A REVIEW ON CORRELATION BETWEEN LIPID PROFILE AND DEPRESSION

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ABSTRACT

Epidemiological and clinical intervention data indicate that low levels of circulating lipids and cholesterol are the risk factors for depressive symptoms. Olie et al 2011(1) showed an association of low cholesterol and self-harm in their study. In the present scenario, depression and anxiety disorders have high prevalence rates and are frequently related. Understanding the subject and concepts/mechanisms related to neurobiological basis for these disorders is very important and the available techniques or methods are ineffective. Lipids generally play an important role in neural function in the brain. The composition of lipid of the brain influences perception, mood and behaviour. Lipids are responsible to regulate the membrane's function which acts as a barrier between the intracellular and extracellular spaces. It is found that membrane lipids determine the local behaviour and characterisation and function of proteins within the membrane. It is found from the literature that lipids can influence both exo-and endocytic processes and work within the membrane as second messengers. This paper discusses some important case studies related to the correlation between lipid profile and the depression.

KEYWORDS

Lipids, Depression, Low Cholesterol, Self-harm.

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INTRODUCTION: Parker et al(2) expressed that historically, Hippocrates was the first to describe melancholia (Depression) as a condition associated with "Aversion to food, Despondency, Sleeplessness, Irritability and Restlessness". Akiskal HS.(3) told that The World Health Organization (WHO) has ranked depression as fourth in a list of most urgent problems worldwide. It is also happening that about 10 to 15% of the patients generally commit suicide with depression. Aetiologically, depression is a neurobiological disorder associated with derangements in neurochemical, neuroendocrine and neuroimmunological functions. The neurobiological basis for several disorders are yet to be fully understood, and available treatments are ineffective some times for the special cases.

Many neurobiological models generally assume that the aspects such as (i) dysfunctions in neuronal proteins and (ii) peptide activities are primarily responsible for these disorders. Brain lipids are found to play key role for the localisation, function of proteins in the cell membrane and regulation of synaptic output in neurons. It is also found that lipids sometimes may also leave the membrane as transmitters and relay signals from the membrane to intracellular compartments or to other cells. It is important to know (i) the complete function of membrane lipids (ii) role in the membrane's function as a barrier (iii) as a signalling medium for classical transmitter signalling (iv) contribution to depression and anxiety disorders and (v) targets for lipid-based treatment approaches.

It is mentioned that preclinical findings are very important for the membrane-forming n-3 polyunsaturated fatty acids, glycerophospholipids, glycerolipids, and sphingolipids in the induction of depression- and anxiety-related behaviours. These polyunsaturated fatty acids found to offer new treatment options, namely, targeted dietary supplementation or pharmacological interference with lipid-regulating enzymes. Effective lipid based therapies are found to need more individualised approaches. In summary, with the available knowledge base, it is found that membrane lipids have crucial and important role in the pathogenesis of depression and anxiety disorders and these lipids could be exploited for improved prevention and treatment.

Membrane lipids have important functions in the brain. Membrane lipids constitute a physical barrier that segregates the inner and outer cellular environments; these lipids are also involved in cell signalling. Although numerous studies have been reported in the literature on aspects related to depression, lipid profiles, exact mechanisms responsible for the same is yet to understand completely Manfredni et al 2000,(4) Maimance and Al-Hazmi.(5) 2009, Paul et al 2000,(6) Pie et al 2012,(7) Maximillian et al 2003,(8) Bell et al 2001.(9)

The Contributing Factors or Mechanisms or Parameters for Depression:

The Following are some of the Important Aspects Responsible for Depression.

1.1. Fatty Acids.

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1.1.1. Preclinical evidence.

1.1.1.a. The lack of n-3 polyunsaturated fatty acids in the brain induces depression/anxiety.

1.1.1.b. Dopaminergic Mechanisms.

1.1.1.c. Serotonergic Mechanisms.

1.1.1.d. Noradrenergic Mechanisms.

1.1.1.e. Increased n-3 Polyunsaturated Fatty Acids Reduce Depression/Anxiety.

1.1.1.f. n-3 Polyunsaturated Fatty Acids in the Depressed/Anxious Organism.

