the 50% of the sample of subjects considered apparently normal.

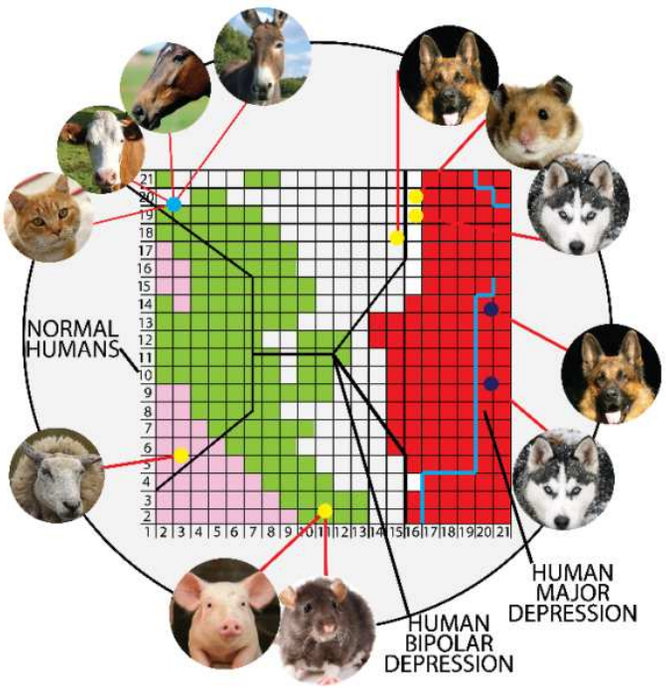

Figure 8. Distribution over the SOM of human subjects and animals. According to the psychiatric diagnosis (when definitive) we can recognize: 1= OCD area, 2= Major Depression area, 3= Bipolar area (the largest), 4= Suicide area, 5= Psychotic area, N= apparently normal area. N area collects about the 50% of the sample of subjects considered apparently normal.

Several different animals have been mapped on the SOM, as well. The molecular similarities [11], observed between animal and man (Figure 8), concern the conditions of Major Depression, Bipolar Disorder, Obsessive Compulsive Disorder (OCD).

To confirm the molecular correspondence between man and animal, observe how, e.g. Cat, Bovine, Horse and Donkey, correspond to the area of maximum Linoleic Acid and of Obsessive Compulsive Disorder.

This area is recognized as the point of maximum concentration of Linoleic not only for diagnostics correspondence, but also because it contains the cat, who, as feline, is known to possess desaturase, but with low activity [12], therefore not to be able to transform Linoleic Acid into Arachidonic Acid, resulting in savings of Linoleic, and long living animals [13]. Further, in the same animals, symptoms of OCD can occur [14, 15]. **See Appendix (Linoleic acid secrets)**.

3. On the non-manipulability of the SOM built for the classification of the psychiatric subjects

Let's suppose we want to build a fake SOM, that is, a SOM driven by us according to a desired result. We should be very lucky, in fact we should guess:

1200 particular numbers (starting weights). By the way, really, it is impossible to know how they could be chosen in order to obtain a particular result.

Above all, we should find a particular order of data that, because of an unknown reason (really unknown), lead to a very particular result. In our case, we have a data base of 144 Subjects (84 depressive and 60 normal). This means that there are 144!=5.5503*10249 combinations. A training process takes about 4 minutes. So, we need about 4.224*10242 centuries to check all possible results thus taking a particular one. A bit difficult.

So, if we want to build a fake SOM, well, it's almost impossible (at least in a reasonable time even using the fastest computer on Earth).

The SOM (Figure 1) shows that major depressive subjects belong to an area which is completely disconnected from that of healthy and bipolar. Looking at the location of the data over the SOM, we find also a region (extreme left corner) which we attribute to psychotic subjects according to the clinical diagnosis. We translated these facts in terms of symmetry breaking [16), confirming that MD is a disease completely trapped apart from healthy, bipolar, psychotic subjects and patients with obsessive compulsive disorder (OCD) (Figure 9).

"What is opposition is reconciled, and by different things the more beautiful harmony is created, and everything is generated by the contrast."

Heraclitus

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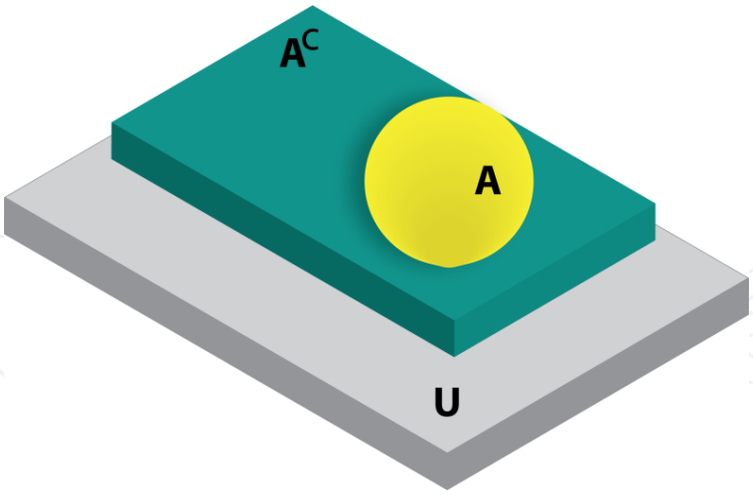

Figure 9. Bipartition of U. U is the Universal set representing humankind. A is the cell whose elements are characterized by a positive value of B2. A^C, which is the complement of A in U, is the cell whose elements are characterized by a negative value of B2. B2 is the index who put in relation the three fatty acids, isolated by the SOM, with the molecular weight and the melting point and that has recognized the Bipolar subjects (B2 positive) from the Major Depressive subjects (B2 negative).

4. Facts and perspectives on quantum neuron molecular research

The Quantum Paradigm Psychopathology Group (QPP) conference in Palermo (26-27 of April, 2013) has marked a definite turning point in the foundational perspective of many of the group's participants regarding the study of psychopathology, particularly mood disorders. One reason for this turning point stems from a realization that two of the most common forms of psychopathology, major depression and bipolar disorder, may be recognizable through bimolecular markers (**see Appendix: from biology to the anthropology of treatment**). Long years of theoretical study – out of the conviction that one should not be, using Feyerabend's words, "thought officer and concept manager", but rather, as Lakatos claims, good creator of theoretical frameworks able of acting "faster than the records of facts that must be collected in them"-by independent investigators have finally culminated in a convergence of their insights though quantum paradigms that now promise to illuminate, through the empirically tangible route of such new bio molecular markers, pathological phenomena of the conscious brain, thus potentially both factually confirming and further harmonizing the diverse prior contributions of these conceptually innovative psychiatrists, biochemists, molecular biologists, philosophers and theologians.

The idea, as stressed during the Conference in Palermo, was to take into consideration consciousness processes, together with their normal and pathological dynamics, without fixating on isolated elements and levels that can be observed by a privileged and detached observer, but rather by thinking and acting effectively through connections, relations, and networks. And all of this, always in the belief that science is the narration of a world that

expresses emerging states, and is therefore never reducible to a simple sum of basics ingredients, where spontaneous symmetry breakings ensure multiplicity, creativity, vitality, in compliance with the concept of natural self-organization and systems evolution, towards growing complex and unpredictable states.

The socio-economic significance of this procedure is undeniable: science takes shape into social and economic structures which, by accepting the transformation from foucaultian monitoring and control instruments (ideological reductionism) into open, fluid, emerging systems (complexity or open logics), could really, when considering mental diseases, understand the often blurred classifications of the DSM and open up to the important connections between consciousness and quantum brain dynamics.

Hence the rejection of any form of ontological reductionism, which is self-referring, linked to metaphysical-ideological cognitive dynamics, and tied to a pervasive will to power which sees research freedom as a worrying system breakdown.

Against this epistemological backdrop, among the foundational innovators we can mention those who have left particularly fertile footprints in terms of basic quantum theories linking brain, behaviour, and consciousness.

