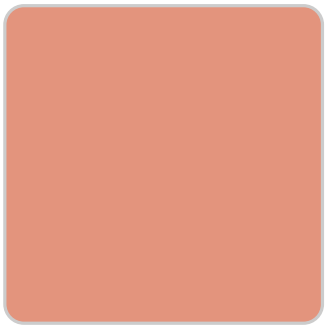
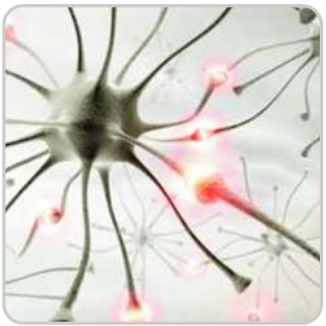
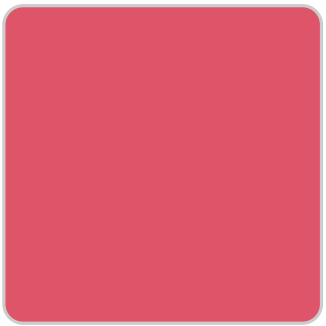
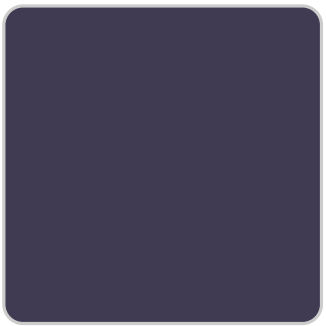
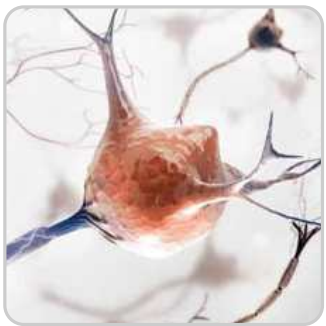
The Ontogeny of Neurodegenerations

Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease - Human Atavistic Archaeal Colonies with Neanderthal Metabolonomics

Ravikumar Kurup and Parameswara Achutha Kurup





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Contents

1

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A Cholesterol and Actinide Dependent Shadow Biosphere of Archaea and Viroids in Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-4]. Endogenous digoxin has been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[4]. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[7, 9].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, dopamine, serotonin,

pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-7 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
PD	23.46	1.87	59.27	8.86	22.67	2.29	57.69	5.29
AD	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
MND	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
PD	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
MND	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on HMG CoA reductase and ATP synthase.*

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy+Cipro)		ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.30	0.20	18.35	0.35	4.40	0.11	18.78	0.11
PD	23.09	1.69	61.62	8.69	23.09	1.90	66.15	4.09
AD	23.43	1.68	61.68	8.32	23.58	2.08	66.21	3.69
MND	22.38	2.38	60.65	5.27	23.00	1.64	66.67	4.21
	F value 319.332 P value < 0.001		F value 199.553 P value < 0.001		F value 449.503 P value < 0.001		F value 673.081 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on digoxin and bile acids.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
PD	0.51	0.05	0.199	0.027	22.61	2.22	66.62	4.99
AD	0.55	0.03	0.192	0.040	22.12	2.19	62.86	6.28
MND	0.53	0.06	0.212	0.045	23.30	1.88	62.49	7.26
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 290.441 P value < 0.001		F value 203.651 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and hexokinase.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
PD	20.94	1.54	62.76	8.52	23.33	1.79	62.50	5.56
AD	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
MND	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and delta amino levulinic acid.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
PD	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MND	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 7 *Effect of rutile and antibiotics on dopamine and serotonin.*

Group	Dopamine % (Increase with Rutile)		Dopamine % (Decrease with Doxy+Cipro)		5 HT % change (Increase with Rutile)		5 HT % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
PD	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
AD	23.66	1.67	65.97	3.36	23.09	1.81	65.86	4.27
MND	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15]. There was also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[8]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[14]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH, serotonin and dopamine was also detected[16]. The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase activity were increased. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[18]. Archaeal pyruvate can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the

noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[19]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[20]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[19, 20]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality[21]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The RNA viroids can regulate mRNA function by RNA interference[18]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression. This can lead to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

NMDA receptors can be modulated by digoxin induced calcium oscillations resulting NMDA activity, PAH increasing NMDA activity as well as viroid induced RNA interference[4]. The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. The dipolar PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state[22] inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world[4, 22]. Extrasensory perception of low level EMF can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaea can regulate limbic lobe transmission with archaeal

cholesterol aromatase/ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline[16]. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance[4]. Right hemispheric dominance can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signaling can activate NFKB producing chronic immune activation[4, 23]. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[24]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[24]. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy

needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway. The archaeal bile acids are steroidal hormones which can bind GPCR and modulate D2 regulating the conversion of T4 to T3 which activates uncoupling proteins, can activate NRF ½ inducing NQO1, GST, HOI reducing redox stress, can bind FXR regulating insulin receptor sensitivity and bind PXR inducing the bile acid shunt pathway of cholesterol detoxification[25]. The digoxin and PAH induced increased intracellular calcium can lead to PT pore dysfunction, cell death and neuronal degeneration[4]. The archaeal cholesterol catabolism can deplete the cell membranes of cholesterol resulting in organelle dysfunction and degeneration. The RNA viroids can recombine with HERV sequences and get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by RNA viroid binding producing Prion Disease. HERV sequences and prions can lead onto neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[4].

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The Archaeal Induced Stem Cell Conversion Produces an Epidemic Benjamin Buttons Reverse Aging Syndrome Leading to in Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

The global warming produces increased acidity and atmospheric carbon dioxide resulting in extremophilic archaeal symbiosis in humans. The archaeal symbiosis results in neanderthalisation of humans. The archaea induced uncoupling proteins producing the primitive Warburg phenotype and stem cell metabolonomics. The archaeal metabolites of cholesterol digoxin, bile acids and short chain fatty acids induce uncoupling proteins. The lysosomal enzymes a marker of stem cell conversion are markedly increased along with genesis of the archaeal phenotype in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. In all these systemic diseases there is somatic cell transformation to stem cell and lose of function. The neurons become immature and lose their dendritic spines and connectivity. This results in loss of neuronal function and reversion to archaeal magnetite mediated extrasensory perception of low level of EMF. Exposure to low level of EMF results in brain changes. This results in prefrontal cortex atrophy. The primitive brain areas of cerebellum and brain stem become hypertrophic. The somatic and neuronal cell proliferates and there is neanderthalisation of the brain and body[1-17].

Reason judgment and logic is a function of the cerebral cortex especially the prefrontal lobe. Prefrontal lobe function needs dynamic synaptic connectivity which is produced by jumping genes mediated by human endogenous retroviral sequences. The cerebellum is the site of impulsive behavior and the unconscious behavior. The cerebellar and subcortical brain connections are predominantly archaeal colony networks. The global warming and exposure to low level of EMF leads to actinidic archaeal growth in the brain and increased archaeal magnetite mediated perception of low level of EMF. This leads to prefrontal cortex atrophy and cerebellar dominance. The conscious becomes minimal and unconscious brain

takes over. The study assessed archaeal growth as assessed by cytochrome F420 activity and stem cell type metabolonomics in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-17].

Materials and Methods

The blood samples were drawn from neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The estimations done in the blood samples collected include cytochrome F420 activity. Blood lactate, pyruvate, hexokinase, cytochrome C, cytochrome F420, digoxin, bile acids, butyrate and propionate were estimated.

Results

The blood samples of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease had increased blood lactate and pyruvate, increased RBC hexokinase, increased serum cytochrome C and serum cytochrome F420, increased serum digoxin, bile acids, butyrate and propionate. The disease state had increased cytochrome F420 activity. The serum cytochrome C levels in the blood were increased. This suggested mitochondrial dysfunction. There was an increased in glycolysis as suggested by increased RBC hexokinase activity and lactic acidosis. Owing to the mitochondrial dysfunction and pyruvate dehydrogenase inhibition there was pyruvate accumulation. The pyruvate was converted to lactate by the Cori cycle and also to glutamate and ammonia. This metabolism is suggestive of the Warburg phenotype and stem cell conversion. The stem cells depend on Warburg anaerobic glycolysis for energetics and have a mitochondrial dysfunction. The

lysosomal enzyme beta galactosidase activity was increased in the disease group suggesting stem cell conversion.

Table 1.

