Early Diagnosis and Nutritional Treatment Stabilizes Neuropsychiatric Disorders

Ian James Martins

Received: 15 December 2017 Accepted: 31 December 2017 Published: 15 January 2018

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.

Index terms— neuropsychiatric; schizophrenia; depression; bipolar disease; diagnosis; mitophagy; endoplasmic reticulum stress

1 Introduction

euroscience 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][5][6]. 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][8][9][10][11][12][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][16][17][18][19][20][21] that may lead to accelerated programmed cell death in neuropsychiatric conditions and global chronic disease.

2 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][23][24]. These

genes may not allow early diagnosis and N Author: School of Medical Sciences, Edith Cowan University, Western Australia 6009, Australia. e-mail: i.martins@ecu.edu.au A 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][30][31][32][33][34][35][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 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][39][40][41][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 stressinduced 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][46][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]. A 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].

3 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][56][57][58][59][60]. The early diagnosis of neuropsychiatric disorders now involves measurements of nuclear, cellular and plasma Sirt 1 levels (Figure **??**) [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 **??**: 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 **??**) may reflect inhibition of Sirt 1 activity and pertinent to activation of autoimmune disease [43]. These biomarker tests (Figure **??**) that are relevant to global chronic illness [65,66] are now appropriate to the early diagnosis and treatment of neuropsychiatric disturbances.

4 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].

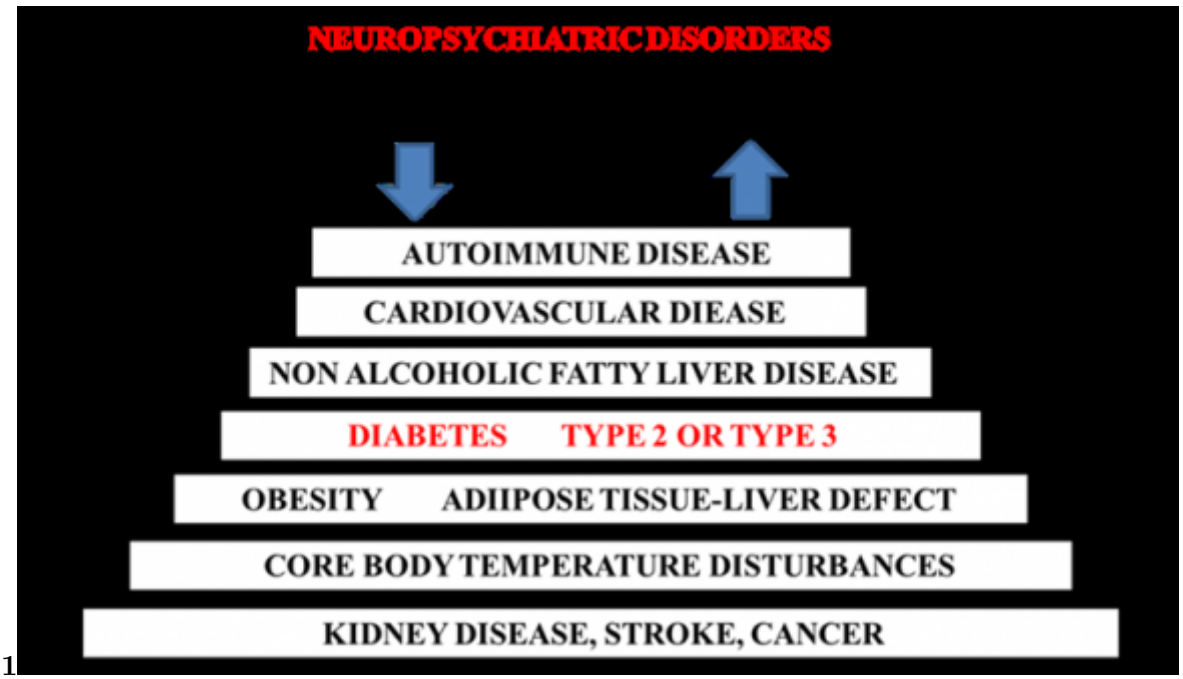
Nutritional biotherapy is now critical to the maintenance of the calorie sensitive gene Sirt 1 with excessive glucose and fatty acid that is involved in Sirt 1 repression. Early interventions with the use of genomic A medicine [71,72] and Sirt 1 activatorsare essential to the treatment of autoimmune 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][45][46][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. II.