Quantum Mind has been an ongoing field of study since the final decades of the last century. Pioneers like the physicists Hiroomi Umezawa, Kunio Yasue, and Giuseppe Vitiello, mathematicians like Roger Penrose, and biomedical investigators like Stuart Hameroff, Gordon Globus, and Gustav Bernroider have plumbed the depths of subatomic structure and its macroscopic amplifications in search of substrates for quantum computation and other capabilities that may match attributes of the normal human psyche better than models advocated by conventional cognitive neuroscience.

In the domain of psychopathology, Gordon Globus has gone on to propound a highly original concept of schizophrenia linked to the “tuning” of quantum vibrations suffusing the brain. Nancy Woolf, along with co-authors including Jack Tuszynski, has offered credible links between psychopathology and quantum-computational dysfunction within the skeletal proteins giving shape to brain cells. Paavo Pylkkanen has related the physical substrates of mental illness to quantum “pilot waves.” Donald Mender has proposed ways of comprehending the neurophysiology of disordered thinking and emotion in terms of quantum "phase transitional" analogies to the freezing and melting of ordinary matter; he has also contributed to a reframing of psychiatric disease nosology in light of the anthropic principle. Ursula Werneke has complimented this anthropic reconsideration through her examination of psychotically “impaired” reality-testing in the context of Hugh Everett’s many-worlds ontology. Massimo Cocchi, Lucio Tonello, Fabio Gabrielli, have forged links between serotonin and quantum phenomena via membrane biophysics in depression and psychosis.

The above honor roll of seminal QPP theoreticians is surely not exhaustive, but these brief remarks are not intended as a complete historical review. Rather, the purpose is an opening into the possibility of turning today’s theoretical potentialities into experimental confirmed

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reality. It should be recalled and emphasized as a guiding principle that the cohesion of a convivial multidisciplinary group operating without the winnowing constraints of competing, mutually exclusive ideas may not remain true to the epistemic rigors of science. QPP can minimize this sort of hazard by maximizing, in the spirit of Karl Popper, exposure of its most cherished conjectures to a fair risk of experimental refutation.

A number of participants in the Palermo conference have signed a document, aptly called "The Declaration of Palermo," whose conclusion asserts:

> *"Even the absence of highly complex synaptic connections among neurons does not preclude the presence of at least rudimentary phenomenal experience in organisms endowed with superposed micro tubular dimers, ordered water, membrane ion channels, and/or crucial lipid raft assemblies connected to selected second messenger systems. In addition, quantum-biophysical aspects of these and/or other yet undiscovered structures and related processes may prove to be potent factors in the deeper etiologies and improved treatments of psychiatric disorders."*
>
> The Declaration of Palermo was written by Donald Mender and Massimo Cocchi and edited by: Don Michele Aramini, Gustav Bernroider, Francesco Cappello, Fabio Gabrielli, Gordon Globus, Mansoor Malik, Efstratios Manousakis, Kary Mullis, Eliano Pessa, Massimo Pregnolato, Paavo Pylkkänen, Mark M. Rasenick, Lucio Tonello, Jack Tuszynski, Giuseppe Vitiello, Ursula Werneke, Paola Zizzi.

This strong theoretical statement invites an opening into possible experimental models that will test the reality of the group's hypotheses by identifying, starting from precise molecular reference points characterizing the two mood disorders mentioned above, a non-trivially quantum pathway of bio molecular changes conditioning brain processes through the most intimate aspects of neuronal, trans neuronal, and sub neuronal function. In particular, membrane viscosity and its role within the interactome may prove to figure centrally in quantum-chemical transduction of neural signals.

The Declaration of Palermo concerning the plausibility of a quantum basis for consciousness entails a lucid analysis of phenomenologies crucial to both human beings and other creatures. The main feature belonging intrinsically to both Homo sapiens and non-human animals is a common core awareness that is nevertheless expressed differently for each kind of organism at divergent levels overseeing management of disparate needs and actions, realized through behaviour in relation to concrete variations of the external environment. The dimension of "self-consciousness" is evolved, step by step, in phylogenetic progression according to an admirable order justifying the survival of each unique life form with respect to the particular tasks which it has to perform.

Today we are equipped with many high-end tools in our attempts to understand all the steps in the evolution of consciousness, but it is through intuition that we will achieve, simply, an adequate interpretation of consciousness itself, that most complex and extraordinary gift. Pending such 'intuition," some members of the QPP group have decided to submit to classical experimental testing those insights that each contributor has independently adduced through

theoretical inquiry, that is, through the construction of an empirical map laying bare the most germane trans neuronal, neuronal, and sub neuronal molecular changes with an eye toward the possibility of inducing and measuring changes in membrane viscosity correlated with in vivo manifestation of mood disorders. As far as we know this will be the first time that such micro-molecular events are to be tied rigorously to molar cognitive phenomena.

The resulting experimental data may offer an enduring empirical anchor in contradistinction to the intersubjective vagaries that have afflicted those various psychiatric disease nosologies, most recently DSM V, issuing from the hollow consensus of committees and cultural contextual fashion. If the experimental program planned by the QPP group succeeds, the goal of psychodiagnostic validity, heretofore sacrificed by DSM to mere inter-rater "reliability", may at last be achieved.

5. A working hypothesis: Quantum Neuron Molecular Mapping (Q-NeMoMa) project

5.1. Numbers and figures of the experimental background

There is full knowledge that each mood disorder will manifest with different states of consciousness [17, 18].

Our platelets results, in their correspondence with the strong diagnostic power between Bipolar Disorder and Major Depression, and in the similarity found between human and animals, give the possibility to investigate the different neuronal genetic expression, and the possible inherited errors in neurons. The working hypothesis should provide neurons, from different animal origin, which are known to have molecular characteristics similar to those of man with mood disorders. Table 1 and Figure 10 [19-24].

This could allow understanding, first, the different gene expression according to the different psychiatric disorders studied; second, culturing the neurons belonging to the different animals, it will be possible to arrange modifications of the cell membrane viscosity. In agreement with the assumption, the path described can reasonably lead to the possibility to artificially create models of membrane viscosity corresponding to changes of the psychopathological phenomenon with the ability to achieve the set of molecular evaluations necessary for the understanding of the modifications of the interactome (*the whole [array of] molecular interactions that take place in an organism and allow the cascade of regulatory molecules including the mechanism of action of enzymes and metabolic reactions)*.

The Q-NeMoMa project, practically, wants to investigate the molecular modifications of the neuron according to different modifications of the viscosity of the neuronal membrane.

Some of the most important world experts have come together to identify the experimental procedures to be carried out.

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Fatty Acids (% mean values)					
Animals	**Cases**	**Palmitic Acid**	**Linoleic Acid**	**Arachidonic Acid**	**B2 Index**
Sheep	4 pool of 3	19.91	8.22	4.73	3. 980
Bovine	4 pool of 3	18.37	26.72	6.77	2.937
Cat	4 pool of 3	17.45	27.75	9.54	2.240
Horse	4 pool of 3	14.8	23.17	6.46	2.173
Donkey	8 pool of 3	14.39	19.68	6.34	2.154
Guinea pig	Literature	17.4	12.4	14.6	1.675
Rat	Literature	24.40	9.5	20	2.567
Pig	80	26.09	8.78	14.12	3.957
German Shepherd	7	18.9	21.5	20.39	0.936
	1	15.13	20.65	22.00	-0.240
Alaskan Malamute	5	18.25	19	21.2	0.688
	1	16.7	17.89	23.93	-0.120
Humans (normal)	60	20.68	19.41	14.06	2.445
Depression 1 (MD+ BD)	84	17.92	16.71	19.03	1.002
Depression 2 (MD)	41	17.22	9.34	26.81	-0.310
Bipolar	67	19.75	8.65	23.79	0.819
Ischemia 1	50	23.32	10.51	15.17	3.072
Ischemia 2	87	19.59	4.74	12.72	2.658
Young adults	45	18.16	21	14.71	1.690
Children	59	23.23	11.82	10.77	3.746

Table 1. Average Fatty Acids and B2 index of different animals and human beings.

