
Research Description and Goals

Psychiatry seems to be one of the few areas of medicine, perhaps the only one, in which treatments such as talk therapies, medication, and peer support are not well supported by more effective technological alternatives, such as ECT (electroconvulsive therapy), which alters brain functions with small, external electrical stimulations, or TMS (transcranial magnetic stimulation), which involves the use of a special electromagnetic device that sends short impulses to the brain. Often, diagnoses and therapies are left to the experience and subjective evaluation of the psychiatrist, whose accuracy is subject to constant criticism of other, skeptic psychiatrists with a different point of view. Conversely, technology nowadays is becoming more and more involved in the scientific community, leading research to solve modern and controversial topics. In the section Platelet's Fatty Acids and Differential Diagnosis of Major Depression and Bipolar Disorder through the Use of an Unsupervised Competitive-Learning Network Algorithm (SOM) of the article *Open Journal of Depression*, Serena Benedetti (et al.) discusses how, from a simple blood sample, it is possible to calculate the quantity of polyunsaturated fatty acids (lipids mostly found in seeds, nuts, or fish) that are present in the human body's platelet membranes, which are small red blood cells that prevent bleeding. The research proposal is well-founded with the help of a mathematical analysis through a non-linear self-organizing map (SOM) that allows a better and more concise use of the information contained in the platelet. The combined application that the project proposes, therefore, could lead to an almost perfect diagnosis of the pathology afflicting the patient.

Project Significance

This is a huge step forward in the prevention of suicides and similar acts of self-harm, which affect not only a patient's own health, but also that of others. Specialists in neurology or psychiatry, however, are less than welcoming to these studies. Instead of see-

ing these studies as a sign of progress in research, they treat them as untrue with everything to prove, since they see technology as a potential threat for their positions. It is not a mystery that in the near future, a functional, tested machine could give an almost perfect result, in which case the human voice will start to lose credibility and power. It is likely that managers would rather buy a new machine than hire a new employee. For this reason, even managers at the level of the Ministry of Health and other medical associations turn a deaf ear and do everything possible to silence these studies, hide their benefits, and hamper their development. It is crucial to keep in mind that a lot of diagnoses, when addressing cases of psychiatric disorders, are dubious at best, if not wrong. For instance, psychiatrists should not tell patients that their anxiety or depressive disorder are caused by a chemical imbalance in the brain when there is no evidence this exists. However, there are currently no other ways to improve the accuracy of these diagnoses, which is why these studies may be useful. It is unimaginable to think of being able to understand such a complex subject as that of the psychiatric pathology without having collaboration between various fields. In fact, this study is the first time that a case can distinguish between a bipolar patient and a depressed patient. The reason this distinction is relevant is because, as stated before, errors often made in the diagnosis of major depression versus that of bipolar disorder, are due to the delay in appearance of symptoms in the latter. Early on, the same patient who is diagnosed as a major depressed case is labeled as bipolar because there is no possible way to distinguish between the separate illnesses. After more than one hundred cases, it was possible to recognize that this kind of depression is characterized in a difference in composition of fatty acids in platelets compared to the one in subjects suffering from bipolar disorder. This is crucial to understanding that the individual does not change throughout life. Therefore, if someone who has major depression but

is misdiagnosed as a child and later said to have bipolar disorder, this someone won't develop the bipolar disorder, but instead the major disorder would just get worse due to lack of appropriate therapeutics.

Study Design, Part 1: Participants.

In order to examine misdiagnoses in mental illness, psychiatrists scrutinized and recruited all volunteer participants, and patients underwent a semi-structured interview based on DSM-IV-TR criteria (Diagnostic and Statistical Manual of Mental Disorders, fifth edition). 132 total subjects were involved, 105 of which had either a bipolar disorder (BD) or a more generic mental disorder (MD), and 27 of which were completely healthy and represented the Control Group (CTR). The subjects were recruited without regard to sex, age, food intake patterns, or pharmacological therapies. Details are shown in Table 1 below:

Subjects Investigated	Males	Females	Total	Average Age
MD	12	28	40	50.5 ± 14.7
BD	22	43	65	50.2 ± 13.1
CTR	17	10	27	***
# of Treated Patients	** 34	** 71	** 105	50.3 ± 13.7

Table 1. ** CTR not included in calculations because considered as NOT-TREATED. *** CTR average age not available. Group matched for age, sex, and socio-cultural group to MD and BD subjects.