1.2. Clinical Evidence.

2.1. Glycerolipids.

2.1.1. Preclinical evidence.

2.2. Glycerophospholipids.

2.2.1. Preclinical evidence.

2.2.2. Clinical evidence.

2.3. Sphingolipids.

2.3.1. Preclinical evidence.

2.3.2. Clinical evidence.

LITERATURE REVIEW: This section presents brief review on the investigations carried out by various researchers. Important studies are presented below. Suna et al 2016[10] studied the impact of Electroconvulsive therapy (ECT) as a non-pharmacological treatment on the peripheral lipid pattern in depressive patients. Authors analysed peripheral lipid profile composition before and after a course of ECT in 27 non-fasting inpatients at a university psychiatric hospital with DSM-IV major depressive episode. A multivariate repeated measurement regression analysis was performed for the impact of ECT treatment on each lipid parameter and evaluated separately for every dependent variable. It was found from the clinical tests that total cholesterol and the cholesterol subtypes HDL and LDL were increased after the treatment compared to baseline. It was also observed from the tests that apolipoprotein A1 was increased after ECT, whereas apolipoprotein B was not. Indices for the prediction of cardiovascular diseases were found unchanged after treatment by ECT. The reduction of depressive psychopathology is found negatively correlated with HDL cholesterol and apolipoprotein A1.

Young-Min Park et al 2014[11] carried out investigations on depressed patients to find the evidence that whether low lipid levels are responsible. The main objective of their study was to identify the relations among low serum lipid levels with suicide ideation or and with central serotonin function. About seventy three patients who were diagnosed with major depressive disorder examined for auditory processing for the loudness dependence of auditory evoked potentials (LDAEP). LDAEP was measured in terms of Hamilton Depression Rating Scale (HAMD) and the Beck Depression Inventory (BDI) for all the patients on the same day. Further, serum levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride (TG) levels were also measured. As per the scores of HAMD and BDI, the depressed subjects were separated in two groups i.e. with and without suicidal ideation.

It was found that TG levels differed significantly between the two groups, whereas body mass index (BMI), LDL, HDL, total cholesterol, and LDAEP did not. It was observed that the scores for HAMD and BDI were negatively correlated with TG levels. The studies confirmed a relationship between TG and suicide ideation which is independent of both body weight and BMI. In addition, serum lipid levels were found to be associated with central serotonergic activity. Floyd et al 2011[12] performed the studies to examine the relationship between depressive behaviour and concentrations of lipids and lipid signalling molecules which is common to both CHD (coronary heart disease) and depression in a cohort of cynomolgus monkeys (Macaca fascicularis). The monkeys were fed with a 'Western' diet, enriched with cholesterol and saturated fat for about 27 months and recorded depressive behaviour on weekly basis. The parameters, namely, body-mass index, body weight and circulating cholesterol profiles were monitored in all animals during the above period, and FA-based signalling molecules & fatty acids (FA) were monitored in the most depressed monkeys. It was observed that monkeys which had Western diet exhibited a broad range of percent time spent in depressive behaviour.

The percent time spent depressed by monkeys was observed positively correlated with total plasma and cholesterol, LDL and also negatively associated with HDL cholesterol. The major observation from the study was that (i) in depressed monkeys, FA ratios revealed that stearoyl Coenzyme A desaturase 1 activity was increased (ii) depressed female monkeys had increased concentrations of serum lipids and lipid signalling molecules that are typically associated with resistance to insulin, obesity, and cardiovascular disease, which could be due to correlation of depression and CHD. Tiao-Lai Huang 2015[13] reported the experimental data between serum lipid profiles in patients with or without suicide attempts, various clinical subtypes of major depression and with single episode or repeated episodes. The study was carried for a period of two years on 168 people among which 109 with major depression and 59 in a healthy group. Blood samples were collected from all the people to determine serum lipid profiles and statistical analysis was determined with body mass index adjustment.

From the results, it was found that there were no considerable differences of any kind in serum lipid profiles between depressive patients or any feature, with or without suicide attempts nor between depressive patients with single episode or repeated episodes. Finally, it was concluded that serum lipid profiles cannot be employed as biological markers to differentiate the suicide attempts, clinical subtypes and episodes in patients with major depression.

Raymonde et al 2004[14] examined the relation of depressive symptoms and HRT (Hormone Replacement Therapy) to lipoprotein lipids among postmenopausal women. Epidemiological studies were carried out for about 70 healthy, postmenopausal women. The parameters measured were depression scale and lipoprotein lipids.

