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Abstract- The reliable diagnostic identification of neuropsychiatric disorders such as schizophrenia, bipolar disease, and depression has been associated with some biological markers (genomics, proteomics, metabolomics) but to date, these markers do not have the sensitivity/specificity of a diagnostic test. Biomarker tests that are relevant to global chronic disease are now applicable to neuropsychiatric diseases to prevent autoimmune disease, endoplasmic reticulum stress associated mitophagy with relevance to neuron apoptosis. Metabolic abnormalities has been linked to neuropsychiatric disorder with the careful nutritional assessment of patients reported in many published studies. Early interventions with genomic medicine now assist in the prevention of autoimmune disease associated with global chronic disease and neuropsychiatric disorders.

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Abstract- The reliable diagnostic identification of neuropsychiatric disorders such as schizophrenia, bipolar disease, and depression has been associated with some biological markers (genomics, proteomics, metabolomics) but to date, these markers do not have the sensitivity/specificity of a diagnostic test. Biomarker tests that are relevant to global chronic disease are now applicable to neuropsychiatric diseases to prevent autoimmune disease, endoplasmic reticulum stress associated mitophagy with relevance to neuron apoptosis. Metabolic abnormalities has been linked to neuropsychiatric disorder with the careful nutritional assessment of patients reported in many published studies. Early interventions with genomic medicine now assist in the prevention of autoimmune disease associated with global chronic disease and neuropsychiatric disorders. Functional foods that contain appropriate doses of activators will allow modulation of neuropsychiatric diseases at the nuclear receptor level with the maintenance of neuron endoplasmic reticulum stress and the prevention of mitophagy associated with accelerated neurodegeneration.

Keywords: neuropsychiatric; schizophrenia; depression; bipolar disease; diagnosis; mitophagy; endoplasmic reticulum stress; amyloid beta; genomic medicine; sirtuin 1; global; chronic disease; neurodegeneration.

Abbreviations: NAFLD, non alcoholic fatty liver disease, ER, endoplasmic reticulum, LPS, bacterial lipopolysaccharides, NO, nitric oxide, Sirt 1, Sirtuin 1.

I. Introduction

Neuroscience research has become crucial to understand the complexity of neuropsychiatry disorders and assist with the diagnosis and treatment of the various disorders [1]. Neuropsychiatric disorders such as schizophrenia, depression, bipolar disease, autism, attention deficit hyperactivity disorder and neurodegenerative diseases such as Parkinson's disease, Huntington's disease, and Alzheimer's disease have increased in various communities. The global chronic disease epidemic has indicated that nonalcoholic fatty liver disease (NAFLD) and diabetes (Figure 1) will reach epidemic levels with 30% of the population affected with complications such as cardiovascular disease, kidney disease and neurodegenerative diseases [2,3]. Neuropsychiatric disorders may now be connected to the global chronic disease epidemic [2] with early diagnosis essential to prevent accelerated neurodegeneration and to improve medical therapy in neuropsychiatric patients [4-6].

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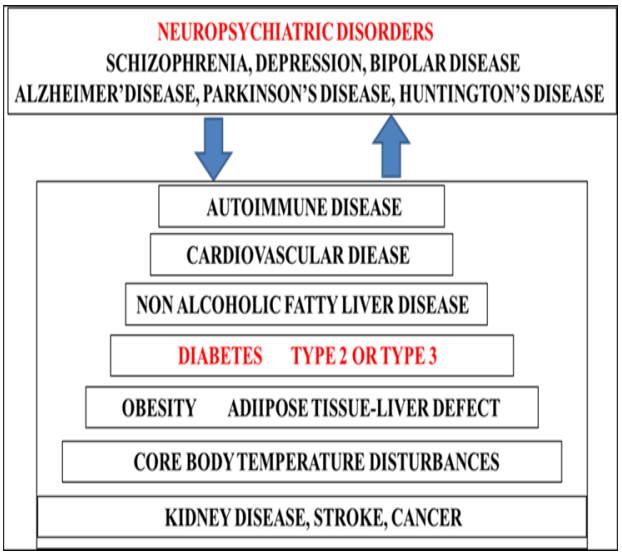

Figure 1: Connections between global chronic disease and neuropsychiatric disorders indicate insulin resistance and immune reactions interfere with the diagnosis and treatment of neuropsychiatric disturbances such as schizophrenia, depression, bipolar disorder, autism, and neurodegenerative diseases.