5 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. [1] [2]

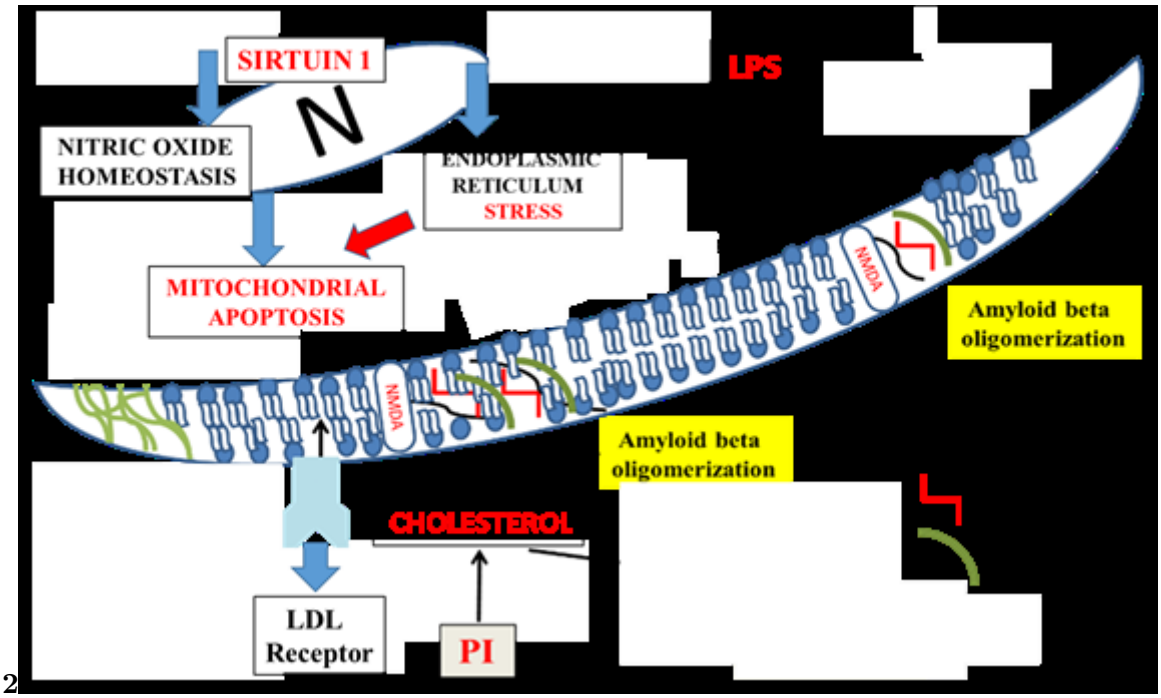
[1] Early Diagnosis and Nutritional Treatment Stabilizes Neuropsychiatric Disorders