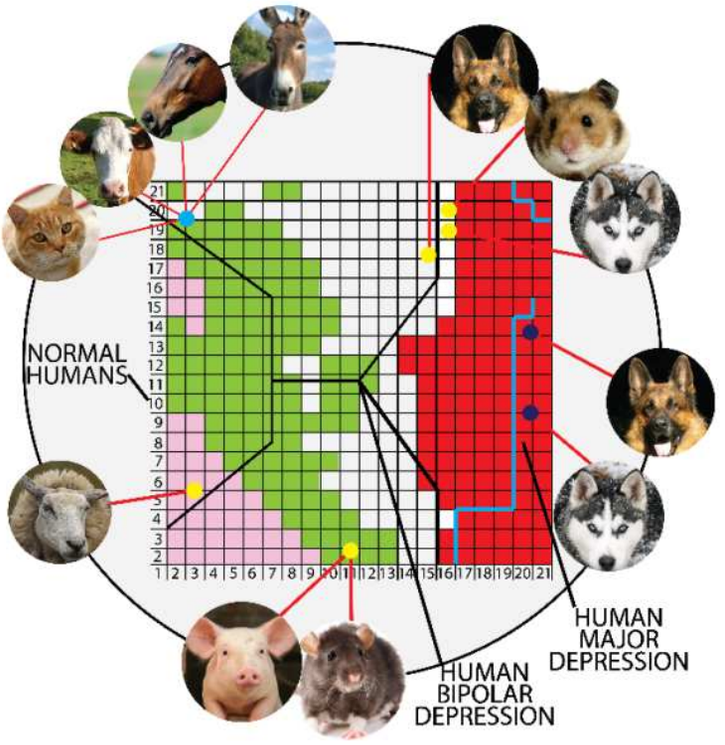

Figure 10. Distribution of animals and humans over the SOM.

From this important research will be possible to obtain data needed to assess whether, corrective actions for the improvement of the devastating conditions of all those who are suffering from mood disorders, will be possible.

A valuable help to the understanding of the neuron functioning can come from quantum molecular computation, by being able to interpret the neuron modifications, in the occurrence of the most important mood disorders such as Major Depression and Bipolar Disorder.

The suggested path could start from the largest scale: the cell membrane.

Five parallel approaches should be addressed, working one with the other, Figure 11:

1. Quantum chemical scale of neural signals by Bernroider [25, 26].
2. The Fatty Acid profile (Palmitic, Linoleic and Arachidonic Acids dynamics) of Cocchi and Tonello [2, 3, 7, 8, 9, 10, 11].
3. The role of lipid raft and G protein of Mark Rasenick [27-29].
4. Cytoskeleton modifications (Microtubules and Tubulins) studied by Tuszynski [30-33].
5. The exosomes studied by Francesco Cappello [34].

The complex dream we are running is to realize the molecular hypothesis of consciousness, designed in 2008 (private meeting in Bologna, Department of Veterinary Medical Sciences) by **Massimo Cocchi, Lucio Tonello, Mark Rasenick, Stuart Hameroff & Kary Mullis**. Figure 12.

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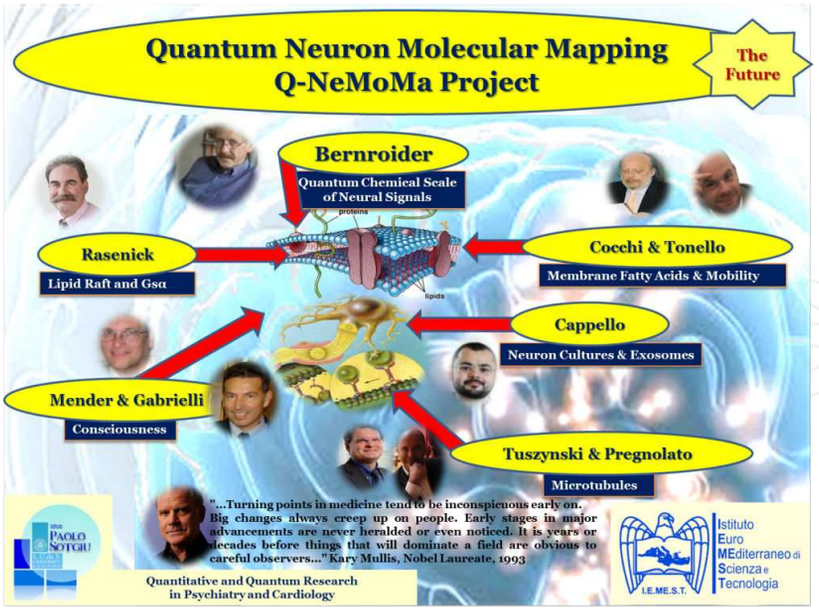

Figure 11. The steps of the project

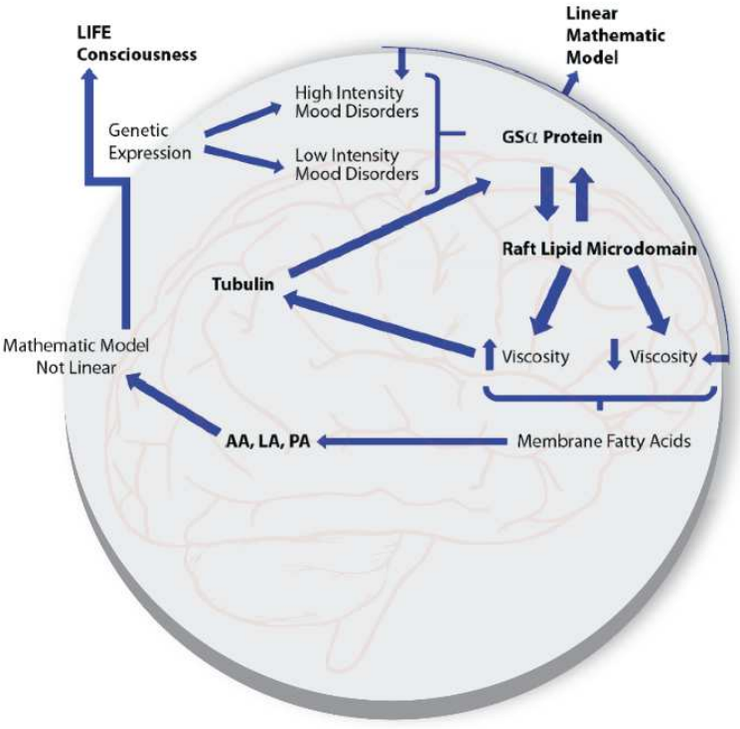

Figure 12. The consciousness molecular path

The whole path could be supervised by Gabrielli (Philosopher [8]) and Mender (Psychiatrist [35]), scientists of rigorous intellectual skills with a profound vision of the theoretical and conceptual aspects of psychopathology and quantum consciousness.

5.2. Final theoretical issues

Although there is evidence of a continuing effort by the international psychiatric community to refine the diagnosis of mood disorders, to date, the traditional diagnostic criteria are not enough sensitive in identifying patients with Bipolar Disorder (BD) from those suffering from Major Depression (MD), in the first diagnosis. Diagnosis remains mostly late and treatments, that may improve symptoms and quality of life, continue to be preceded by interventions which, in addition to not providing adequate relief, often worsen the BD course, increasing the likelihood of inducing rapid cycles or suicidal behaviour [50, 51].

Differential diagnosis of BD symptoms from other diagnoses has been documented as difficult [52-55]. Diagnosing BD from MD, psychosis, borderline personality disorders, obsessive-compulsive disorder, etc.) or neuropsychological disorders (cognitive impairment, dementia, etc.) or neuropsychological disorders, has presented challenges. Moreover, manifestations are highly variable not only from patient to patient, but also in the same subject at different stages of the clinical course and in later life.