Insulin resistance in NAFLD, obesity, and diabetes involve autoimmune alterations in various tissues such as the adipose tissue, heart, liver and kidney that may determine accelerated brain aging and lifespan with relevance to neuropsychiatric disorders (Figure 1) [7-13]. The role of nutrition, lifestyle and environmental factors on increased oxidative stress, overactive immune system, and inactivation of anti-aging genes [14] has increased interest in the treatment, care, and diagnosis of neuropsychiatric disorders-early diagnosis with relevance to anti-aging genesis critical to prevent autoimmune reactions [3,7,14] associated withmajor subcellular alterations such as mitochondrial apoptosis and endoplasmic reticulum (ER) stress in neurons [15-21] that may lead to accelerated programmed cell death in neuropsychiatric conditions and global chronic disease.

a) Sirtuin 1 and Global chronic disease with relevance to ER stress and mitophagy in neuropsychiatric disorders

Specific genes and novel mutations were identified in neuropsychiatric conditions with gene variants involved in cognitive disorders in these patients [22-24]. These genes may not allow early diagnosis and

reversal of the complications of these neuropsychiatric disorders. In recent years the discovery of anti-aging genes and their inactivation [25, 26] may now be relevant to the epigenetics of neuropsychiatric disorders [27, 28]. The anti-aging gene Sirtuin 1 (Sirt 1) has become important to neuropsychiatric conditions with its connections to schizophrenia, depression, bipolar disease and autism [29-36]. Sirt 1 dysregulation is critical to the development of global chronic disease with Sirt 1 effects on chromatin alterations (modeling) that influence the DNA sequence, DNA repair, DNA methylation and histone modifications [25, 26]. Sirt 1 is a nicotinamide adenine dinucleotide dependent-class III histone deacetylase that targets transcription factors such as peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC 1-<alpha>), mitochondrial biogenesis, p53, pregnane X receptor (PXR) to adapt gene expression to metabolic activity, insulin resistance and inflammation [25, 26]. Sirt 1 mediated deacetylation of the transcriptional factor FoxO3a represses Rho-associated protein kinase-1 gene expression was associated with the reduction of amyloid beta generation [14]. In mammalian cells, Sirt 1 is linked to autoimmune disease [3, 7] and the regulation of telomere maintenance and length [26]. Sirt 1 and its association with neuron senescence [37] was connected to Alzheimer's disease and other neurodegenerative diseases.

Inactivation of anti-aging genes such as Sirt 1 may supersede the genetic findings in neuropsychiatric disorders and the Sirt 1 gene now associated with cell abnormalities (Figure 2) in neuropsychiatric conditions. Mitochondrial alterations and ER stress in global chronic disease have become of principal concern to neuroinflammation in neuropsychiatric conditions and neurodegenerative diseases. The repression of Sirt 1 in global illness [2, 3] and ER stress-induced mitophagy (Figure 2) [38-42] may be relevant to the diagnosis and treatment of neuropsychiatric patients in various global communities. Sirt 1 in neurons is critical for the prevention of cholesterol dyshomeostasis with toxic amyloid beta formation (Figure 2) involved in ER stress-induced mitophagy and neuron survival [43]. The connections between Sirt 1 and neuropsychiatric conditions are relevant to Sirt 1's role in autoimmune disease and amyloid beta aggregation [3, 7, 43]. In the developing with increased plasma bacterial lipopolysaccharides (LPS), Sirt 1 may be repressed [44] with relevance to LPS in cell membranes that bind to cholesterol/sphingomyelin domain with an acceleration of toxic amyloid beta oligomerization in neuropsychiatric disorders [45-47].