[2] Year 2018



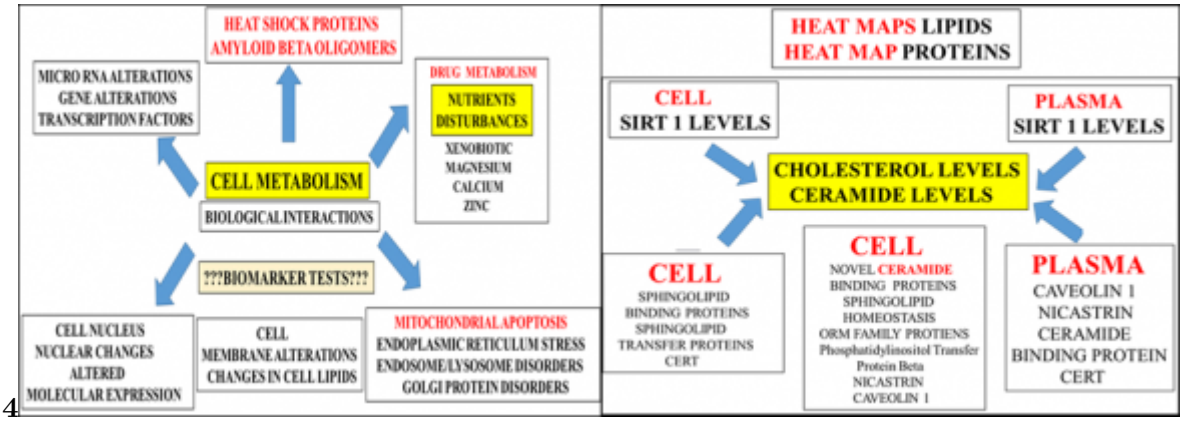
1

Figure 1: Figure 1 :



2

Figure 2: Figure 2 :



4

Figure 3: Figure 4 :

Figure 4:

.1 Acknowledgements

[BioMed Res Int] , *BioMed Res Int* 2017 p. .

[Mahgoub and Monteggia ()] , M Mahgoub , L M Monteggia . *Epigenetics and psychiatry* 2013. 10 p. . (Neurotherapeutics)

[Abe-Higuchi et al. ()] , N Abe-Higuchi , S Uchida , H Yamagata , F Higuchi , T Hobara . Hippocampal Sirtuin 1. 2016.

[Schaeffer et al. ()] 'Alterations of brain membranes in schizophrenia: impact of phospholipase A (2)'. E L Schaeffer , W F Gattaz , G P Eckert . *Curr Top Med Chem* 2012. 12 p. .

[Martins ()] 'Anti-Aging Genes Improve Appetite Regulation and Reverse Cell Senescence and'. I J Martins . *Apoptosis in Global Populations. AAR* 2016. 5 p. .

[Martins ()] 'Antimicrobial activity inactivation and toxic immune reactions induce Epilepsy in human'. I J Martins . *J Med Discov* 2017. 2 p. .

[Martins ()] 'Appetite Regulation and the Peripheral Sink Amyloid beta Clearance Pathway in Diabetes and Alzheimer's Disease. Top 10 Commentaries in Alzheimer's Disease'. I J Martins . www.avidscience.com *Avid Science* 2018. 2 p. .

[Goldman et al. ()] 'Awareness, Diagnosis, and Treatment of Depression'. L S Goldman , N H Nielsen , H C Champion . *J Gen Intern Med* 1999. 14 p. .

[Martinsi ()] 'Bacterial Lipopolysaccharides Change Membrane Fluidity with Relevance to Phospholipid and Amyloid Beta Dynamics in Alzheimer's Disease'. J Martinsi . *J Microb Biochem Technol* 2016. 8 p. .

[Kidd ()] 'Bipolar disorder and cell membrane dysfunction. Progress toward integrative management'. P M Kidd . *Altern Med Rev* 2004. 9 p. .

[Müller et al. ()] 'Brain membrane lipids in major depression and anxiety disorders'. C P Müller , M Reichel , C Mühle , C Rhein , E Gulbins . *Biochim Biophys Acta* 2015. 1851 p. .

[Patel et al. ()] 'Crosstalk between endoplasmic reticulum stress and oxidative stress in schizophrenia: The dawn of new therapeutic approaches'. S Patel , D Sharma , K Kalia , V Tiwari . *Neurosci Biobehav Rev* 2017. 83 p. .

[Martins ()] 'Diabetes and Organ Dysfunction in the Developing and Developed World'. I J Martins . *GJMR* 2015. 15 p. .

[Balhara ()] 'Diabetes and psychiatric disorders'. Y P S Balhara . *Indian J Endocrinol Metab* 2011. 15 p. .

[Taber et al. ()] 'Diagnosis and treatment of neuropsychiatric disorders'. K H Taber , R A Hurley , S C Yudofsky . *Annu Rev Med* 2010. 61 p. .

[Strassnig et al. ()] 'Dietary Intake of Patients with Schizophrenia'. M Strassnig , J S Brar , R Ganguli . *Psychiatry (Edgmont)* 2005. 2 p. .