Group	Cytochrome F 420		Serum cyto C (ng/ml)		Lactate (mg/dl)		Pyruvate (umol/l)		RBC hexokinase (ug glu phos/ hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal population	1.00	0.00	2.79	0.28	7.38	0.31	40.51	1.42	1.66	0.45
MND	4.00	0.00	12.65	1.06	24.28	1.69	95.44	12.04	9.30	3.98
AD	4.00	0.00	11.94	0.86	22.04	0.64	97.26	8.26	8.46	3.63
PD	4.00	0.00	12.81	0.90	26.20	5.29	97.77	13.24	8.99	3.27
Low level background radiation	4.00	0.00	12.26	1.00	23.31	1.46	103.28	11.47	7.58	3.09
F value	0.001		445.772		162.945		154.701		18.187	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 2.

Group	ACOA (mg/dl)		Glutamate (mg/dl)		Se. ammonia (ug/dl)		RBC digoxin (ng/ml RBC Susp)		Beta galactosidase activity in serum (IU/ml)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal population	8.75	0.38	0.65	0.03	50.60	1.42	0.58	0.07	17.75	0.72
MND	1.95	0.06	3.14	0.32	94.60	8.52	1.34	0.31	51.16	7.78
AD	2.19	0.15	3.53	0.39	95.37	4.66	1.10	0.08	51.56	3.69
PD	2.13	0.17	3.25	0.40	94.77	2.86	1.50	0.20	46.82	4.73
Low level background radiation	2.14	0.19	3.47	0.37	102.62	26.54	1.41	0.30	51.01	4.77
F value	1871.04		200.702		61.645		60.288		194.418	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

The neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease tend to have a predominant anaerobic glycolytic metabolism and mitochondrial oxidative phosphorylation is suppressed. The metabolism is

similar to the metabolism of the stem cell. The pyruvate and lactate levels are increased with a decrease in acetyl coenzyme A and ATP. The glycolytic pathway and hexokinase is increased. This indicates a Warburg phenotype depending upon anaerobic glycolysis for energetics. The lysosomal enzymes beta galactosidase a stem cell marker is increased. The cytochrome F420 is also increased as well as the archaeal catabolite digoxin which suppresses sodium potassium ATPase. Bacteria and archaea are supposed to induce stem cell transformation. The induction of uncoupling proteins leads to stem cell transformation. The uncoupling proteins inhibit oxidative phosphorylation and the substrates are directed to anaerobic glycolysis. Digoxin by inhibiting sodium potassium ATPase can increase intracellular calcium, induce mitochondrial permeability transient pore function and uncouple oxidative phosphorylation. The side chain of cholesterol is catabolised by archaea to butyric acid and propionic acid which uncouple oxidative phosphorylation. The archaeal side chain hydroxylase convert cholesterol to bile acids which uncouple oxidative phosphorylation. Thus archaeal symbiosis in the cell results in cholesterol catabolism and the catabolites digoxin, bile acids and short chain fatty acids uncouple oxidative phosphorylation, inhibit mitochondrial function and promote anaerobic glycolysis. The conversion of somatic cells to stem cell helps in archaeal persistence within the cell and symbiosis. Mycobacterium leprae infection can convert Schwann cells to stem cells. Archaeal infection produces somatic cell conversion to stem cells for archaeal persistence. The conversion to stem cell results in proliferation and loss of function resulting in neurodegenerations-alzheimer’s disease, parkinson’s disease and motor neuron disease. Stem cell conversion of neurons and loss of function results in development of a new neuronal phenotype[1-17].

The neuronal cell in neurodegenerations-alzheimer’s disease, parkinson’s disease and motor neuron disease behaves like the stem cell. It is plausible to

hypothesize a somatic cell conversion to stem cell in these disorders. The differentiated cells by archaeal induction get converted to stem cell. The stem cell is an immature cell with loss of function. The neurons lose their dendritic spines and loss of connectivity. The brain function becomes primitive. The neurons are adendritic and disconnected. This results in complex brain structures like the modern cerebral cortex and prefrontal cortex atrophy. The primitive parts of the brain the brain stem and cerebellum hypertrophies. This results in neanderthalisation of the brain with a prominent occipital bun and atrophied prefrontal cortex. The prefrontal cortex atrophy results in loss of logic, judgment, reasoning and executive functions. The hypertrophy of the cerebellum and brain stem results in dominance of impulsive behavior. The loss of function of the neurons results in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increased archaeal induced proliferation of stem cells results in a big sized brain and trunk as in Neanderthals. This archaeal symbiosis produces neanderthalisation and a stem cell syndrome. This produces reverse aging which can be called as an epidemic Benjamin Button syndrome. The lymphocytic stem cells have uncontrolled proliferation and results in autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Stem cell markers are increased in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease and the neurons lack dendritic spines. The unconscious brain is formed of an archaeal colony network and is adynamic and inflexible. There is an epidemic of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The loss of function of neurons leads to increased extrasensory perception via archaeal magnetite. The perception of low level EMF leads to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-17].

The development of cerebral cortex requires synaptic plasticity and is modulated by HERV mediated jumping genes. This needs a dynamic brain and the human cerebral cortex evolved due to the jumping genes generated from human endogenous retroviral sequences. The cerebellar world is mediated by the archaeal colony network. The stem cell transformation of somatic cells results in HERV resistance and retroviral resistance. Archaeal digoxin inhibits reverse transcriptase by producing magnesium deficiency as well as modulates RNA viral editing inhibiting retroviral replication. This produces lack of HERV jumping genes in this stem cell brain and lack of synaptic plasticity and dynamicity. The stem cell syndrome is characterized by retroviral resistance. Archaeal symbiosis inhibits retroviral infection. The homo sapiens with less of archaeal symbiosis becomes susceptible to retroviral and other RNA viral infection and gets wiped out. The homo neoneanderthalis are resistance to retroviral and other RNA viral infection and persists. The homo neoneanderthalis dominates all over the world. But the homo neoneanderthalis are prone to civilisational disease like neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The homo neoneanderthalis becomes extinct after a period of time[1-17].

The archaeal induced stem cell syndrome or neanderthalisation is due to global warming and acid rains resulting in increased extremophilic archaeal symbiosis. The archaea catabolises cholesterol and generates digoxin, bile acids and short chain fatty acids which produce induction of uncoupling proteins. This produces mitochondrial dysfunction and the cell obtains its energetics from glycolysis. Archaeal digoxin produces membrane sodium potassium ATPase inhibition which also contributes to stem cell conversion. The whole body somatic and brain undergoes stem cell conversion and becomes a stem cell phenotype with Warburg metabolic phenotype. The generalized acidity due to global warming and increased atmospheric carbon dioxide also facilitates archaeal growth and

stem cell transformation. The acidic pH due to the Warburg phenotype and increased atmospheric carbon dioxide also results in stem cell conversion. The somatic differentiated cell getting converted to stem cells lose their function and become dysfunctional metabolically, neurologically, immunologically and endocrine-wise. This produces the epidemic Benjamin button syndrome and the human species becomes neanderthalic and a collection of immature stem cells. This results in epidemic neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The brain becomes converted to a collection of stem cells which are dedifferentiated with loss of function and is like an archaeal colony network. The perception becomes extrasensory and quantal depending on archaeal magnetite. The increased amount of low level EMF perception results in prefrontal cortical atrophy. It also produces cerebellar hypertrophy and the cerebellar cognitive function takes over. This leads on to an epidemic of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-17].

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3

##

Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease – Relation to Archaeal Mediated RNA Viroids and Amyloidosis

Introduction

Prion proteins have been implicated in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The beta amyloid in alzheimer's disease, alpha synuclein in parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. Prion diseases are conformational diseases. The abnormal prion protein seeded into the system converts the normal proteins with prion like domains to abnormal configuration. This abnormal protein resists digestion by lysosomal enzymes after its half life is over and results in deposition of amyloid plaques. This produces organ dysfunction. Prion phenomena were initially described for Creutzfeldt Jakob's disease (CJD), but now it is found to be wide spread in chronic disease pathogenesis. Ribonucleoproteins are well known to behave like prion proteins and form amyloid. We have demonstrated actinidic archaea which secretes RNA viroids in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The RNA viroids can bind with normal proteins with prion like domains eg., superoxide dismutase and produce a ribonucleoprotein resulting in prion phenomena and amyloidogenesis. The actinidic archaeal growth results in increased digoxin synthesis and phenotypic conversion of homo sapiens to homo Neanderthals as reported earlier. The increased actinidic archaeal growth is due to global warming and this results in neanderthalisation. Homo neanderthalis tend to have more of civilisational diseases like neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Actinidic archaeal secreted RNA viroids may play a crucial role in amyloid formation and pathogenesis of these disorders[1-16].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+cerium 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of cerium increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of cerium increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Results

The results show that there was increase in cytochrome F420 in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease indicating increased archaeal growth. There was also an increase in free RNA indicating self replicating RNA viroids in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The RNA viroid generation was catalysed by actinides. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid.