In neuropsychiatric disorders [12, 13, 48, 49] alterations in neuron membranes have become of prime concern with relevance to defective phospholipid metabolism in these patients. Lipid membrane abnormalities may affect dopamine signaling in schizophrenia and phospholipase A2 abnormalities responsible for altered brain membranes. The defective neuron amyloid beta pathway (Figure 2) is now relevant to neuropsychiatric disorders such as schizophrenia, depression and bipolar disease and applicable to disturbed membrane cholesterol homeostasis and toxic amyloid beta oligomer formation in neurons (Figure 2). In chronic diseases such as NAFLD, obesity, and diabetes alterations in membrane phospholipids are connected to the defective amyloid beta clearance pathway [43, 47] with effects on neuron membranes with toxic amyloid beta oligomerization associated with neuron cell apoptosis (Figure 2). Phospholipid composition such as phosphatidylinositol lower membrane cholesterol (Figure 2) and amyloid beta with prevention of toxic amyloid beta aggregation [50].

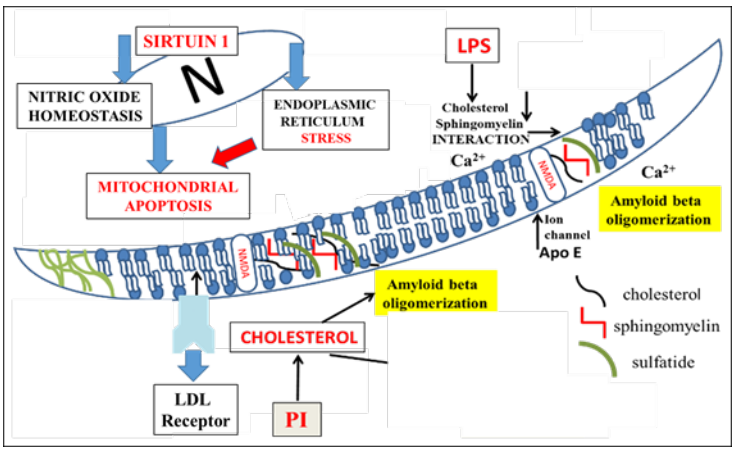

Figure 2: Inactivation of genes such as Sirtuin 1 (Sirt 1) is associated with ER stress and the induction of mitophagy in neuropsychiatric disorders. Cholesterol dysregulation and toxic amyloid beta formation are associated with Sirt 1 inactivation by LPS with relevance to neuropsychiatric diseases in the developing world. Phosphatidylinositol (PI) may reduce membrane cholesterol levels and amyloid beta oligomers to treat mitophagy and ER stress in liver and brain diseases (2). N- Nucleus.

Nitric oxide (NO) is now a crucial player in neuropsychiatric disease and associated with schizophrenia, bipolar disorder and major depression [51, 52]. NO as a lipophile acts as an intracellular and intercellular messenger that is critically regulated by cellular Sirt 1 [53, 54] with NO involved in cell communication between neuron cells in the brain. The connections between the immune system and neuropsychiatric diseases involve NO and implicate Sirt 1 regulation of NO in autoimmune disease [51]. The importance of Sirt 1 in neuropsychiatric disorders is relevant to NO homeostasis as the primary defect (Figure 2) with connections to secondary subcellular and membrane alterations in neuropsychiatric disturbances [51, 52].

b) *Diagnosis of mitophagy in neuropsychiatric patients with global chronic disease*

The criteria are allowing reliable diagnostic identification of schizophrenia, bipolar disease and depression are defined by subjective experiences (symptoms), loss of function (behavioral impairments) and variable patterns of the disease. Some biological markers (genomics, proteomics, metabolomics) were associated with the disorder, but to date, these markers do not have the sensitivity/specificity of a diagnostic test [55-60]. The early diagnosis of neuropsychiatric disorders now involves measurements of nuclear, cellular and plasma Sirt 1 levels (Figure 3) [43, 61]. Measurements of magnesium [62, 63] and zinc may be vital to prevent inactivation of brain Sirt 1 activity. Sirt 1 nuclear receptor control of ER-mitochondria interaction may need to assess plasma LPS levels to avoid complete repression of Sirt 1 and induction of mitophagy induced ER stress in neuropsychiatry diseases.