[Koga et al. ()] 'Endoplasmic Reticulum (ER) Stress Induces Sirtuin 1 (SIRT1) Expression via the PI3K-Akt-GSK3? Signaling Pathway and Promotes Hepatocellular Injury'. T Koga , M A Suico , S Shimasaki , E Watanabe , Y Kai . *J Biol Chem* 2015. 290 p. .

[Sprenkle et al. ()] 'Endoplasmic reticulum stress and inflammation in the central nervous system'. N T Sprenkle , S G Sims , C L Sánchez , G P Meares . *Mol Neurodegener* 2017. 12 p. 42.

[Ptak and Petronis ()] 'Epigenetic approaches to psychiatric disorders'. C Ptak , A Petronis . *Dialogues Clin Neurosci* 2010. 12 p. .

[Martins ()] 'Functional Foods and Active molecules with relevance to Health and Chronic disease'. I J Martins . *FFHD* 2017. 7 p. .

[Martins ()] 'Genomic medicine and acute cardiovascular disease progression in diabetes'. I J Martins . *Res Chron Dis* 2018. 2 p. .

[Martins ()] 'Genomic Medicine and Endocrine Autoimmunity as Key to Mitochondrial Disease'. I J Martins . *Glob J Endocrinol Metab* 2018. 2 p. .

[Harvey et al. ()] P D Harvey , R K Heaton , W T Carpenter , M F Green , J M Gold . *Diagnosis of Schizophrenia: Consistency Across information Sources and Stability of the Condition*, 2012. 140 p. .

[Martins ()] *Heat Shock Gene Inactivation and Protein Aggregation with Links to Chronic Diseases*, I J Martins . 2018. 6 p. .

[Li et al. ()] 'Hepatic over expression of SIRT1 in mice attenuates endoplasmic reticulum stress and insulin resistance in the liver'. Y Li , S Xu , A Giles , K Nakamura , J W Lee . *FASEB J* 2011. 25 p. .

[Herskovits and Guarente ()] A Z Herskovits , L Guarente . *SIRT1 in neurodevelopment and brain senescence*, 2014. 81 p. .

[Martins ()] 'Increased Risk for Obesity and Diabetes with Neurodegeneration in Developing Countries. Top 10 Contribution on'. I J Martins . www.avid.science.com *Genetics. Avid Science* 2018. 1 p. .

[Kishi et al. ()] T Kishi , Y Fukuo , T Kitajima , T Okochi , Y Yamanouchi . *SIRT1 gene, schizophrenia and bipolar disorder in the Japanese population: an association study*, 2011. 10 p. .

[Lo Iacono et al. ()] L Lo Iacono , F Visco-Comandini , A Valzania , M T Viscomi , M Coviello . *Adversity in childhood and depression: linked through SIRT1*, 2015. 5 p. e629.

[Martins ()] *Magnesium Therapy Prevents Senescence with the Reversal of Diabetes and Alzheimer's Disease. Health*, I J Martins . 2016. 8 p. .

[Martins ()] I J Martins . *LPS Regulates Apolipoprotein E and A? Interactions with Effects on Acute Phase Proteins and Amyloidosis. AAR*, 2015. 4 p. .

[Martins ()] I J Martins . *Biomarker Tests and Ageing Science*, 2017. 1 p. .

[Tessier et al. ()] 'Membrane lipidomics in schizophrenia patients: a correlational study with clinical and cognitive manifestations'. C Tessier , K Sweers , A Frajerman , H Bergaoui , F Ferreri . *Transl Psychiatry* 2016. 6 p. e906.

[Marazziti et al. ()] 'Mitochondrial alterations and neuropsychiatric disorders'. D Marazziti , S Baroni , M Picchetti , P Landi , S Silvestri . *Curr Med Chem* 2011. 18 p. .

[Wallace ()] 'Mitochondrial Etiology of Neuropsychiatric Disorders'. D C A Wallace . *JAMA Psychiatry* 2017. 74 p. .

[Pei and Wallace ()] 'Mitochondrial Etiology of Neuropsychiatric Disorders'. L Pei , D C Wallace . *Biol Psychiatry* 2018. 83 p. .

[Dick et al. ()] 'Nature and nurture in neuropsychiatric genetics: where do we stand?'. D M Dick , B Riley , K S Kendler . *Dialogues Clin Neurosci* 2010. 12 p. .