To overcome this impasse various strategies have been identified and more sensitive and specific assessment tools have been searched for discriminating the BD condition and overcome the delay of an accurate diagnosis has been particularly difficult with MD. The BRIDGE study indicated a first way to go [56], and highlight the strength of some variables such as: mania/hypomania developing during therapy with an antidepressant or other drug, mood lability developing during antidepressant therapy, 2 or more prior mood episodes, and positive family history of mania/hypomania. 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 nonrelated psychiatric conditions are still characterised and defined by descriptive and non-biological criteria, but it is hoped that we can adequately characterise this and other psychiatric disorders with the addition of new quantitative approaches.

Cocchi and Tonello have studied platelet membranes of depressed subjects, enlisting profiles of FAs as a possible measure of the membrane status and to determine whether fatty acids could provide indications of diagnostic help between normal subjects and subjects affected by mood disorders. In the first experimental phase, two mathematical tools were identified, a complex one (Self Organizing Map (SOM)) and a simple one (the B2 Index), which will prove valuable not only to define the condition of the Major Depression and Bipolar Disorder, but also to provide the possibility of reasonable inferences about the biological significance of the two molecular mood disorders.

We see the emergence, in summary, of some stringent theoretical and anthropological focuses:

- Firstly, the distinction between first-level ontological Depression and second-level ontological Depression.
- The first kind of depression, of an existential nature, expressed by the most varied cultural traditions, is rooted in our structural contingency, which in time and in becoming recognises the mark of its own finiteness (man as an anguished and depressed “natural” animal).

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- Second-level ontological Depression, on the other hand, refers to MD, understood as a molecular, bio-existential niche, marked cogently by serotonin and fatty acids, with its own specific "emotive tonality" [57, 58].
- The centrality of the concept of situation, that is of man as a being located "here and now", starting from biological markers able to offer the diagnosis of MD and BD an extremely real substrate, to be faced on an empirical, therefore public base, to construct a DSM that is not pregnant with pseudo-phenomenology or ideology, but which looks at the *dasein* of consciousness in its true biomolecular flesh [57, 58].
- The continuity between biology and culture, which finds full confirmation in the phenomenon of depression, whose original (ontological) biological nature (serotonin, fatty acids) thoroughly intercepts the structural (ontological) precariousness of living that the great cultural narrations have rooted in flesh and blood (ontic) existence.
- The view of man as a synthesis of *Körper* and *Leib*: life experience is always rooted in biology, the phenomenological "losability" and "impossibility" [59] are also, and firstly, biological "losability" and "impossibility".

To remain in the distinction, often denied only in the intentions, between *erklären* (causal explanation) and *verstehen* (psychological comprehension) means ignoring the prolific acquisitions of complexity theory; above all it means remaining prisoner to the "myth of the sense", on whose basis life experiences, the phenomenological approaches, the philosophical articulations, on which an authentic interpretation of the psychopathology should depend, are hypostatised. The reification of the metaphors, the empty sentimentalism of the interior resonances, the veneration of the illness *as a fruitful production of alternative worlds, the dilution of the tragedy of depression in the imaginative vis of melancholy*: this is the most injurious product of pseudo-phenomenology.

Also biology produces sense, indeed it is the original meaning on which to graft other forms of meaning, of which philosophy is undoubtedly a strong interlocutor, but alongside other forms of knowledge (biochemistry, quantum physics, biomathematics, anthropology, sociology…), as an overall, heuristic synthesis, expressive of an autonomous, therefore "adult", approach to psychopathology [57, 58].

Lastly, it is necessary that the scientific community and the world of the clinical profession commit themselves increasingly so that psychiatry and psychology can constitute themselves as heuristic bio-analytical-existential knowledge, where the diagnosis is not placed under the Heideggerian "yoke of the idea" [60, 61] (classificatory ideology and diagnostic imperialism), but refers to convincing biological markers. In this context, comparison with the neurosciences appears inescapable, particularly in their quantistic standpoint [62-67], with all the implications, also of an ethical nature, that this involves [68-78].

In other words, to start from biology to move towards increasingly complex systems, able to integrate biochemical expressions, living and irreducible existential experiences, social and cultural contexts. Depression therefore needs to be inscribed within a horizon of unmythicised, polyvocal meaning where the biological, physiological, clinical, existential, psycho-social and anthropological aspects are set as objective a hermeneutic framework as possible.

This is all the more so at a time like the present, when a person is often appraised only on the basis of successes achieved, of objects flaunted, of products voraciously consumed, in the instant, of his social visibility, of relentless efficacy, of perfect adaptation of the "thinkable to the possible": all contexts where the genetic and biological psychopathologies of mood are disproportionately amplified [79-83].

If the mechanistic-reductionist cognitive approaches have been characterised by the metaphor of the "edifice", of the solid Cartesian rock, all the forms of knowledge founded on complexity theory have been characterised by the metaphor of the "network", of thinking in relationships, in a dynamic, fluid, open manner. In the field of mental illness, this means setting aside both the organicist paradigm and the pseudo-phenomenological, "sentimentalistic", and therefore ideological, paradigm, in order to have an integrated view of biological objectiveness and humanistic psychotherapy.

That is to say, an expression of diverse interrelated contributions from the various disciplines (psychiatry, psychology, biochemistry, anthropology, quantum physics, mathematics, philosophy).

The observer thus becomes a builder of models, a manager of complexity, giving treatment the character of a truly empathic relationship. This is all the more so where distressing pathologies are involved, such as Major Depression and Bipolar Disorder, "caput mortuum" of psychiatry, because the absence of cogent biological markers seriously compromises every form of therapy. Hence the identification of a biological platform (fatty acids of platelets) as a starting point for a correct classification of MD with respect to BD.

6. Conclusion

The identification of three platelet fatty acids (Palmitic Acid-PA, Linoleic Acid-LA and Arachidonic Acid-AA), in addition to allowing the identification of subjects affected by Mood Disorders, brought about some hypotheses which, over the time, have been proven by robust experimental data concerning also the concept of serotonin uptake on the basis of membrane viscosity. Platelets, considered cells with high affinity to neurons, have the same embryonic origin of brain and skin (ectoderm). Over the last thirty years, numerous and influential works have reported a similarity between platelet and neuron's serotonin concentration, mainly in MD and BD.

This evidence, together with the possibility of classifying the two main mood disorders (Major Depression, MD and Bipolar Disorder, BD), led to some considerations on the molecular uniqueness of MD, generally understood as a phenomenon affecting only human beings, and, more precisely, just part of them. The identification of the characteristics that distinguish MD subjects from BD ones occurs through the different position on the SOM of the triplet of fatty acids, above mentioned, detected for each subject, and through the B2 chemical index.

In this context, we can trace the human states between normality, BD and MD, the latter considered as a bio-molecular and existential niche. Looking into the undeniable distinction made between depressed and bipolar subjects thanks to the neural network (SOM) and the

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chemical index (B2) for indirect assessment of platelet membrane viscosity, we asked ourselves the question of whether the molecular characteristics of subjects with MD were completely different from those of all other living beings both humans or animals. In the light of the experimental data, humans can have either positive or negative values of the B2 index. Those humans having positive values of B2 are normal (N), bipolar (B) and psychotic (P) people. On the contrary, major depressed subjects (MD) have negative B2 values. On the basis of our hypothesis, MD would be, at this point, the real disease, among all Mood Disorders, with specific molecular features and expressions of consciousness, according to the concept of Symmetry Breaking. The use of biochemistry, non-linear mathematics, and human-animal comparison leads to some reflections that are not only really close to a cultural and biological interpretation of mood disorders, but also pave the way for diagnostic perspectives and predictive interpretation patterns of the disease known as "Mood Disorder".

Appendix — From biology to the anthropology of treatment

It is undeniable that the depth of the *ens sofferens*, to be approached with a curative word [36], cannot be traced only to *disease*—pathology or biomedical classification—but also to *illness*—experience of the malaise as lived—and *sickness*—the social determination of the condition [37-39].

For all societies, illness is an event to be interpreted; it is not just a biological fact but also a cultural one. Basically, illness is representation, interpretation, of a portion or of all reality by individuals in a certain social context. The medical description of the human body and the illness always refer back to culturally peculiar meanings.