The statistical analysis for body mass index, age, HRT status, the interaction of depression, depressive symptoms, and HRT exhibited 17% variance in low-density lipoprotein cholesterol and 16% variance in total cholesterol. It was also found that larger levels of depressive symptoms are related with lower cholesterol levels only among women who are not taking HRT. Mohammad et al 2014[15] carried out investigations on symptoms of depression in patients suffering from MDD (Maniac Depressive Disorder). Patients were selected on random process. Mean age of 32.25 years and fifty two percent of males were selected in a total of 60 patients. All were suffering from MDD. For all the patients, a standard medication of 40 mg/day citalopram were given and randomly assigned either to the atorvastatin group (20 mg/day) or to the placebo group. Periodically, blood lipid values were determined. Experts gave ratings on depressive symptoms via Hamilton Depression Rating Scales (HDRS) at different times.

It was found that HDRS scores reduced over a period of time. The significant Time by Group interaction exhibited that symptoms of depression reduced more in the atorvastatin group than in the placebo group. Further, it was noted that in the atorvastatin group triglyceride, cholesterol, and Low Density Lipids significantly decreased, and High Density Lipids significantly increased over time compared to placebo group. Further, it was observed that blood lipid and HDRS scores were not associated.

It was revealed from the studies that adjuvant atorvastatin group favourably influences symptoms of depression among patients suffering from severe MDD. Shili Chen et al 2014[16] performed studies on the anti-depressive effect of the conventional Chinese medicine Allium macrostemon. Studies were carried out in a rat model of depression simulated by exposure to chronic immobilisation stress. The focus of the main study was on lipid and acylcarnitine metabolism, which has a key role in the pathogenesis of depression.

Plasma lipid profiling was determined by ultrafast liquid chromatography and ion trap-time of flight mass spectrometry. Ultra-high performance liquid chromatography and triple quadruple mass spectrometry was employed to synthesise the plasma acylcarnitine profile. It was noted from the principal component analysis that there are distinct differences in plasma lipid and acylcarnitine profiles of depressed rats compared to control rats. This was validated by univariate analysis. It was further noted that several lysophosphatidylcholines, most medium- and long-chain acylcarnitines were found to increase while some phosphatidylcholines and triglycerides and TG were found to decrease in the plasma of depressed rats. These changes could be attributed to (i) depressed rats are part with inflammatory conditions and (ii) an incomplete β-oxidation of fatty acids. Figure 1 shows graphical view of the study carried out by the authors.