Table 1 *Effect of cerium and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Cerium)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.06	1.61	57.81	6.04
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of cerium and antibiotics on free RNA.*

Group	RNA % change (Increase with Cerium)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.37	0.13	18.38	0.48
PD	23.08	1.87	65.09	3.48
AD	23.29	1.92	65.39	3.95
MND	23.11	1.52	66.68	3.97
F value	427.828		654.453	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source. The archaeal origin of the self replicating RNA was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by cerium induced increase in enzyme activities. There was an increase in free RNA indicating self replicating RNA viroids. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. The RNA viroids can bind with proteins having prion like domains forming ribonucleoproteins. These ribonucleoproteins can give an abnormal conformation to the protein resulting in generation of abnormal prions. The abnormal prions can act as a template to convert normal proteins with normal configuration to abnormal conformation. This can result in amyloidogenesis. The abnormal configured proteins will resist lysosomal digestion and accumulate as amyloid. This can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Amyloidogenesis has been implicated in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The beta amyloid in alzheimer's disease, alpha synuclein in parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. Prion diseases are conformational diseases.

The RNA viroids generated from actinidic archaea can bind to proteins with prion like domains resulting in generation of ribonucleoproteins.

Ribonucleoproteins with abnormal conformation can act as a template for normal proteins with prion like domains to change to abnormal conformation. This results in generation of prion proteins with abnormal conformation resisting lysosomal digestion and generating amyloid. These neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease are due to actinidic archaeal generated RNA viroid induced prion protein generation and amyloidogenesis. Prion proteins have been implicated in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The beta amyloid in alzheimer's disease, alpha synuclein in parkinson's disease, the TAR protein in frontotemporal dementia and copper zinc dismutase in motor neuron disease behaves like prion proteins. The present study shows that the same prion protein mechanism can operate in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Sporadic CJD is also induced by actinidic archaea induced RNA viroids. Actinidic archaeal induced RNA viroids generated prions can be transferred between individuals indicating the infective nature of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The global warming results in increased growth of actinidic archaea and neanderthalisation of the homo sapien species. The actinidic archaea secreted viroids can generate ribonucleoproteins by binding to proteins with prion like domains. This generates amyloidogenesis and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The widespread incidence of these systemic diseases leads to extinction of the neanderthalised species.

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4

##

Neo-Neanderthalisation and Human Disease – The Origins of in Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinidic archaea has been related to global warming and human diseases especially neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The growth of endosymbiotic actinidic archaea in relation to climate change and global warming leads to neanderthalisation of the human mind-body system. Neanderthal anthropometry and metabolonomics has been described in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease especially the Warburg phenotype and hyperdigoxinemia. Digoxin produced by archaeal cholesterol catabolism produces Neanderthalisation. Prefrontal cortical atrophy and cerebellar hyperplasia has been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease in this communication. This leads on to dysautonomia with sympathetic hyperactivity and parasympathetic neuropathy in these disorders. Actinidic archaeal related cerebellar dominance leads to changes in brain function[1-16]. The data is described in this paper.

Materials and Methods

Fifteen cases, each of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease and internet addicts were selected for the study. Each case had an age and sex matched control. Neanderthal anthropometric and phenotypic measurements which included protruding supra-orbital ridges, dolichocephalic skull, small mandible, prominent mid face and nose, short upper and lower limbs, prominent trunk, low index finger-ring finger ratio and fair complexion were evaluated in the cases study. Autonomic function tests were done to assess the sympathetic and parasympathetic system in each case. CT scan

of the head was done to have a volumetric assessment of the prefrontal cortex and cerebellum. Blood cytochrome F420 activity was assessed by spectrophotometric measurement.

Results

All the case groups studied had higher percentage of Neanderthal anthropometric and phenotypic measurements. There was low index finger-ring finger ratio suggestive of high testosterone levels in all the patient population studied. In all the case groups studied, there also was prefrontal cortex atrophy and cerebellar hyperplasia. Similarly in the all the case groups studied, there was dysautonomia with sympathetic over activity and parasympathetic neuropathy. Cytochrome F420 was detected in the entire case group studied showing endosymbiotic archaeal overgrowth.

Table 1 *Neanderthal phenotype and systemic disease.*

Disease	Cyt F420	Neanderthal phenotype	Low index finger-ring finger ratio
Alzheimer's disease	89%	65%	75%
Parkinson's disease	70%	71%	80%
MND	80%	75%	75%
Internet users	65%	72%	69%

Table 2 *Neanderthal phenotype and brain dysfunction.*

Disease	Dysautonomia	Prefrontal cortex atrophy	Cerebellar hypertrophy
Alzheimer's disease	60%	72%	60%
Parkinson's disease	62%	71%	68%
MND	69%	74%	76%
Internet users	74%	84%	82%

Discussion

Neanderthal metabolonomics contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were Neanderthal phenotypic features in all the case groups studied as well as low index finger-ring finger ratios suggestive of increased testosterone levels. Neanderthalisation of the mind-body system occurs due to increased growth of actinidic archaea as a consequence of global warming. Neanderthalisation of the mind leads to cerebellar dominance and prefrontal cortex atrophy. This leads to dysautonomia with parasympathetic neuropathy and sympathetic hyperactivity.

Global warming and the ice age produces increased growth of extremophiles. This leads to increased growth of actinidic archaeal endosymbiosis in humans. There is archaeal proliferation in the gut which enters the cerebellum and brain stem by reverse axonal transport via the vagus. The cerebellum and brain stem can be considered as an archaeal colony. The archaea are cholesterol catabolising and use cholesterol as a carbon and energy source. The actinidic archaea activates the toll receptor HIF alpha inducing the Warburg phenotype resulting in increased glycolysis with generation of glycine as well as pyruvate dehydrogenase suppression. The accumulated pyruvate enters the GABA shunt generating of succinyl CoA and glycine. The archaeal catabolism of cholesterol produces ring oxidation and generation of pyruvate which also enters the GABA shunt scheme producing glycine and succinyl CoA. This leads to increased synthesis of porphyrins. In the setting of digoxin induced sodium potassium ATPase inhibition the dipolar porphyrins produce a pumped phonon system resulting in the Frohlich model Bose-Einstein condensate and quantal perception of low level EMF. Low level EMF pollution is common with internet usage. Perception of low level of EMF leads to neanderthalisation of the brain with

prefrontal cortex atrophy and cerebellar hyperplasia. The archaea which reaches the cerebellum from the gut via the vagus nerve proliferates and makes the cerebellum dominant with resultant suppression and atrophy of the prefrontal cortex. This leads to wide spread incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The actinidic archaea induces the Warburg phenotype with increased glycolysis, PDH inhibition and mitochondrial suppression. This produces neanderthalisation of the mind-body system. The actinidic archaea secretes RNA viroids which block HERV expression by RNA interference. The HERV suppression contributes to the inhibition of prefrontal cortex development in Neanderthals and cerebellar dominance. Archaeal digoxin produces sodium potassium ATPase inhibition and magnesium depletion causing reverse transcriptase inhibition and decreased generation of HERV. The HERV contributes to the dynamicity of the genome and are required for the development of the prefrontal cortex. The HERV suppression contributes to retroviral resistance in Neanderthals. The actinidic archaea catabolises cholesterol leading to cholesterol depleted state. Cholesterol depletion also leads to poor synaptic connectivity and decreased development of prefrontal cortex. This is not genetic change but a form of symbiotic change with endosymbiotic actinidic archaeal growth in the body and brain. This leads onto the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Internet use and low level EMF pollution is common in this century. This results in increased low level EMF perception by the brain by the digoxin-porphyrin mediated pumped phonon system created Bose-Einstein condensates contributing to prefrontal cortex atrophy and cerebellar dominance. Cerebellar dominance leads to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There is an epidemic of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease in the present day community. The