In strict terms, we could say that the pain articulates its meanings in suffering, which is a restless reflection on the ineluctable, and nevertheless unexpected, occurrence of the illness.

It can be understood, then, that only medical practice that does not limit itself to the biomedical dimension, which is in any case an indisputable point of departure, but is able to meet with the suffering person in his or her intimacy, can ensure, if not salvation against the perverse myth of recovery, at least dignity of the treatment as a profound ethical and existential relationship.

Hence the opening towards intimacy as a dual construction of meaning, the planning of significances contributed to both by the patient, in trusting abandon, and by the physician, as a warm, experienced responsibility. The intimacy is inhabited by the treatment (sphere of essential meanings of living) and not by anxiety (sphere of intra-worldly commerces), precisely because the experience of illness is experience of a relational wound which destructures the biological and existential narration of the subject:

- Wounded in relation to his own body, in *Der Zauberberg* Thomas Mann says that "illness makes men more corporeal, it makes them all body" [40], from which, on the one hand, we wish to distance ourselves as it is a sign of the precariousness of existence, while on the other hand we want to master it as we never did when in good health, because the anguish of

feeling expropriated by it, not only by the almost fleshly possibility of death, but also by its medical visibility (the anguish—increasingly flaunted, for that matter, and reiterated like a mantra—of the reification of the medical approach), makes us feel the full weight of our vulnerability;

- A relational wound with respect to everyday life, whose narrative laceration provokes at first dismay, then a steady eclipse towards an indeterminate space-time, which for this reason is anguishing and inhospitable, and requires an approach that is not simply clinical but, precisely, one of intimacy, which, as a profound expression of empathy, configures itself as discretion, the word held back, the gesture experienced, total attention for the suffering countenance in a mutual exchange of meanings.

In the case of mental illnesses, then, the social, cultural weight takes on an almost transcendent value, due to the often blurred correspondences between classification and natural object, between nosology and effective reality of the illness.

When all this is recognised, what remains, excluding the interpretations of meaning, is the structural necessity, when coping with the illness—in our case the psychopathology—of starting from the biological fact, from objective biological markers, without which experience, biographical narrations, cultural rootings would be empty just as biology, on the other hand, would be blind.

The meaning is not only the prerogative of philosophy, which certainly remains a strong interlocutor, but also of biology and biochemistry: the corporeal meaning/significance of a pathological event.

Certainly, a medicine limited to the biological fact cannot be extensive and ostensive of the illness. At the same time, however, no one should doubt—as however happens unfailingly—that starting from a bio-medical platform can *ipso facto* reduces the physician to a pure functionary of the body and of the pathology connected with it.

Ultimately, we need to remind the alleged monolithic custodians of the thought of Husserl, Heidegger, Jaspers, Minkowski and Binswanger that rooting the pathology in biology does not mean expropriating the sick person of his illness and making the physician a mere functionary of the organism, an all-out pathologist who ignores biographies, experiences, corporeal dynamics and relational ontologies.

If anything, biographies, relationships, cultural expressions can be preserved in all their dignity, once their genuine biological matrix has been determined.

On the other hand, we risk only metaphysical hypostatisation and, therefore, a treatment rooted in an immobile metempirical "elsewhere".

A fruitful heuristic synthesis between *Körper* and *Leib*, *erklären* and *verstehen* [41], as a true commitment to healing the "living flesh" (*Fr. chair*) [42], is possible only if we start from the biological roots of our *being in the world* (*in der Welt sein*).

Heidegger's figures of omnipotence *(Allmacht)* and impotence *(Ohnmacht*) [43], can be taken up and re-elaborated in a synthesis between the naturalistic, classificatory power of science

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and the ever-open possibility of phenomenology, avoiding the same Heidegger's anti-technicist derailments and the exacerbated revivals of Binswanger's phenomenology as a mere therapeutic praxis, without theoretical rigour.

Like psychiatry and psychology—bio-reductionist and limited to the illness—so too "antipsychiatry", which reduces the illness only to a social construction, process of control, of exclusion/inclusion managed by bio-power [44-48], unable to recognise the productivity/creativity of schizophrenic processes [49], ends up by prejudicing the genuine dynamics of the treatment.

Hence the need for an objective biological reference able to act as a cogent platform in the treatment relationship, with reference to two distressing psychopathologies: MD and BD [1].

Appendix: Linoleic acid secrets

Linoleic acid, a regulator of the fine tuning?

On why you can read in the platelet, what happens in the neuron in the case of mood disorders, we are not, up to now, able to give complete answer.

It will help in trying to understand the phenomenon, the configuration of the level curves of the various fatty acids made in the SOM (Figure 13). The values of C20: 4 (Arachidonic Acid) stored in each artificial neuron ADAM were interpolated and distributed all over the map, depending on the distance weighted of minimum squares. A graphic profile, therefore, has been made and expressed in a 2D plane (Figure 14).

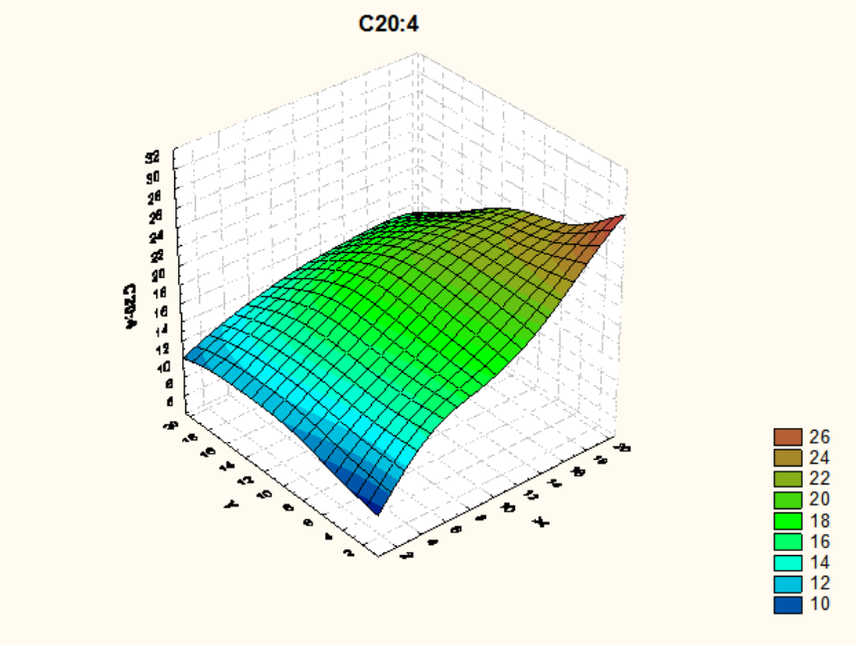

Figure 13. The value of C20: 4 stored in each artificial neuron of ADAM

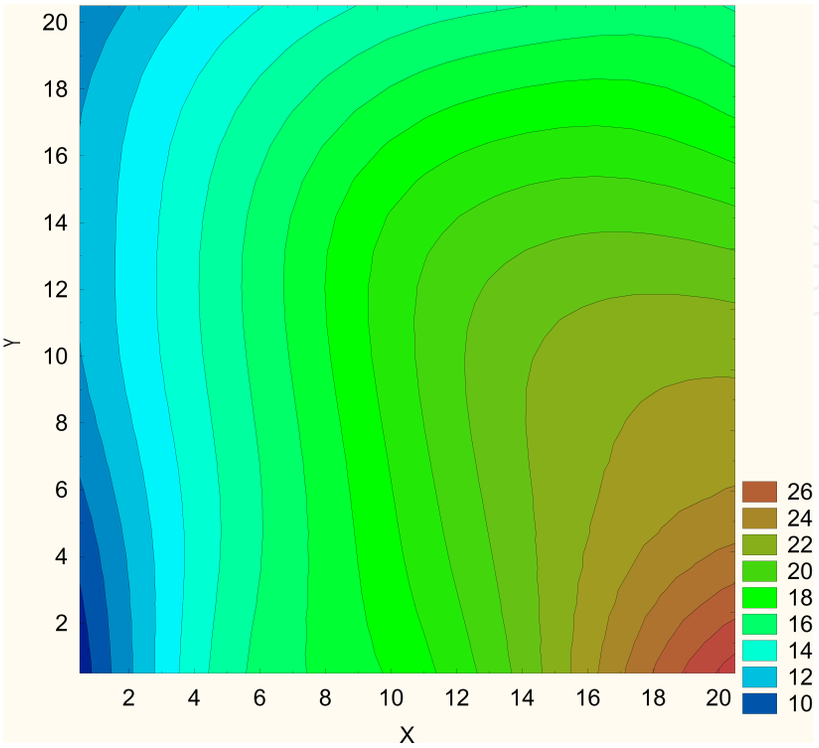

Figure 14. The level curves were made and expressed in a two-dimensional

Following the same procedure we have identified the maximum and minimum levels of the other fatty acids (Figure 15).