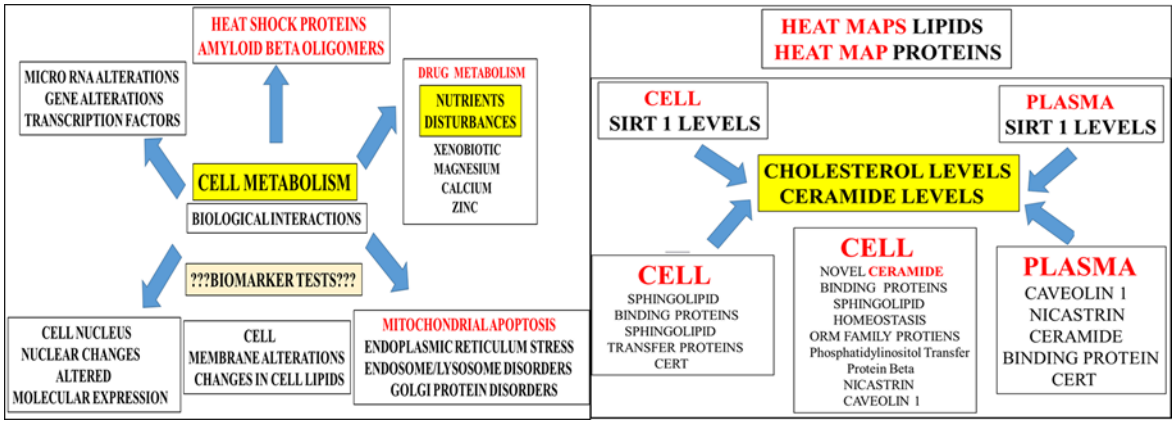

Figure 3: Biomarker tests for mitophagy and ER stress in neuropsychiatric disorders were required for reversal and stabilization of the disease. Genomic, proteomic and lipidomic experiments are critical to assess the induction of mitophagy with relevance Sirt 1 and lipid binding protein analysis in plasma and tissues. Plasma lipid measurements of cholesterol, ceramide, sphingolipids, and phospholipids (phosphatidylinositol) are essential to determine early mitophagy-ER stress disorders in neuropsychiatric disorders.

Lipidomic analysis [64] of plasma lipids (sphingolipids/ceramides) may reflect changes in the periphery and central nervous system and correlation with plasma Sirt 1, ceramide binding proteins and sphingolipid transfer proteins may be important in neuropsychiatric diseases. Measurements of micro RNA (mir-34a, mir-122, mir-132) may indicate repression of Sirt 1 [3] and relevant to the lipidomic analysis. The levels of plasma heat shock protein (Figure 3) may reflect inhibition of Sirt 1 activity and pertinent to activation of autoimmune disease [43]. These biomarker tests (Figure 3) that are relevant to global chronic illness [65,66] are now appropriate to the early diagnosis and treatment of neuropsychiatric disturbances.

c) *Nutritional Biotherapy and Management of neuropsychiatric114 patients*

In neuropsychiatric disorders such as schizophrenia, a healthy and low carbohydrate diet with careful nutritional assessment [67, 68] is required to prevent obesity, diabetes, and NAFLD and stabilize complications of the disease. A systematic review of the literature indicates that metabolic abnormalities were linked to schizophrenia [69]. In depression and mental illness a complete nutritional diet [70] is required to improve behavior, emotion, and cognition with consumption of low carbohydrates, proteins (amino acids/brain function, essential fatty acids (omega-3), vitamins (B, B12, folate) and minerals (calcium, chromium, iodine, iron, lithium, selenium, zinc). Diets that contain functional foods such as biologically active Sirt 1 activator are now essential to maintain patients with neuropsychiatric disorders [64].