porphyrin mediated extrasensory perception can contributes to low level EMF related neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The modern population is a hybrid of homo sapiens and homo neanderthalis. This contributes to 10 to 20 per cent dominant hybrids who tend to have increase incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. This correlated with the generation of Neanderthal hybrids when the Eurasian Neanderthal male mated with homo sapiens African females. The extrasensory/quantal perception due to dipolar porphyrins and digoxin induced sodium potassium ATPase inhibition and the generated pumped phonon system mediated quantal perception leads to low level EMF related neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaeal cholesterol catabolism leads to increased synthesis of digoxin. Digoxin promotes tryptophan transport over tyrosine. Tyrosine deficiency leads to dopamine deficiency and morphine deficiency. This leads to a morphine deficiency syndrome in Neanderthals. This leads to increased incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The Neanderthals were essentially meat eaters taking a ketogenic diet. The acetoacetic acid is converted to acetyl CoA which enters the TCA cycle. When the Neanderthal hybrids consume a glucogenic diet owing to the spread of settled civilisation it produces pyruvate accumulation owing to PDH suppression in Neanderthals. The increased archaeal growth activates the toll receptor and induces HIF alpha resulting in increased glycolysis, PDH suppression and mitochondrial dysfunction-the Warburg phenotype. The pyruvate enters the GABA shunt pathway producing glutamate, ammonia and porphyrins resulting in neuropathology of neurodegenerations-alzheimer's disease, parkinson's

disease and motor neuron disease. There is dominance of cerebellar function. The Neanderthal hybrids have cerebellar dominance and less of conscious behaviour. The predominant homo sapiens had prefrontal cortex dominance over the cerebellum resulting in more of conscious behaviour. Neanderthalisation leads to increased incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The Neanderthals consuming a glucogenic diet produces increased glycolysis in the setting of PDH inhibition. This produces the Warburg phenotype. There is increased lymphocytic glycolysis and immune activation producing autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increased levels of GAPD result in nuclear cell death and neurodegeneration. The predominance of glycolysis and suppression of mitochondrial function results in glycemia and insulin resistance. The glycolytic intermediate 3-phosphoglycerate is converted to glycine resulting in NMDA excitotoxicity contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Cerebellar dominance is seen in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The cerebellar hyperplasia results in sympathetic hyperactivity and parasympathetic neuropathy. Vagal neuropathy results in immune activation and autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Vagal neuropathy and sympathetic over activity can contribute to glycogenolysis and lipolysis resulting in insulin resistance. Insulin resistance leads to increased incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Cerebellar dominance and cerebellar cognitive affective dysfunction can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron

disease. The increased porphyrin synthesis resulting from succinyl CoA generated by GABA shunt and glycine generated by glycolysis contributes to increased extrasensory perception of low level EMF important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Sympathetic over activity and parasympathetic neuropathy can contribute to neurodegeneration.

The archaeal cholesterol catabolism generates digoxin which produces sodium potassium ATPase inhibition and increase in intracellular calcium and decrease in intracellular magnesium. The increase in intracellular calcium produces oncogene activation and NFKB activation resulting in autoimmunity important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increase in intracellular calcium opens the mitochondrial PT pore resulting in cell death and neurodegeneration. The increase in intracellular calcium can modulate the neurotransmitter release from presynaptic vesicles. This can modulate neurotransmission. Digoxin induced magnesium depletion can remove the magnesium block on the NMDA receptor resulting in NMDA excitotoxicity. This can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Digoxin induced magnesium depletion can inhibit reverse transcriptase activity and HERV generation modulating the dynamicity of the genome. Digoxin induced intracellular calcium accumulation and magnesium depletion can modulate G-protein and protein tyrosine kinase dependent neurotransmitter and endocrine receptors. This can produce digoxin induced neuro-immuno-endocrine integration. Digoxin functions as a Neanderthal master hormone. This defective neuro-immuno-endocrine integration can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The actinidic archaea are cholesterol catabolising and leads to low levels of testosterone and estrogen. The Neanderthals consume a low fibre diet with low lignan content. The actinidic archaea has cholesterol catabolising enzymes generating more of testosterone than estrogens. This contributes to estrogen deficiency and testosterone over activity. The Neanderthal population are hypermales with concommitant right hemispheric dominance and cerebellar dominance. Testosterone suppresses left hemispheric function. The high testosterone levels in Neanderthals contribute to a bigger brain. The Neanderthals males as well as females had a higher level of testosterone contributing to gender equality and gender neutral states. There was group identity and group motherhood with no differences between roles of both males and females. This also resulted in matrilinearity. The homo sapiens eat a high fibre diet with low cholesterol and high lignan content contributing to estrogen dominance, left hemispheric dominance and cerebellar hypoplasia. Homo sapiens had higher reproductive rates and overtook the Neanderthal population resulting in its extinction. The homo sapien population was conservative with normal sexual mores, family values and patriarchal type of behaviour. The role of females the homo sapien community was inferior to males. The increasing generation of Neanderthal hybrids due to climate change mediated archaeal overgrowth leads to gender equality and equidominance of male and female in this century. This change in endocrine status leads to increased incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The cholesterol catabolism results in cholesterol depletion and bile acid deficiency. Bile acids bind to VDR and are immunomodulatory. Bile acid deficiency leads to immune activation and autoimmunity important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Bile acids bind to FXR, LXR and PXR modulating lipid and carbohydrate metabolism. This leads to insulin resistance in the presence of bile

acid deficiency. Bile acid uncouples oxidative phosphorylation and its deficiency leads to insulin resistance. Insulin resistance is important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Cholesterol depletion also leads to vitamin D deficiency. Vitamin D binds to VDR and produces immunomodulation. Vitamin D deficiency leads to immune activation and autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Vitamin D deficiency can also produce rickets and contribute to the phenotypic features of Neanderthals. Vitamin D deficiency can contribute to brain development resulting in macrocephaly. Vitamin D deficiency contributes to insulin resistance and truncal obesity of Neanderthals. Vitamin D deficiency contributes to the fairness of the Neanderthal skin as a phenotypic adaptation. The Neanderthal phenotypic features are due to vitamin D deficiency and insulin resistance. Vitamin D deficiency leads on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Thus global warming and increased endosymbiotic actinidic archaeal growth leads to cholesterol catabolism and generation of the Warburg phenotype resulting in increased porphyrin synthesis, extrasensory low EMF perception, prefrontal cortex atrophy, insulin resistance and cerebellar dominance. This leads on to neanderthalisation of the body and brain. This leads on to an epidemic of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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Porphyrins and Quantal Perception – Role of Porphyrins in Environmental Communication/Modulation of Digital Information Storage/Processing System – Low Level of Electromagnetic Fields and Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinidic archaea has been described as endosymbionts in humans. Actinidic archaea have a mevalonate pathway and are cholesterol catabolising. They can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can generate porphyrins via the cholesterol ring oxidase generated pyruvate and GABA shunt pathway. Archaea can produce a secondary porphyria by inducing the enzyme heme oxygenase resulting in heme depletion and activation of the enzyme ALA synthase. The archaea can induce the enzyme heme oxygenase resulting in depletion of heme and induction of ALA synthase. This can lead to porphyrinogenesis. Low level of electromagnetic fields and geomagnetic fields can induce porphyrin synthesis by inhibiting the enzyme ferrochelatase which has got a ferromagnetic core. Inhibition of ferrochelatase produces deficiency of heme resulting in induction of ALA synthase. Low level of EMF can also induce heme oxygenase depleting heme and inducing ALA synthase. Porphyrins can undergo auto-oxidation generating biophotons and a quantal state. Porphyrin auto-oxidation is modulated by low level of electromagnetic fields and geomagnetic fields. Porphyrin microarrays can function as quantal computers storing information and can serve the purpose of extrasensory perception. Porphyrins can serve as a two way communicating bridge between digital information storage systems generating low level electromagnetic fields and human systems. The low level of EMF produced by digital system enhances porphyrin synthesis and serves the purpose of two way extrasensory perception and communication. The porphyrin quantal computers can in turn by biophoton emission modulate digital information storage system. Actinidic archaea have been related to the pathogenesis of schizophrenia, malignancy, metabolic syndrome x, autoimmune disease and neuronal degeneration. An actinide dependent shadow biosphere of archaea and

viroids in the above mentioned disease states is described. Porphyrins have been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyrins can mediate the pathogenesis of low level electromagnetic fields inducing the above mentioned disease states. A hypothesis regarding the role of porphyrins and quantal perception as well as the role of porphyrins in environmental communication/modulation of digital information storage/processing system is presented. The relationship between low level of electromagnetic fields and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease is highlighted[1-5].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. There were also 10 normal people with right hemispheric dominance, left hemispheric dominance and bi-hemispheric dominance included in the study selected from the normal population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, polycyclic aromatic hydrocarbon, hydrogen peroxide, pyruvate, ammonia, glutamate, delta aminolevulinic acid, succinate, glycine and digoxin. Cytochrome