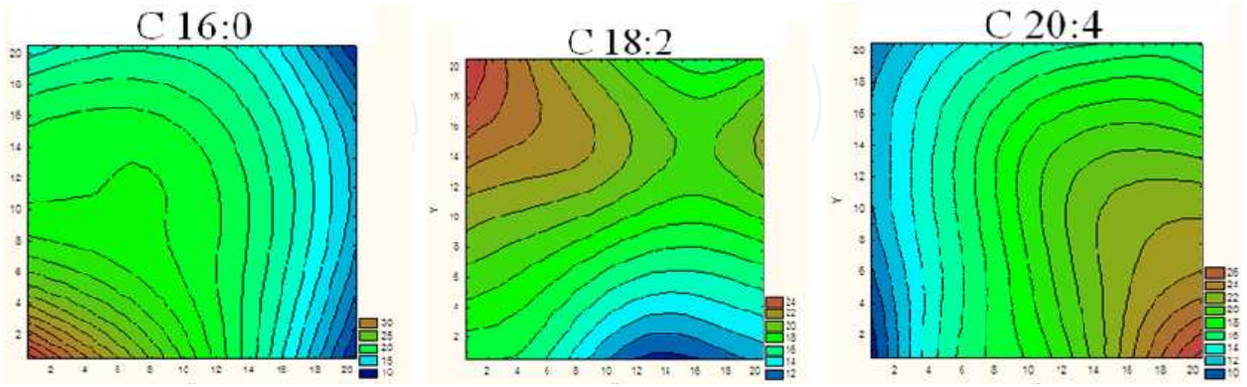

Figure 15. Minimum level (blue) and maximum (brown) of the fatty acids identified by the SOM

If we plot all three fatty acids expressed as index B2 we obtain Figure 16.

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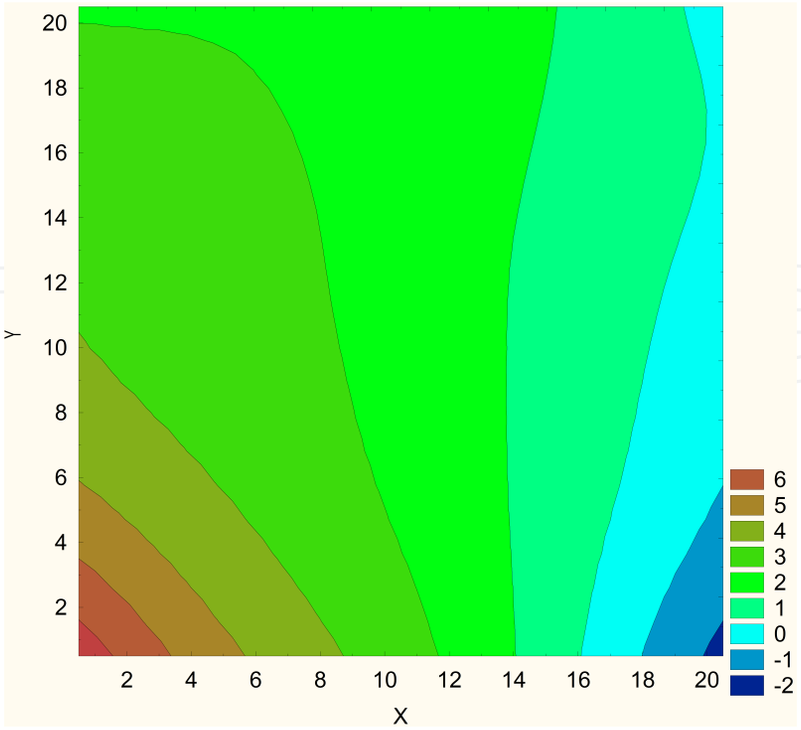

Figure 16. B2 index distribution over the SOM

The index B2, seems to be a good predictor of the macro-areas (Figure 17)

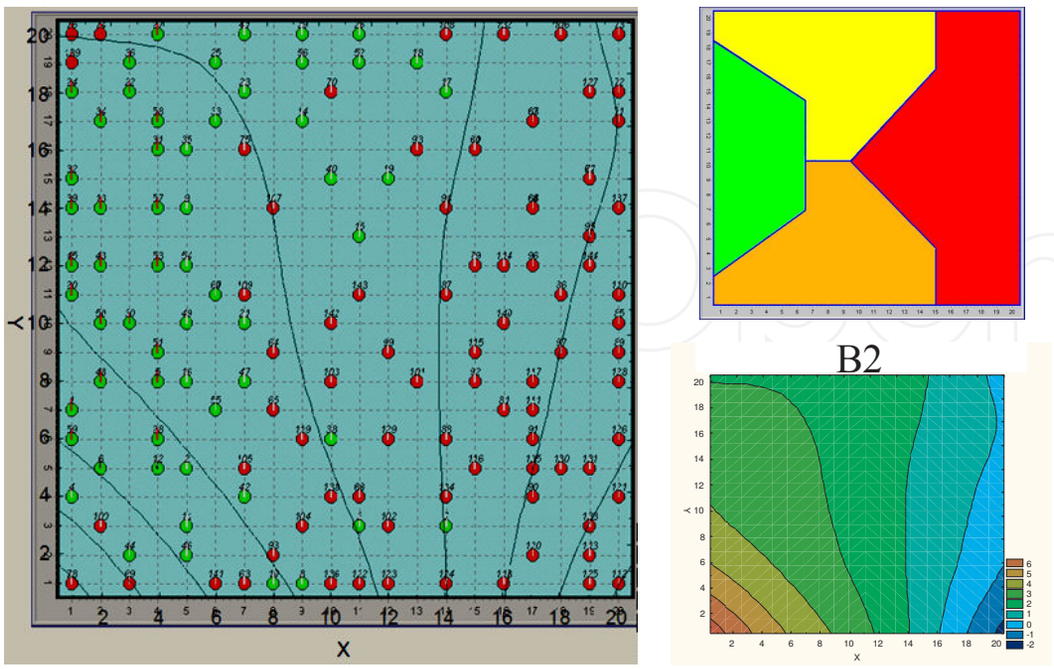

Figure 17. Level curves of the B2 Index over the SOM

A glimmer of light appears when we realize that only with the SOM and the B2 index, together, we can accurately identify the characteristic of the subject (SOM and B2 do not know of each other but converge on the same target). This observation becomes necessary when more than one subject, with the same B2 index have two different positions in the SOM, i.e., the same index can classify subjects in different areas. This finding is very important because it means that, in addition to the reasoning on the mobility of the membrane, there is another element of conditioning, and since everything revolves around the three fatty acids previously mentioned, must necessarily be one of them, in its concentration, that makes the difference and can affect the mood profile of the subject. Even in these cases we have accurate diagnostic findings.