[Katz et al. ()] 'Neuropsychiatric disorders at the presentation of type 2 diabetes mellitus in children'. Levitt Katz , L E Swami , S Abraham , M Murphy , K M Jawad , AF . *Pediatr Diabetes* 2005. 6 p. .

[Marin and Saneto ()] 'Neuropsychiatric Features in Primary Mitochondrial Disease'. S E Marin , R P Saneto . *Neurol Clin* 2016. 34 p. .

[Kota et al. ()] 'Neuropsychiatric screening in type 2 diabetes mellitus'. S K Kota , L K Meher , S Jammula , S V S Krishna , S K Kota . *Indian J Endocrinol Metab* 2012. 16 (Suppl1) p. .

[Akyol et al. ()] 'Nitric oxide as a physiopathological factor in neuropsychiatric disorders'. O Akyol , S S Zoroglu , F Armutcu , S Sahin , A Gurel . *In Vivo* 2004. 18 p. .

[Martins ()] 'Nutrition Therapy Regulates Caffeine Metabolism with Relevance to NAFLD and Induction of Type 3 Diabetes'. I J Martins . *J Diabetes Metab Disord* 2017. 4 p. 19.

[Martins ()] *Nutritional diets accelerate amyloid beta metabolism and prevent the induction of chronic diseases and Alzheimer's disease. Photon ebooks*, I J Martins . 2015. p. .

[Martins ()] 'Over nutrition Determines LPS Regulation of Mycotoxin Induced Neurotoxicity in Neurodegenerative Diseases'. I J Martins . *Int J Mol Sci* 2015. 16 p. .

[Rush ()] 'Problems associated with the diagnosis of depression'. A J Rush . *J Clin Psychiatry* 1990. 51 p. .

[Radtke et al. ()] F A Radtke , G Chapman , J Hall , Y A Syed . *Modulating Neuroinflammation to Treat Neuropsychiatric Disorders*, 2017.

[Ratnaseelan et al. ()] A M Ratnaseelan , I Tsilioni , T C Theoharides . *Effects of Mycotoxins on Neuropsychiatric Symptoms and Immune Processes*, 2018. 40 p. .

[Lindholm et al. ()] 'Recent Insights into the Role of Unfolded Protein Response in ER Stress in Health and Disease'. D Lindholm , L Korhonen , O Eriksson , S Kõks . *Front Cell Dev Biol* 2017. 5 p. 48.

[Lu et al. ()] 'Role and Possible Mechanisms of Sirt1 in Depression'. G Lu , J Li , H Zhang , X Zhao , L-J Yan . *Oxidative Medicine and Cellular Longevity* 2018. 2018 p. .

[Bu et al. ()] 'Role of SIRT1/PGC-1? in mitochondrial oxidative stress in autistic spectrum disorder'. X Bu , D Wu , X Lu , L Yang , X Xu . *Neuropsychiatr Dis Treat* 2017. 13 p. .

[Song and Kim ()] 'Role of Sirtuins in Linking Metabolic Syndrome with Depression'. J Song , J Kim . *Front Cell Neurosci* 2016. 10 p. 86.

[Kraft and Westman ()] 'Schizophrenia, gluten, and low-carbohydrate, ketogenic diets: a case report and review of the literature'. B D Kraft , E C Westman . 6:10. *Nutr Metab* 2009.

[Signaling Mediates Depression-like Behavior Biol Psychiatry] 'Signaling Mediates Depression-like Behavior'. *Biol Psychiatry* 80 p. .

[Martins ()] 'Single Gene Inactivation with Implications to Diabetes and Multiple Organ Dysfunction Syndrome'. I J Martins . *J Clin Epigenet* 2017. 3 p. 24.

.1 Acknowledgements

[Jung et al. ()] 'SIRT1 attenuates palmitate-induced endoplasmic reticulum stress and insulin resistance in HepG2 cells via induction of oxygen-regulated protein 150'. T W Jung , K T Lee , M W Lee , K H Ka . *Biochem Biophys Res Commun* 2012. 422 p. .