F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The study also involved estimating the following parameters in the patient population-digoxin, bile acid, hexokinase, porphyrins, pyruvate, glutamate, ammonia, acetyl CoA, acetyl choline, HMG CoA reductase, cytochrome C, blood ATP, ATP synthase, ERV RNA (endogenous retroviral RNA), H_2O_2 (hydrogen peroxide), NOX (NADPH oxidase), TNF alpha and heme oxygenase[6-9]. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients and those with exposure to low level of EMF showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma and those with exposure to low level of EMF caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables section 1: 1-6 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was upregulated archaeal porphyrin synthesis in the patient population and those with exposure to low level of EMF which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt

pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase.

The study showed the patient's blood, those with exposure to low level of EMF and right hemispheric dominance had increased heme oxygenase activity and porphyrins. The hexokinase activity was high. The pyruvate, glutamate and ammonia levels were elevated indicating blockade of PDH activity, and operation of the GABA shunt pathway. The acetyl CoA levels were low and acetyl choline was decreased. The cyto C levels were increased in the serum indicating mitochondrial dysfunction suggested by low blood ATP levels. This was indicative of the Warburg's phenotype. There was increased NOX and TNF alpha level indicating immune activation. The HMG CoA reductase activity was high indicating cholesterol synthesis. The bile acid levels were low indicating depletion of cytochrome P450. The normal population with right hemispheric dominance had values resembling the patient population with increased porphyrin synthesis. The normal population with left hemispheric dominance had low values with decreased porphyrin synthesis.

Section 1: Experimental Study

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
PD	23.46	1.87	59.27	8.86	22.67	2.29	57.69	5.29
AD	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
MND	22.06	1.61	57.81	6.04	23.46	1.91	61.56	4.61
Low level EMF	22.70	1.87	60.46	8.06	23.73	1.38	65.20	6.20
F value	306.749		130.054		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
PD	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
MND	23.30	1.42	65.07	4.95	23.11	1.52	66.68	3.97
Low level EMF	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and delta aminolevulinic acid.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.40	0.10	18.48	0.39
PD	0.51	0.05	0.199	0.027	22.83	1.90	67.23	3.45
AD	0.55	0.03	0.192	0.040	23.67	1.68	66.50	3.58
MND	0.53	0.06	0.212	0.045	23.17	1.88	68.53	2.65
Low level EMF	0.51	0.05	0.213	0.033	22.29	2.05	61.91	7.56
F value	135.116		71.706		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 4 *Effect of rutile and antibiotics on succinate and glycine.*

Group	Succinate % (Increase with Rutile)		Succinate % (Decrease with Doxy+Cipro)		Glycine % change (Increase with Rutile)		Glycine % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
PD	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
AD	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
MND	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
Low level EMF	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
F value	403.394		680.284		348.867		364.999	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and glutamate.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Glutamate (Increase with Rutile)		Glutamate (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
PD	20.94	1.54	62.76	8.52	23.33	1.79	62.50	5.56
AD	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
MND	21.07	1.79	63.90	7.13	22.47	2.17	65.97	4.62
Low level EMF	22.29	2.05	62.37	5.05	21.66	1.94	67.03	5.97
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and ammonia.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		Ammonia % (Increase with Rutile)		Ammonia % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
Schizo	22.50	1.66	60.21	7.42	22.52	1.90	66.39	4.20
PD	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MND	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Low level EMF	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Section 2: Patient Study

Table 1

Group	RBC digoxin (ng/ml RBC Susp)		Cytochrome F 420		HERV RNA (ug/ml)		H_2O_2 (umol/ml RBC)		NOX (OD diff/hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.58	0.07	1.00	0.00	17.75	0.72	177.43	6.71	0.012	0.001
RHCD	1.41	0.23	4.00	0.00	55.17	5.85	278.29	7.74	0.036	0.008
LHCD	0.18	0.05	0.00	0.00	8.70	0.90	111.63	5.40	0.007	0.001
MND	1.23	0.26	4.00	0.00	50.04	3.91	278.90	11.20	0.038	0.007
PD	1.34	0.31	4.00	0.00	51.16	7.78	295.37	3.78	0.035	0.011
AD	1.10	0.08	4.00	0.00	51.56	3.69	277.47	10.90	0.036	0.007
Exposure to EMF	1.41	0.30	4.00	0.00	51.01	4.77	276.49	10.92	0.038	0.007
F value	60.288		0.001		194.418		713.569		44.896	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 2

Group	TNF ALP (pg/ml)		ALA (umol24)		PBG (umol24)		Uroporphyrin (nmol24)		Coproporphyrin (nmol/24)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	17.94	0.59	15.44	0.50	20.82	1.19	50.18	3.54	137.94	4.75
RHCD	78.63	5.08	63.50	6.95	42.20	8.50	250.28	23.43	389.01	54.11
LHCD	9.29	0.81	3.86	0.26	12.11	1.34	9.51	1.19	64.33	13.09
MND	79.28	4.55	68.28	6.02	46.54	4.55	290.44	57.65	436.71	52.95
PD	82.13	3.97	67.30	5.98	47.25	4.19	286.84	24.18	432.22	50.11
AD	79.65	5.57	67.32	5.40	49.83	3.45	259.61	33.18	433.17	45.61
Exposure to EMF	76.41	5.96	68.41	5.53	47.27	3.42	288.21	26.17	444.94	38.89
F value	427.654		295.467		183.296		160.533		279.759	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 3

Group	Protoporphyrin (Ab unit)		Heme (uM)		Bilirubin (mg/dl)		Biliverdin (Ab unit)		ATP synthase (umol/gHb)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	10.35	0.38	30.27	0.81	0.55	0.02	0.030	0.001	0.36	0.13
RHCD	42.46	6.36	12.47	2.82	1.70	0.20	0.067	0.011	2.73	0.94
LHCD	2.64	0.42	50.55	1.07	0.21	0.00	0.017	0.001	0.09	0.01
MND	49.59	1.70	13.03	0.70	1.84	0.07	0.070	0.015	3.09	0.65
PD	49.36	4.18	11.81	0.80	1.83	0.09	0.071	0.014	3.34	0.84
AD	49.68	3.30	12.09	1.12	1.77	0.13	0.073	0.016	3.34	0.75
Exposure to EMF	50.59	1.71	12.36	1.26	1.75	0.22	0.073	0.013	3.39	1.03
F value	424.198		1472.05		370.517		59.963		54.754	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 4

Group	SE ATP (umol/dl)		Cyto C (ng/ml)		Lactate (mg/dl)		Pyruvate (umol/l)		RBC hexokinase (ug glu phos/ hr/mgpro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	0.42	0.11	2.79	0.28	7.38	0.31	40.51	1.42	1.66	0.45
RHCD	2.24	0.44	12.39	1.23	25.99	8.10	100.51	12.32	5.46	2.83
LHCD	0.02	0.01	1.21	0.38	2.75	0.41	23.79	2.51	0.68	0.23
MND	1.66	0.56	12.06	1.09	21.78	0.58	90.46	8.30	6.29	1.73
PD	1.27	0.26	12.65	1.06	24.28	1.69	95.44	12.04	9.30	3.98
AD	2.06	0.19	11.94	0.86	22.04	0.64	97.26	8.26	8.46	3.63
Exposure to EMF	1.37	0.27	12.26	1.00	23.31	1.46	103.28	11.47	7.58	3.09
F value	67.588		445.772		162.945		154.701		18.187	
P value	< 0.001		< 0.001		< 0.001		< 0.001		< 0.001	