Nutritional biotherapy is now critical to the maintenance of the calorie sensitive gene Sirt 1 with excessive glucose and fatty acid that is involved in Sirt 1 repression. Early interventions with the use of genomic

medicine [71, 72] and Sirt 1 activatorsare essential to the treatment of autoimmune disease and neurodegeneration. Appropriate doses of Sirt 1 activators such as pyruvic acid, resveratrol, leucine, rutin, and alpha lipoic acid will prevent mitophagy and ER stress by modulation at the cellular level of neuropsychiatric disease. Phosphatidylinositol (4gm/day) should be consumed [50] to halt neuron membrane cholesterol and amyloid beta disturbances. Appetite control (Figure 4) with cautious nutrient (glucose/fatty acid) intake will maintain the calorie sensitive Sirt 1 activity and stabilize schizophrenia, depression and bipolar disease. The contents of caffeine (Figure 4) in the diet in neuropsychiatric patients should be carefully controlled to prevent caffeine associated neuron disturbances in the brain [63]. In the developing world with elevated LPS levels [44-47] nutritional biotherapy is critical to maintaining Sirt 1 activity and rapid hepatic drug and xenobiotic metabolism [14]. The use of anti-depressants, antipsychotics and other drug therapy in neuropsychiatric patients require intact hepatic and brain Sirt 1 activity. Sirt 1 inhibitors [43, 63] may nullify drug therapy with drug-drug interactions (Figure 4) as complications of neuropsychiatric disorders. Prevention of stress and maintenance of core body temperature were required for the prevention of autoimmune disease [43, 54] in these patients.

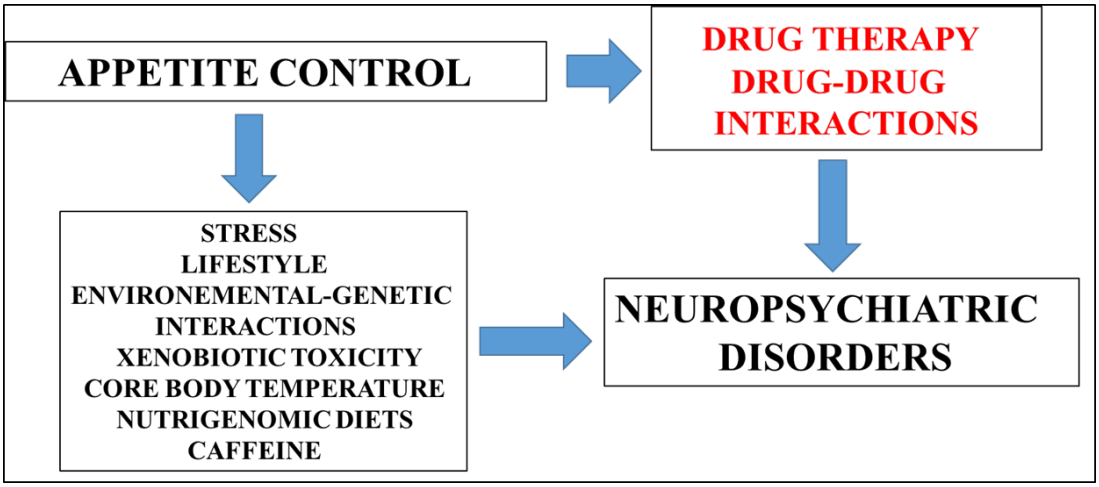

Figure 4: Appetite control is essential to maintain Sirt 1 activityand therapeutic drug metabolism with the prevention of drug-drug interactions in neuropsychiatric disorders. Nutrigenomic diets that contain Sirt 1 activators are vital for the treatment of neuropsychiatric disease and the prevention of mitophagy induced ER stress. Caffeine intake should be controlled to maintain therapeutic drug treatment. Excessive anxiety and pressure should be avoided to preserve nitric oxide homeostasis and immune reactions with relevance to autoimmune and neurodegenerative diseases.

II. Conclusion

Early diagnosis and the measurement of plasma/tissue Sirt 1 levels in neuropsychiatric disorders will allow treatment of schizophrenia, depression and bipolar disease. Plasma analysis of Sirt 1 with extensive lipidomic analysis may indicate the risk of mitophagy and ER stress with relevance to autoimmune disease in neuropsychiatric disorders. Nutritional biotherapy and genomic medicine that involves the activation of Sirt 1 at the nuclear receptor level may allow modulation/reversal of mitophagy and ER stress in psychiatric disorders and neurodegenerative diseases such as Alzheimer/s disease, Parkinson's disease, and Huntington's disease.

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