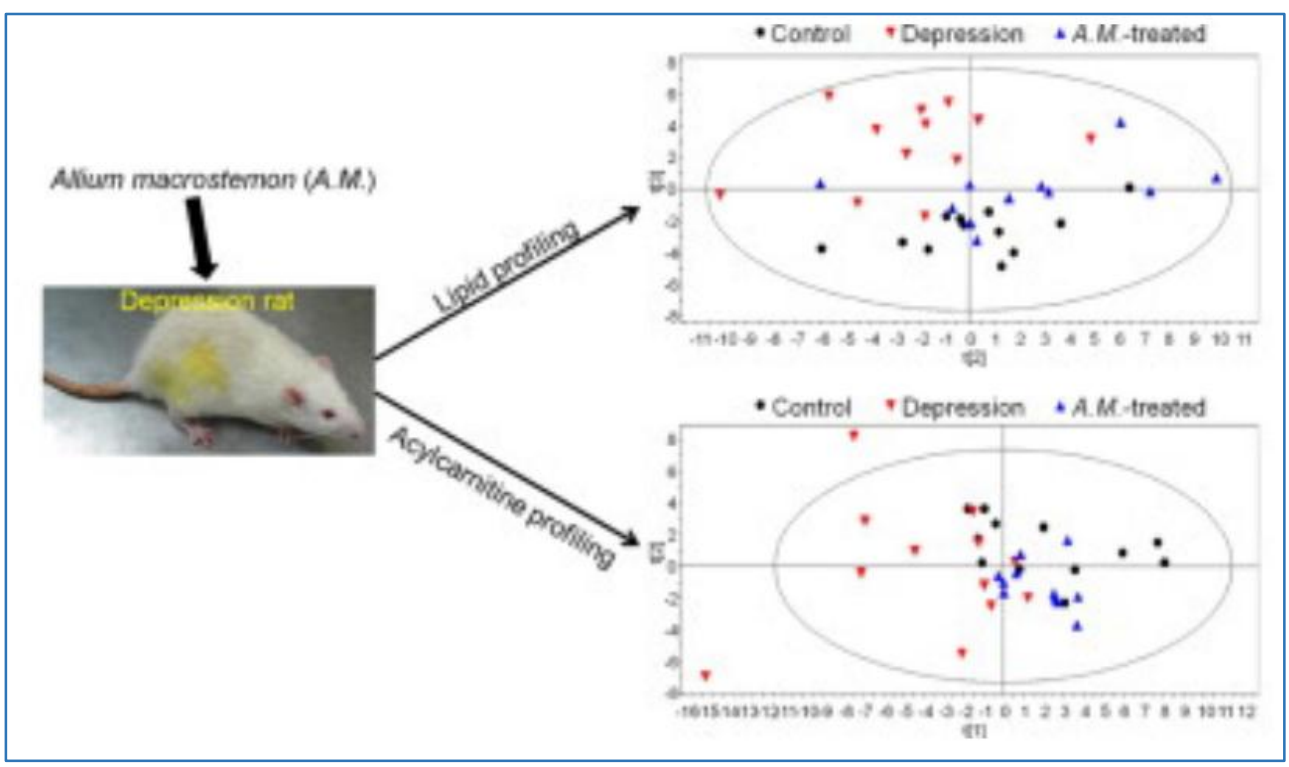

Fig. 1: Graphical Representation of Study carried out Shili Chen et al (2014)

Ahmad et al 2012[17] conducted investigations on 99 patients with major depressive disorder, Schizophrenia, bipolar mood disorder, Two time blood samples were taken, among which the first blood sample was taken before ECT and the second one was taken during 20 min. after ECT while the patients were on fasting. The parameters such as the cholesterol, blood glucose, LDL, triglyceride, HDL, and creatinine levels were determined. The blood glucose and cholesterol levels after ECT were found more than those of pre-ECT.

Significant difference was not found between pre- and post-ECT with respect to the levels of HDL, LDL, triglyceride, and creatinine. Further, the type of psychiatric disorder, height, weight, age, and gender could not be related to the post-ECT glucose level. In general, ECT might immediately increase the total cholesterol levels and blood glucose, while it does not affect any of the other specified parameters. From the study, it can be inferred that these increases appear to be independent of the type of psychiatric disorders. Tiao et al 2003[18] made investigations to know the relations between serum lipid, lipoprotein concentrations and depressive state, anxious state, and major depressive disorder. Authors performed studies on a total of 207 patients who have admitted for general health checkup over a period of one year. One Psychiatrist carried out all the investigations for all the patients to know the anxiety and depressive orders with the help of the Chinese Health Questionnaire, the Taiwanese Depression Questionnaire and the semi-structured clinical interview for DSM-IV.

For estimation of serum lipid and lipoprotein concentrations and physical examination, blood samples were collected simultaneously. It was found that for patients (i) who did not have regular checkup, had low high-density lipoprotein (HDL) cholesterol (ii) the ratio of total cholesterol TC/HDL differed significantly between depressive state, anxious state and normal groups in men after taking care of age adjustment (iii) the ratios of TC/HDL and low-density lipoprotein (LDL)/HDL showed significant differences between patients having major depressive disorder and normal controls in the case of women.

SUMMARY AND CONCLUDING REMARKS: It is found from the literature that there is correlation between depression and low lipid profile. But, the mechanisms or factors responsible for this relationship or depression are not understood properly. There are some evidences or proofs that low lipid levels may cause suicide in depressed patients. The research gap is to identify whether low serum lipid levels are in relation with suicide ideation or are with central serotonin function. Study on low serum lipid levels and suicide ideation yielded a relationship between low lipids and suicide ideation which is independent of both body mass index and body weight.

Cholesterol is found to be reduced in depressed patients. Electroconvulsive therapy (ECT) is found to be a highly effective treatment option for specific forms of depression. Like for other non-pharmacological therapies, targeting depression such as psychotherapy or sleep deprivation, there is a lack of evidence about the effects on peripheral lipid parameters. The role of serum lipid profiles as biological markers to differentiate the clinical subtypes, suicide attempts and episodes in patients with depression is found to be minimum. It is further noted from the literature that naturally occurring low cholesterol levels were related to increased depressive symptoms predominantly in men. However, depression is found to be more common among women, which enhances during the menopause, and may be influenced by hormone replacement therapy.

Liquid chromatography or mass spectrometry-based quantitative metabolic profiling method is observed to be a useful tool to estimate the metabolic changes in depression. It is noted that there are controversies about the effect of ECT on blood glucose level apart from the other effects such as blood cholesterol, LDL, HDL, and triglyceride levels. These aspects can be investigated for future studies. A role for glycerolipids is one of the emerging areas in the control of anxiety-related behaviours, whereas glycerophospholipids appear to be important for the therapeutic action of antidepressant drugs.

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