Study Design, Part 2: Investigations.

It is necessary to recognize the significant correlation between the biochemical mechanisms present in the blood and those existing in the brain--in particular in those brain areas most affected by the depression--so that the diagnosis of depression by the blood is reliable and a valid and essential diagnostic support to the clinic. Benedetti's study examined the circulating platelets and posited that it could bring an innovative contribution to the psychiatric diagnosis with the introduction of a "biological marker of depression and bipolar disorder." As a support of the diagnosis of the neuropsychiatric clinic, this study takes into account three fundamental scientific assumptions. The first is a new evaluation of the unique relationship of

body and mind as a result of the discovery that many circulating cells, such as white blood cells and platelets, have the same receptors for the neurotransmitters that are present in neurons. Specifically, platelets and neurons have a very similar metabolism of serotonin. The second assumption is a new evaluation of the informational role of cell membranes. As highlighted in the research, subjects with depression present a different composition of fatty acids in platelets compared to those who suffer from bipolar disorder. Consequently, this different composition can modulate the responses to serotonin and antidepressant drugs. In support of the above-cited assumptions, the markers would allow a better understanding of the role of nutrition, inflammation and oxidative stress in the pathogenesis of depression.

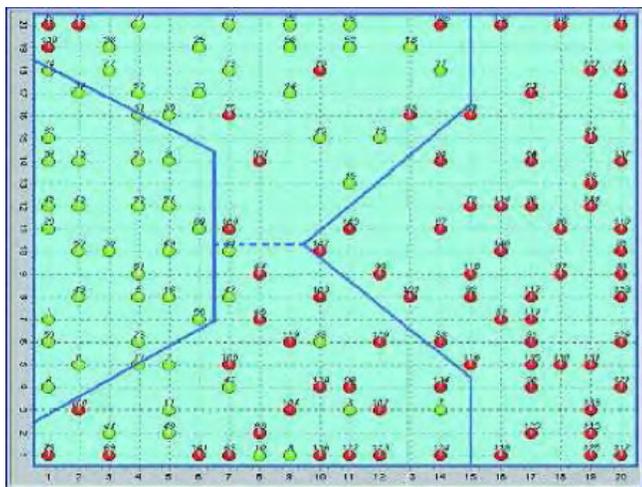
The mathematical analysis the research is proposing, the SOM (Self Organizing Map), is a data visualization technique that reduces the dimensions of data through the use of artificial neural networks (ANN), and it is now needed to give a clearer picture of the above investigations. This particular algorithm allows you to view the results graphically by constructing a two-dimensional map that has the subjects analyzed in a continuous manner, not necessarily divided in specific categories or under strict criteria. This approach will evaluate the fatty acids of the platelet membranes of subjects diagnosed with Major Depression against a population control theoretically lacking this pathology.

Study Design, Part 3: Procedures.

1. Blood Sampling
2. Platelet Isolation
3. Platelet Membrane Fatty Acid Composition A
4. Mathematical Method:
 1. Self Organizing Map (SOM)
 2. On the Non-Manipulability of the SOM Built for the Classification of the Subjects
 3. B2 Index
 4. Plasma and Platelet Serotonin Levels
 5. Oxidative Stress and Inflammation Markers
 6. Statistics and Data Processing

Outcomes

After selection, 105 subjects were included. Among MD, 19 patients were on treatment with serotonergic drugs, 10 with non-serotonergic and 11 received no therapy. Among BD, 28 patients were on treatment with serotonergic drugs, 14 with non-serotonergic, and 23 received no therapy. The control group (CTR) comprised of 27 apparently healthy volunteers (M = 17, F = 10) matched for age, sex and socio-cultural condition to pathological subjects.



the information concerning their pathological state. The results obtained was that, using three particular fatty acids (Palmitic, Linoleic, and Arachidonic), the SOM has been able to construct a map of the two populations, recognizing as similar the subjects belonging to the same population and, at the same time, those different among the two populations.