Table 5

Group	ACOA (mg/dl)		ACH (ug/ml)		Glutamate (mg/dl)	
	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	8.75	0.38	75.11	2.96	0.65	0.03
RHCD	2.51	0.36	38.57	7.03	3.19	0.32
LHCD	16.49	0.89	91.98	2.89	0.16	0.02
MND	2.15	0.22	33.27	5.99	3.67	0.38
PD	1.95	0.06	35.02	5.85	3.14	0.32
AD	2.19	0.15	42.84	8.26	3.53	0.39
Exposure to EMF	2.14	0.19	37.75	7.31	3.47	0.37
F value	1871.04		116.901		200.702	
P value	< 0.001		< 0.001		< 0.001	

Table 6

Group	Se. ammonia (ug/dl)		HMG Co A (HMG CoA/MEV)		Bile acid (mg/ml)	
	Mean	± SD	Mean	± SD	Mean	± SD
NO/BHCD	50.60	1.42	1.70	0.07	79.99	3.36
RHCD	93.43	4.85	1.16	0.10	25.68	7.04
LHCD	23.92	3.38	2.21	0.39	140.40	10.32
MND	95.61	7.88	1.14	0.07	22.98	5.19
PD	94.60	8.52	1.08	0.13	28.93	4.93
AD	95.37	4.66	1.10	0.07	26.26	7.34
Exposure to EMF	102.62	26.54	1.00	0.07	22.58	5.07
F value	61.645		159.963		635.306	
P value	< 0.001		< 0.001		< 0.001	

Abbreviations

NO/BHCD: Normal/Bi-hemispheric chemical dominance

RHCD: Right hemispheric chemical dominance

LHCD: Left hemispheric chemical dominance

AD: Alzheimer’s disease

MND: Motor neuron disease

PD: Parkinson’s disease

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[2, 10]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[11]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis[12]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[10]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevlunic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[13]. This can lead on

to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Low level electromagnetic fields and its porphyrin messengers can regulate the brain mediating quantal perception. Porphyrin microarrays serve the purpose of quantal perception. Porphyrin photo-oxidation can generate free radicals which can modulate NMDA transmission. Free radicals can increase NMDA transmission. ALA blocks GABA transmission and upregulates NMDA. Thus porphyrins can produce NMDA excitotoxicity contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The dipolar porphyrins in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrin molecules have a wave particle existence and can bridge the dividing line between quantal state and particulate state. Thus the porphyrins can mediate quantal perception and perception of low level EMF contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyrins binding to proteins, nucleic acids and cell membranes can produce biophoton emission. Porphyrins by auto-oxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Thus porphyrin microarrays can function as a quantal computer mediating extrasensory perception of low level EMF contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The porphyrins can modulate hemispheric dominance. There is

increased porphyrin synthesis and RHCD and decreased porphyrin synthesis in LHCD. RHCD can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Altered porphyrin metabolism has been described in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3, 4, 16]. Thus porphyrins microarrays can function as a quantal brain modulating extrasensory quantal perception. Porphyrin microarrays can function as a quantal brain in communication with digital world and geomagnetic fields. This can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The dipolar porphyrins in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world. ALA can produce sodium potassium ATPase inhibition resulting in a pumped phonon system mediated quantal state involving dipolar porphyrins. Porphyrins by auto-oxidation can generate biophotons and are involved in quantal perception. Biophotons can mediate quantal perception. Porphyrin auto-oxidation is modulated by low level of electromagnetic fields and geomagnetic fields. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Porphyrins can thus contribute to quantal perception. Low level electromagnetic fields and light can induce porphyrin synthesis. Low level EMF can produce ferrochelatase inhibition as well as heme oxygenase induction contributing to heme depletion, ALA synthase induction and increased porphyrin synthesis. Light also induces ALA synthase and porphyrin synthesis. The increased porphyrin synthesized can contribute to increased quantal perception and can modulate conscious perception. The human porphyrin microarrays induced biophotons and quantal fields can modulate the source from which low level EMF and photic fields were

generated. Thus the porphyrin generated by extraneous low level EMF and photic fields can interact with the source of low level EMF and photic fields modulating it. Thus porphyrins can serve as a bridge between the human brain and the source of low level EMF and photic fields. This serves as a mode of communication between the human brain and digital EMF storage devices like internet. The porphyrins can also serve as the source of communication with the environment. Environmental EMF and chemicals produce heme oxygenase induction and heme depletion increasing porphyrin synthesis, quantal perception and two-way communication. Thus induction of porphyrin synthesis can serve as a mechanism of communication between human brain and the environment by extrasensory perception. Porphyrin microarrays can function as quantal computers storing information and can serve the purpose of extrasensory perception. Porphyrins can serve as a two way communicating bridge between digital information storage systems generating low level electromagnetic fields and human systems. The low level of EMF produced by digital system enhances porphyrin synthesis and serves the purpose of two way extrasensory perception and communication. The human porphyrin quantal computers can in turn by biophoton emission modulate digital information storage system. The quantal perception of low level EMF can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Low level of electromagnetic fields and its porphyrin messengers can induce the Warburg phenotype. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described. The archaea can synthesize porphyrins and induce porphyrin synthesis. Porphyrins have been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyrins can mediate the effect of low level electromagnetic fields inducing the Warburg phenotype leading to the above mentioned disease states. The Warburg phenotype results in inhibition of pyruvate dehydrogenase and

the TCA cycle. The pyruvate enters the GABA shunt pathway where it is converted to succinyl CoA. The glycolytic pathway is upregulated and the glycolytic metabolite phosphoglycerate is converted to serine and glycine. Glycine and succinyl CoA are the substrates for ALA synthesis. The archaea induces the enzyme heme oxygenase. Heme oxygenase converts heme to bilirubin and biliverdin. This depletes heme from the system and results in upregulation of ALA synthase activity resulting in porphyria. Heme inhibits HIF alpha. The heme depletion results in upregulation of HIF alpha activity and further strengthening of the Warburg phenotype. The porphyrin self oxidation results in redox stress which activates HIF alpha and generates the Warburg phenotype. The Warburg phenotype results in channelling acetyl CoA for cholesterol synthesis as the TCA cycle and mitochondrial oxidative phosphorylation are blocked. The archaea uses cholesterol as an energy substrate. Porphyrin and ALA inhibits sodium potassium ATPase. This increases cholesterol synthesis by acting upon intracellular SREBP. The cholesterol is metabolized to pyruvate and then the GABA shunt pathway for ultimate use in porphyrin synthesis. The porphyrins can self organize and self replicate into macromolecular arrays. The porphyrin arrays behave like an autonomous organism and can have intramolecular electron transport generating ATP. The porphyrin macroarrays can store information and can have quantal perception. The porphyrin macroarrays serves the purpose of archaeal energetics and sensory perception. The Warburg phenotype is associated with neurodegenerations-alzheimer’s disease, parkinson’s disease and motor neuron disease. Low level electromagnetic fields can induce the Warburg phenotype contributing to neurodegenerations-alzheimer’s disease, parkinson’s disease and motor neuron disease.

The role of porphyrins and low level electromagnetic fields in regulation of cell functions and neuro-immuno-endocrine integration is discussed. Low levels of EMF fields can induce digoxin synthesis. Protoporphyrin binds to the

peripheral benzodiazepine receptor regulating steroid and digoxin synthesis. Increased porphyrin metabolites can contribute to hyperdigoxinemia. Digoxin can modulate the neuro-immuno-endocrine system. Low level of EMF fields can modulate membrane, nucleic acid and protein structure and function via induction of porphyrin synthesis. Porphyrins can combine with membranes modulating membrane function. Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. Porphyrins can complex with DNA and RNA modulating their function. Porphyrin interpolating with DNA can alter transcription and generate HERV expression. Low level of EMF fields through modulation of porphyrin metabolism can produce heme deficiency by inhibiting heme oxygenase and ferrochelatase. Heme deficiency can also result in disease states. Heme deficiency results in deficiency of heme enzymes. There is deficiency of cytochrome C oxidase and mitochondrial dysfunction. The glutathione peroxidase is dysfunctional and the glutathione system of free radical scavenging does not function. The cytochrome P450 enzymes involved in steroid and bile acid synthesis have reduced activity leading to steroid-cortisol and sex hormones as well as bile acid deficiency states. The heme deficiency results in dysfunction of nitric oxide synthase, heme oxygenase and cystathione beta synthase resulting in lack of gasotransmitters regulating the vascular system and NMDA receptor-NO, CO and H_2S. Heme has got cytoprotective, neuroprotective, anti-inflammatory and antiproliferative effects. Heme is also involved in the stress response. Heme deficiency leads to metabolic syndrome, immune disease, degenerations and cancer[3-5]. Low level electromagnetic fields can modulate cell functions and neuro-immuno-endocrine-genetic integration via induction of porphyrin synthesis. This can contribute to neurodegenerations-alzheimer’s disease, parkinson’s disease and motor neuron disease.