For a variety of reasons that we will try to make explainable, attention is especially drawn to the linoleic acid, an essential fatty acid which is not manufactured by the human or animal organism. The level curves, which have been previously mentioned, show as the absolute minimum of linoleic acid, as shown below, corresponds to the minimum point of the B2 index (Figure 18):

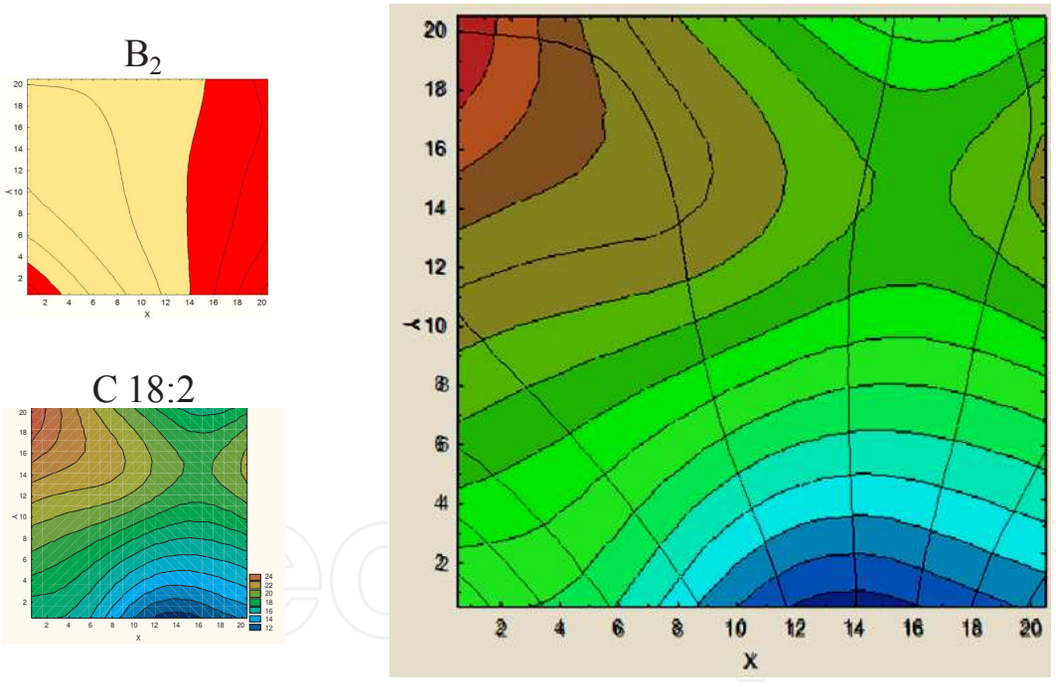

Figure 18. B2 index and linoleic acid distribution over the SOM

The fan produced by the SOM, from right to left, shows that the B2 is in progression from-2.64 To 8.23 (Figure 19).

The apparently healthy subjects are characterized by a mean value of B2 equal to 2.80.

This value is the midpoint between the extremes-2.64 (absolute minimum given by the map) and 8.23 (absolute maximum expressed by the map).

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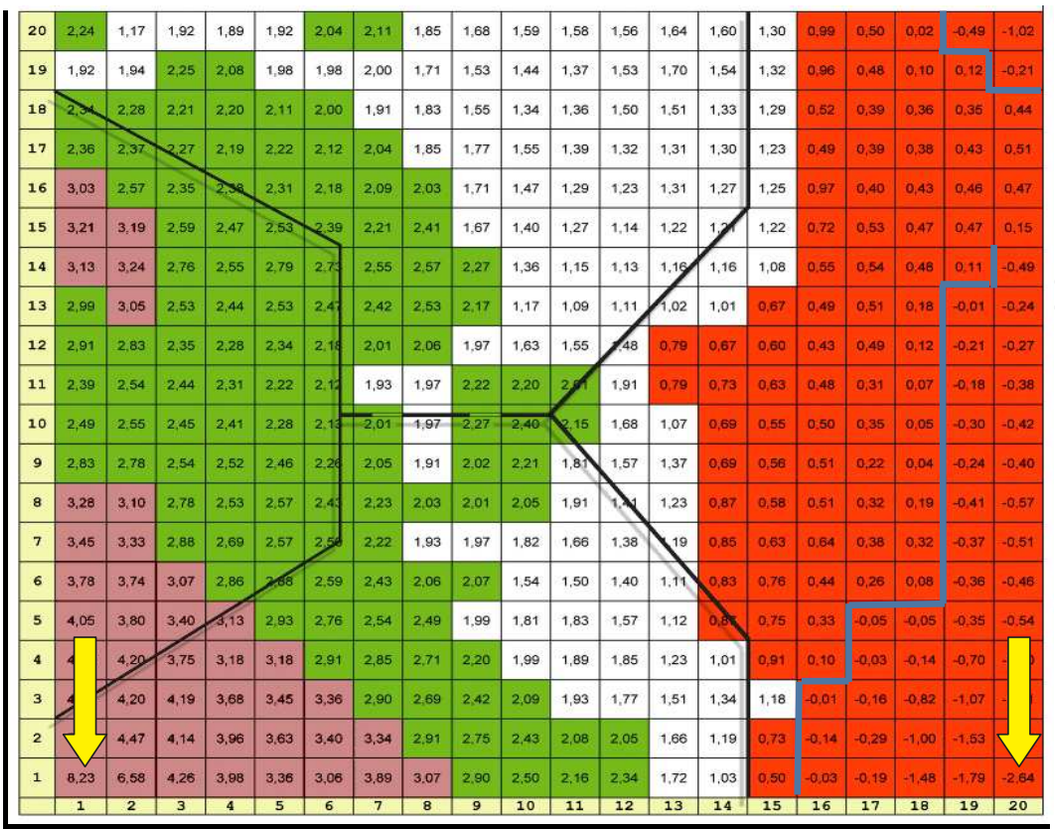

20	2,24	1,17	1,92	1,89	1,92	2,04	2,11	1,85	1,68	1,59	1,58	1,56	1,64	1,60	1,30	0,99	0,50	0,02	-0,49	-1,02
19	1,92	1,94	2,25	2,08	1,98	1,98	2,00	1,71	1,53	1,44	1,37	1,53	1,70	1,54	1,32	0,96	0,48	0,10	0,12	-0,21
18	2,34	2,28	2,21	2,20	2,11	2,00	1,91	1,83	1,55	1,34	1,36	1,50	1,51	1,33	1,29	0,52	0,39	0,36	0,35	0,44
17	2,36	2,37	2,27	2,19	2,22	2,12	2,04	1,85	1,77	1,55	1,39	1,32	1,31	1,30	1,23	0,49	0,39	0,38	0,43	0,51
16	3,03	2,57	2,35	2,38	2,31	2,18	2,09	2,03	1,71	1,47	1,29	1,23	1,31	1,27	1,25	0,97	0,40	0,43	0,46	0,47
15	3,21	3,19	2,59	2,47	2,53	2,39	2,21	2,41	1,67	1,40	1,27	1,14	1,22	1,21	1,22	0,72	0,53	0,47	0,47	0,15
14	3,13	3,24	2,76	2,55	2,79	2,73	2,55	2,57	2,27	1,36	1,15	1,13	1,16	1,16	1,08	0,55	0,54	0,48	0,11	-0,49
13	2,99	3,05	2,53	2,44	2,53	2,47	2,42	2,53	2,17	1,17	1,09	1,11	1,02	1,01	0,67	0,49	0,51	0,18	-0,01	-0,24
12	2,91	2,83	2,35	2,28	2,34	2,18	2,01	2,06	1,97	1,63	1,55	1,48	0,79	0,67	0,60	0,43	0,49	0,12	-0,21	-0,27
11	2,39	2,54	2,44	2,31	2,22	2,12	1,93	1,97	2,22	2,20	2,01	1,91	0,79	0,73	0,63	0,48	0,31	0,07	-0,18	-0,38
10	2,49	2,55	2,45	2,41	2,28	2,13	2,01	1,97	2,27	2,40	2,15	1,68	1,07	0,69	0,55	0,50	0,35	0,05	-0,30	-0,42
9	2,83	2,78	2,54	2,52	2,46	2,26	2,05	1,91	2,02	2,21	1,81	1,57	1,37	0,69	0,56	0,51	0,22	0,04	-0,24	-0,40
8	3,28	3,10	2,78	2,53	2,57	2,43	2,23	2,03	2,01	2,05	1,91	1,71	1,23	0,87	0,58	0,51	0,32	0,19	-0,41	-0,57
7	3,45	3,33	2,88	2,69	2,57	2,58	2,22	1,93	1,97	1,82	1,66	1,38	1,19	0,85	0,63	0,64	0,38	0,32	-0,37	-0,51
6	3,78	3,74	3,07	2,86	2,88	2,59	2,43	2,06	2,07	1,54	1,50	1,40	1,11	0,83	0,76	0,44	0,26	0,08	-0,36	-0,46
5	4,05	3,80	3,40	3,13	2,93	2,76	2,54	2,49	1,99	1,81	1,83	1,57	1,12	0,87	0,75	0,33	-0,05	-0,05	-0,35	-0,54
4	4	4,20	3,75	3,18	3,18	2,91	2,85	2,71	2,20	1,99	1,89	1,85	1,23	1,01	0,91	0,10	-0,03	-0,14	-0,70	
3	4	4,20	4,19	3,68	3,45	3,36	2,90	2,69	2,42	2,09	1,93	1,77	1,51	1,34	1,18	-0,01	-0,16	-0,82	-1,07	
2	4,47	4,14	3,96	3,63	3,40	3,34	2,91	2,75	2,43	2,08	2,05	1,66	1,19	0,73	-0,14	-0,29	-1,00	-1,53		
1	8,23	6,58	4,26	3,98	3,36	3,06	3,89	3,07	2,90	2,50	2,16	2,34	1,72	1,03	0,50	-0,03	-0,19	-1,48	-1,79	-2,64
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20