The SOM interpretation consisted of the map shown in Figure 1. The subjects in red in the two intermediate areas (yellow and orange) have been interpreted

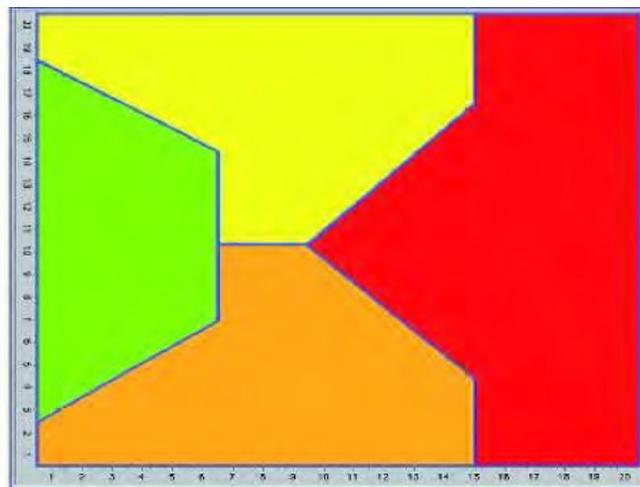


Figure 1. Distribution of human subjects, normal and depressed, in the self-organizing map (SOM) [LEFT], and some respective areas [RIGHT]. Fatty Acids of the Platelet (markers): Palmitic (C16: 0), Linoleic (C18: 2) and Arachidonic (C20: 4), they may discriminate against mood disorders and have diagnostic power. The distribution of 144 subjects studied on the SOM, 60 apparently normal (green) and 84 diagnosed with major depression, allowed the psychiatrists to identify four areas: two specific (only normal and only pathological) and two mixed areas with different concentrations of pathological and apparently normal individuals. Areas of SOM: Green = normal, red = mood disorders, Yellow = high density of normal individuals, Orange = high density of pathological individuals.

Controls, assessed by a semi-structured psychiatric interview, were free of psychiatric illness or, at least, a psychiatric condition was not expressed. None of them were using anti-depressant therapy. These subjects were classified according to negative or positive values. In short, the control group was selected among subjects with positive and negative B2 index (a simple mathematical tool used to establish degrees of viscosity and/or unsaturation within platelet membranes), without expression of psychopathology and without antidepressant assumption. In this way, researchers would be able to identify biomarker differences compared to drug treatment.

The SOM were administered with the values of the fatty acids of the two populations, mixing normal (healthy) and pathological individuals, and hiding all

as misdiagnoses of major depression. The SOM has demonstrated a great capacity of correlation in the diagnosis of major depression and, within the same diagnosis, has also revealed the existence of unambiguous, different biochemical characteristics of the fatty acids of the platelet. Nonetheless, the results are in accordance with the thesis that the diagnosis of major depression is often inaccurate and must be converted to a diagnosis of bipolar disorder.

Limitations

However, this research brings up an ethical issue. When we hear from the media about cases of murder, infanticide, uxoricide, or simple aggressions, they are often considered and defined as voluntary acts. Still, if the aforementioned blood tests were given to these individuals, a jury could not have the

same level of confidence of the motives of the person who gave out the diagnosis, especially if there were no priors of mental conditions. In this case the acts of the convict would not be thought as voluntary and premeditated, but it might be classified as a consequence of the disease, therefore proving innocence. This means that a simple blood test can lead to an effective prevention of harsh sentences in a court of law, especially of borderline subjects, where the test could be the only solution to eventually justify their criminal act as involuntary.

Current psychiatrists are against this type of prevention, even if it would bring significant benefits to their patients through more accurate and precise diagnoses. In fact, some might object that this new diagnostic possibility could create discrimination in employment considering that the employer may require a negative test for his employees. However, in reality, there are no or few social repercussions. The “marker” is not evidence of the disease, but evidence of a predisposition to it, which can lead to prevention of the disorder.

Conclusion and future research

In conclusion, the experiment conducted tries to distinguish the disease at the first visit with the patient, so that the psychiatrist can better target the course of therapy because, at a certain point, treating a patient with major depression the same way as a patient with bipolar disorder is implausible. Due to physical-chemical characteristics in the neuronal membrane that are completely different between these two disorders, the same therapy may have devastating effects in one patient or the other. Kary Mullis, 1993 Nobel Prize in Chemistry, enthusiastically commented on the extraordinary importance of this research; in fact, this method may eventually allow the doctor to know if a patient has the intention to commit suicide, which is the leading cause of death in patients with bipolar disorder. In addition, an incorrect diagnosis and the wrong therapeutic intervention increase suicide risk by about 4 times. With developing research in this field, it seems that we are about to experience a tremendously promising turning point,

References

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