Low level electromagnetic fields via modulating porphyrin metabolism can produce an autonomic neuropathy. Protoporphyrins block acetyl choline transmission producing a vagal neuropathy with sympathetic over activity. Vagal neuropathy results in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. A vagal neuropathy underlines neoplastic and autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low level electromagnetic fields by modulating porphyrin metabolism can induce cell death. Porphyrin induced increased NMDA transmission and free radical injury can contribute to neuronal degeneration. Free radicals can produce mitochondrial PT pore dysfunction. This can lead to cyto C leak and activation of the caspase cascade leading to apoptosis and cell death. Altered porphyrin metabolism has been described in Alzheimer's disease. The increased porphyrin photo-oxidation generated free radicals mediated NMDA transmission can also contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate brain function and cell death[3, 4, 16].

Low level electromagnetic fields by modulating porphyrin metabolism can generate redox stress to regulate cell functions. The porphyrins can undergo photo-oxidation and auto-oxidation generating free radicals. The archaeal porphyrins can produce free radical injury. Free radicals produce NFKB activation, open the mitochondrial PT pore resulting in cell death, activate NMDA receptor and generates the Warburg phenotypes activating glycolysis and inhibiting TCA cycle/oxphos. Porphyrins have been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low level electromagnetic fields by modulating porphyrin metabolism can regulate cell membrane sodium potassium ATPase. The porphyrins can complex and intercalate with the cell membrane producing sodium potassium ATPase inhibition adding on to digoxin mediated inhibition. Porphyrins can

complex with proteins and nucleic acid producing biophoton emission. Low level electromagnetic fields by modulating porphyrin metabolism can regulate DNA, RNA and protein structure and function. Porphyrins complexing with proteins can modulate protein structure and function. Porphyrins complexing with DNA and RNA can modulate transcription and translation. Low level electromagnetic fields by modulating porphyrin metabolism can regulate mitochondrial function, peripheral benzodiazepine receptor and steroidogenesis. The porphyrin especially protoporphyrins can bind to peripheral benzodiazepine receptors in the mitochondria and modulate its function, mitochondrial cholesterol transport and steroidogenesis. Peripheral benzodiazepine receptor modulation by protoporphyrins can regulate cell death, cell proliferation, immunity and neural functions. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress can regulate enzyme systems. The porphyrin photo-oxidation generates free radicals which can modulate enzyme function. Redox stress modulated enzymes include pyruvate dehydrogenase, nitric oxide synthase, cystathione beta synthase and heme oxygenase. Free radicals can modulate mitochondrial PT pore function. Free radicals can modulate cell membrane function and inhibit sodium potassium ATPase activity. Thus the porphyrins are key regulatory molecules modulating all aspects of cell function[3-5]. Low level of electromagnetic fields by modulating porphyrin metabolism can induce viroidal and HERV expression. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides and porphyrins modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities. Porphyrin photo-oxidation induced redox stress can produce HDAC

inhibition. Archaeal pyruvate producing histone deacetylase inhibition and porphyrins intercalating with DNA can produce endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses. The archaea and viroids can also induce cellular porphyrin synthesis. Bacterial and viral infections can precipitate porphyria and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Thus porphyrins can regulate genomic function. The increased expression of HERV RNA can result in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[14, 15].

Low level electromagnetic fields by modulating porphyrin metabolism and generating redox stress can produce immune activation. The porphyrin photo-oxidation can generate free radicals which can activate NFKB. This can produce immune activation and cytokine mediated injury. The increase in archaeal porphyrins can lead to autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate immune function. Porphyrins can combine with proteins oxidizing their tyrosine, tryptophan, cysteine and histidine residues producing crosslinking and altering protein conformation and function. Porphyrins can complex with DNA and RNA modulating their structure. Porphyrin complexed with proteins and nucleic acids are antigenic and can lead onto autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress can produce insulin resistance. The porphyrin photo-oxidation mediated free radical injury can lead to insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Glucose has got a negative

effect upon ALA synthase activity. Therefore hyperglycemia may be reactive protective mechanism to increased archaeal porphyrin synthesis. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate mitochondrial steroidogenesis and metabolism. Altered porphyrin metabolism has been described in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism and inducing redox stress/heme deficiency can activate HIF alpha. The porphyrin photo-oxidation can generate free radicals inducing HIF alpha and producing neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3, 4]. Low level electromagnetic fields by modulating porphyrin metabolism can regulate prion protein conformation. The porphyrin can combine with prion proteins modulating their conformation. This leads to abnormal prion protein conformation and degradation. Archaeal porphyrins can contribute to prion disease important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low level electromagnetic fields by modulating porphyrin metabolism can produce redox stress and regulate HERV expression. The porphyrins can also intercalate with DNA producing HERV expression. The HERV particles generated can contribute to the retroviral state. HERV sequences can produce neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3, 4].

Porphyrins also have evolutionary significance since porphyria is related to Scythian races and contributes to the behavioural and intellectual characteristics of this group of population. Porphyrins can intercalate into DNA and produce HERV expression. HERV RNA can get converted to DNA by reverse transcriptase which can get integrated into DNA by integrase. This tends to increase the length of the non coding region of the DNA. The increase in non coding region of the DNA is involved in primate and human evolution. Thus, increased rates of porphyrin synthesis would correlate with increase in non

coding DNA length. The alteration in the length of the non coding region of the DNA contributes to the dynamic nature of the genome. Thus genetic and acquired porphyrias can lead to alteration in the non coding region of the genome. The alteration of the length of the non coding region of the DNA contributes to the racial and individual differences in populations. An increased length of non coding region as well as increased porphyrin synthesis leads to increased cognitive and creative neuronal function. Porphyrins are involved in quantal perception and regulation of the thalamocorticothalamic pathway of conscious perception. Thus genetic and acquired porphyrias contribute to higher cognitive and creative capacity of certain races. Porphyrias are common among Eurasian Scythian races who have assumed leadership roles in communities and groups. Porphyrins have contributed to human and primate evolution[3, 4]. The increased porphyrin synthesis in the Scythian races contributes to higher level of extrasensory quantal perception in this racial group. This contributes to higher level of cognitive and spiritual function of the brain in this racial group. This racial group has increased incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The porphyrins can contribute to the role of low level electromagnetic fields in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states-neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease is described. Archaeal porphyrin synthesis and induction of endogenous porphyrin synthesis is crucial in the pathogenesis of these disorders. Porphyrins may serve as regulatory molecules modulating immune, neural, endocrine, metabolic and genetic systems. The porphyrins photo-oxidation generated free radicals can produce immune activation, produce cell death, activate cell proliferation, produce insulin resistance and modulate conscious/quantal perception. Porphyrins can regulate hemispheric

dominance. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role. Thus the porphyrins contribute to the inducing role of low level electromagnetic fields in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low level electromagnetic fields and its porphyrin messengers can regulate immune, neural, endocrine, metabolic and genetic systems[3, 4]. A hypothesis regarding the role of porphyrins and quantal perception as well as the role of porphyrins in environmental communication/modulation of digital information storage/processing system is presented. Thus porphyrin microarrays can function as a quantal computer mediating extrasensory perception. Porphyrin microarrays in human systems and brain owing to the wave particle nature of porphyrins can bridge the quantal world and particulate world. The relationship between low level of electromagnetic fields and human disease is highlighted. This can lead on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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6

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Actinidic Archaea Mediates Biological Transmutation in Human Systems – Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Biological transmutation has been postulated by several groups of workers in microbial systems[1, 2]. Quantizing structures of optimal size and shape are necessary for non barrier nuclear interactions. The situation is realized in microbial cultures. During the growth process, the replication of DNA and other biomacromolecules takes place. In the region of growth, the interatomic potential holes with slowly changing sizes are constantly appearing and in this situation non barrier nuclear interactions can take place. Actinidic archaea has been described in human systems from our laboratory and function as cellular endosymbionts regulating multiple cellular functions. The actinidic archaea utilizes an alternate biochemistry depended on actinides for enzyme catalysis. The seashores of Kerala are rich in actinidic elements present as rutile, illmenite and monazite. The actinidic archaea is an endosymbiont of the human cell and it is possible that the organism can mediate biological transmutation. Transmutation of magnesium to calcium can serve as a mechanism of regulation of the neuro-immuno-endocrine system. Deficiency of magnesium is seen in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3]. The actinidic archaea can exist as nanoarchaea which can undergo magnetite and calcium mineralization. It is possible that magnesium is being transmuted biologically to calcium to produce amounts sufficient for calcium mineralization. Calcified nanoarchaea can produce a systemic immune activation contributing to the diverse pathologies of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. This section studies the biological transmutation of magnesium to calcium and cerium. The results are presented in this paper.