[Kim et al. ()] 'SIRT1 Mediates Depression-Like Behaviors in the Nucleus Accumbens'. H-D Kim , J Hesterman , T Call , S Magazu , E Keeley . *J Neurosci* 2016. 36 p. .

[Prola et al. ()] 'SIRT1 protects the heart from ER stress-induced cell death through eIF2? deacetylation'. A Prola , J Pires Da Silva , A Guilbert , L Lecru , J Piquereau . *Cell Death Differ* 2017. 24 p. .

[Martins ()] *Sirtuin 1, a Diagnostic Protein Marker and its Relevance to Chronic Disease and Therapeutic Drug Interventions*, I J Martins . 2018. p. .

[Corvin et al. ()] 'The cognitive genetics of neuropsychiatric disorders'. A Corvin , G Donohoe , A Hargreaves , L Gallagher , M Gill . *Curr Top Behav Neurosci* 2012. 12 p. .

[Culpepper ()] 'The Diagnosis and Treatment of Bipolar Disorder: Decision-Making in Primary Care'. L Culpepper . PCC.13r01609. *Prim Care Companion CNS Disord* 2014. 16.

[Smith et al. ()] 'The diagnosis of depression: current and emerging methods'. K M Smith , P F Renshaw , J Bilello . *Compr Psychiatry* 2013. 54 p. .

[Jablensky ()] 'The diagnostic concept of schizophrenia: its history, evolution, and future prospects'. A Jablensky . *Dialogues Clin Neurosci* 2010. 12 p. .

[Dipasquale et al. ()] 'The dietary pattern of patients with schizophrenia: a systematic review'. S Dipasquale , C M Pariante , P Dazzan , E Aguglia , P Mcguire . *J Psychiatr Res* 2013. 47 p. .

[Martins ()] 'The Future of Biomarkers Tests and Genomic Medicine in Global Organ Disease'. I J Martins . *Microbiology and Infectious Diseases* 2017. 1 p. .

[Martins ()] 'The Future of Genomic Medicine Involves the Maintenance of Sirtuin 1 in Global Populations'. I J Martins . *Int J Mol Biol* 2017. 2 p. 13.

[Heinzen et al. ()] 'The genetics of neuropsychiatric diseases: looking in and beyond the exome'. E L Heinzen , B M Neale , S F Traynelis , A S Allen , D B Goldstein . *Annu Rev Neurosci* 2015. 38 p. .

[Kerr et al. ()] 'The immune system and neuropsychiatric diseases'. D Kerr , C Krishnan , M L Pucak , J Carmen . *Int Rev Psychiatry* 2005. 17 p. .

[Morris and Berk ()] 'The many roads to mitochondrial dysfunction in neuroimmune and neuropsychiatric disorders'. G Morris , M Berk . *BMC Med* 2015. 13 p. 68.

[Horrobin et al. ()] 'The membrane hypothesis of schizophrenia'. D F Horrobin , A I Glen , K Vaddadi . *Schizophr Res* 1994. 13 p. .

[Karatinos et al. ()] 'The nitric oxide pathway: potential implications for treatment of neuropsychiatric disorders'. J Karatinos , R B Rosse , S I Deutsch . *Clin Neuropharmacol* 1995. 18 p. .

[Chan et al. ()] 'The role of de novo protein synthesis and SIRT1 in ER stress-induced Atf4 and Chop mRNA expression in mammalian cells'. S M H Chan , X Zhao , A Elfowiris , C Ratnam , T P Herbert . *Biochimie* 2017. 138 p. .

[Chatterjee and Abel ()] 'To Stay Happy, Keep Your SIRT1 Active'. S Chatterjee , T Abel . *Biol Psychiatry* 2016. 80 p. .

[Rao et al. ()] 'Understanding nutrition, depression and mental illnesses'. Sathyanarayana Rao , T S Asha , M R Ramesh , BN , Jagannatha Rao , KS . *Indian J Psychiatry* 2008. 50 p. .

[Martins ()] 'Unhealthy Nutrigenomic Diets Accelerate NAFLD and Adiposity in Global communities'. I J Martins . *J Mol Genet Med* 2015. 9 p. .