Figure 19. Distribution of the B2 index over the SOM

A careful analysis of the mathematical formulation of the index B2 shows that it is governed almost entirely by the Arachidonic and Palmitic Acid. Intuitively this is deduced by expressing the average values of the two fatty acids of ADAM, using level curves, which appear qualitatively symmetrical (Figure 20).

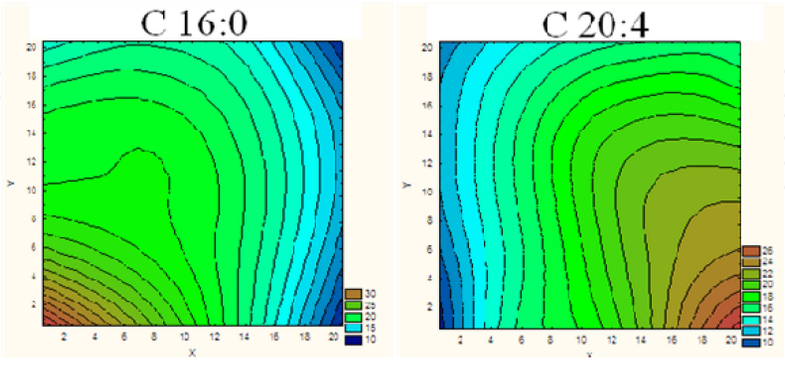

Figure 20. Demonstration of the symmetry of the distribution of palmitic acid (C16: 0) and arachidonic acid (C20: 4).

Are these two fatty acids that determine the macro area of a subject? Within a macro area is the intervention of linoleic acid that modulates with precision the position of the subjects. Maybe C18: 2 is the main actor in the "fine tuning"? (Figure 21).

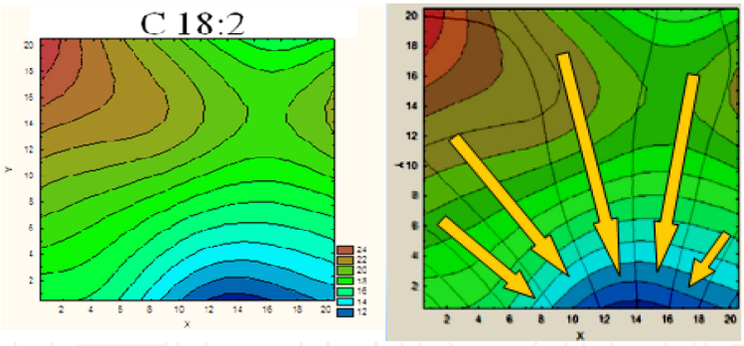

Figure 21. The distribution of linoleic acid on the map represents the core of the SOM

It is likely that in the circumstances that discriminate a healthy person from a pathological, the difference of linoleic determines, however, a modification of the biochemical factors involved and / or responsible for the biochemical and pathological determinism of the "Depression", of course declinable also on the basis of environmental / cultural influences. It should also be noted that the effects of linoleic acid on disease are relevant because of the configurations, equally balanced, of both, Arachidonic Acid and Palmitic Acid. Practically, referring to the positions of the subjects in the map ADAM, for values beyond a certain limit of Arachidonic Acid, the subject is surely depressed, as also happens for values beyond a certain limit Palmitic Acid. When B2 is in a neighbourhood of the normal value, it becomes decisive the percentage of linoleic acid. These configurations introduce, however, the concept of hyper saturation of the platelet in the case of Palmitic and that of hyper unsaturation in the case of Arachidonic. Another discriminant, between the two mentioned for the connotation of the disease, must be identified in Linoleic Acid which, in case of excess, restates the biochemical conditions for the development of the pathology. Certainly the network works beyond these operations, not yet known and interpreted probabilistically, of connection among the values that were administered.

A key point, that of linoleic acid, which requires the opening of a new chapter of considerations.

To better understand the reasoning on the data of linoleic acid, as well as his involvement in the molecular determinism of mood disorders, we must draw attention to some scientific findings that have linked, adversely, excess of linoleic acid, even for not very high concentrations, with some biological functions [84] and molecular interactions, i.e. the microtubules disruption [85].

A series of studies of cellular nutrition [86], on the effect of different amounts of phospholipids, extracted from various organs of calf (diencephalon, retina, cerebral cortex and heart), were made on chick embryo myocardial cultures.

From numerous tests, it was observed that the heart phospholipids, differently from the others, reduced, strongly, the migration speed of the cultures.

We did not understand at that time that the cardiac phospholipids, unlike the others (midbrain, retina and cerebral cortex), are very rich in linoleic acid, and that their addition, in addition to the amount naturally present, could be responsible for profound changes observed.

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This effect could confirm once again the criticality of linoleic acid. Obviously, the consequences of the condition of excess will focus on the biological system in which the phenomenon occurs.

Even in case of reduction of linoleic acid may occur undesirable phenomena, as happens for example in the process of hibernation, in regulating the flow of calcium into the cardiac cell [87, 88].

The lipid structure of the brain as well as investigated [Cocchi and Noble, data not published, [89]] manifests the same characteristics in the extreme positions of the evolution of warm-blooded animal (from birds to humans) in the course of phylogeny [90], i.e. the level of Linoleic Acid is very low (about 0.3%).

It is possible to assume, reasonably, that while the manifestation of Mood Disorders is recognizable by the increase or decrease of specific fatty acids, Linoleic acid, even in its consolidated stability, could be the element capable of inducing, for small changes, amplifications of pathological brain responses.

Perhaps, within the concept of symmetry breaking and within the considerations on the linoleic acid, we can find answers to questions that the work done raises.

In particular we have, for a long time, faced the problem of how the set of three fatty acids could correspond with absolute precision to a condition of DM or DB. The perception that the set of identified molecular mechanisms might underlie the implications of quantum consciousness has been widely debated, finding aspects of great consistency in the molecular interactions involving membrane Gsα protein and cytoskeleton [9, 29, 28, 91, 92].

If we look at the map of the B2 index and the distance between the indexes (the expression of a molecular properties) we can realize how, in biology, the mathematical measure can express appreciable variations, in a numeric around, relatively close, as well as the positive and negative sign that characterizes respectively DB and DM, can never be interchangeable, consistent with the demonstration of the symmetry breaking between DM and DB.

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