Materials and Methods

Informed consent was obtained from all patients included in the study. The permission of the Ethics Committee of the Institute was obtained. Fasting blood was drawn for the study from normal individuals without any systemic disease.

Experimental system was as follows: The basic system contained patient's serum 0.5 ml + normal serum 0.25 ml + physiological buffered saline + cerium chloride 0.1 mg/ml. To the basic system $MgSO_4$ 0.1 mg/ml was added.

The Mg^{++} and Ca^{++} were estimated at 0 hour. The remaining portion was incubated for 16 hours at 37 ℃ for 16 hours. The Mg^{++} and Ca^{++} were estimated at the end of 16 hours. The estimation of Mg^{++} and Ca^{++} were done by using commercial kits. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm).

Results

The results showed that there was a decrease in magnesium and a concomitant increase in calcium in incubated serum samples from normal individuals. The percentage decrease in magnesium was 15.68 to 31.48%. The percentage increase in calcium was 10.43 to 9.79%. There was detection of cytochrome F420 in the system by fluorescence indicating archaeal growth dependent on actinidic cerium. This showed that the actinidic archaea was mediating the biological transmutation of magnesium to calcium.

Table 1 *Experimental biological transmutation.*

Case	Time	Mg (mEq/l)	% change in Mg	Ca (ng/dl)	% change in Ca
Case 1	0 hr	1.415		0.796	
	16 hrs	1.193	15.68 ↓	8.310	10.43 ↑
Case 2	0 hr	2.290		0.764	
	16 hrs	1.569	31.48 ↓	7.480	9.79 ↑

Discussion

The results showed that there is biological transmutation of magnesium to calcium in human systems mediated by actinidic archaea dependent on cerium for its growth. Regulation of calcium and magnesium levels in the cell by archaeal mediated biological transmutation can regulate multiple physiological systems. Calcium can modulate the mitochondrial PT pore and cell death. Cellular calcium levels are also involved in oncogene activation. Magnesium levels in the cell can regulate glycosylation and protein processing modulating golgi body and lysosomal function. Presynaptic calcium levels can regulate synaptic transmission as well as neurotransmitter release into the synapse. Cellular calcium levels can activate NFKB producing immune activation. Magnesium and calcium levels can modulate mitochondrial function and metabolism[3]. This is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

There is magnesium depletion from the system and calcium accumulation which can predispose to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[3]. The increased intracellular calcium can open up the mitochondrial PT pore producing a mitochondrial dysfunction. Magnesium deficiency can produce a mitochondrial ATP synthase defect. The opening of the mitochondrial PT pore produces volume dysregulation of the mitochondria, hyperosmolarity and expansion of the mitochondrial matrix space

producing outer membrane rupture. This leads to release of cytochrome C into the cytoplasm, activating the caspase cascade and cell death. Mitochondrial dysfunction and related apoptosis as well as free radical generation has been related to neuronal degeneration. Decreased intracellular magnesium can lead to altered glyconjugate synthesis and a protein processing dysfunction. Protein processing golgi body dysfunction as well as ER stress has been related to neuronal degeneration. Altered glyconjugates can lead to defective MHC antigen presenting pathway and autoimmunity important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. A defective presentation of viral antigens can lead to immune evasion by the virus and viral persistence contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Both of these can contribute to oncogenesis. Increased calcium within the presynaptic neuron can lead to increased glutamate release into the synapse and increased postsynaptic neuronal calcium can increase the NMDA signal transduction. NMDA signal transduction is important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Increased NMDA signal transduction can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. An increase in intracellular calcium can activate the NFKB signal transduction producing immune activation and autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Immune activation has also been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

A calcium excess related PT pore dysfunction of mitochondria can generate free radicals. Free radicals can produce apoptosis, immune activation, insulin resistance and NMDA activity. Free radicals can activate NFKB producing immune activation and autoimmunity in neurodegenerations-alzheimer's disease,

parkinson's disease and motor neuron disease. Free radicals can activate the NMDA receptor modulating conscious perception and leading on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Free radicals can produce mitochondrial dysfunction and cell death. Free radicals can activate HIF alpha and lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Free radicals can produce insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

A shadow biosphere of actinidic archaea has been described in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaea transmutates magnesium to calcium for the purpose of biological mineralisation. The archaea can exist as nanoarchaea which can get calcified to form calcified nanoarchaeal forms. Calcified nanoarchaeal particles can induce NFKB. This can produce a state of systemic immune activation important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. This activates the AKT PI3 cascade inducing the Warburg phenotype with anaerobic glycolysis which is the basis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The lymphocytes depend of glycolysis for its energy needs. Increased glycolysis can lead to immune activation. The glycolytic enzyme glyceraldehyde 3 phosphate dehydrogenase mediates nuclear cell death. The glycolysis generated NADPH activates the NOX enzyme important in insulin receptor function and NMDA activity. This can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Thus the creation of Warburg phenotype can produce neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Thus the transmutation related free radical generation and altered calcium-magnesium ratios in the cell can alter synaptic transmission, mitochondrial function, golgi body/ER function, lysosomal function, immune activation, cell proliferation, insulin resistance and cell death. The actinidic archaea related biological transmutation is an important regulatory mechanism of the cell whose dysfunction can produce altered neuro-immune-endocrine regulation. This can lead to human disease. The biological transmutation gives the actinidic archaea energy to survive and generates calcium for its biological mineralization. This can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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7

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Endosymbiotic Archaeal Generated RNA Viroids Can Regulate Cell Function and Contribute to Disease State – Role in Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease [1, 2]. Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease [3, 4]. RNA viroids could contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[2]. The possibility of generation of RNA viroids by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea and viroids in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease is described[6]. The role of RNA viroids generated by actinidic archaea in regulation of body functions and the pathogenesis of human disease is discussed.

Materials and Methods

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol

substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond10. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA and free DNA11-14. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: – cytochrome F420, free RNA and free DNA. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.70	1.87	60.46	8.06
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
PD	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
MND	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[15, 16]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[17, 18]. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[19]. This can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[20]. Archaea induced immune activation and redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[21]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[22]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[21, 22]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters[23]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The RNA viroids can regulate mRNA function by RNA interference[20]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/heterochromatin expression. This can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and ebstein barr virus by recombining with archaeal, eukaryotic and human genes resulting in viral speciation[24, 25, 26]. The RNA viroids

can also recombine with endogenous commensal RNA and DNA viruses producing speciation. Viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of viral speciation. These viruses and bacteria can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The multicellular eukaryotes are like archaeal biofilms. The archaea with a mevalonate pathway uses the extracellular RNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes[27, 28]. The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids for the regulation of multicellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth[29]. Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality[30]. The integration of

nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new neuronal, metabolic, immune and tissue phenotype leading to human disease. This leads on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

NMDA receptors can be modulated by viroid induced RNA interference[2]. The dipolar viroids combined with actinides in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world[2, 31]. This can lead to perception of low level EMF contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The viroids can regulate limbic lobe transmission by RNA viroid mediated RNA interference modulating norepinephrine, dopamine, serotonin and acetyl choline receptors[18]. This can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The higher degree of integration of the archaea and viroids into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance[2]. Right hemispheric dominance can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The viroid RNA interference mediated altered monoamine and NMDA transmission contributes to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion[2, 32]. The archaea and viroid induced chronic immune activation and generation of

superantigens can lead on to autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea and viroids can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[33]. This Warburg phenotype contributes to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and metabolic syndrome. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[33]. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway[34]. Viroid induced RNA interference can modulate the mRNAs concerned with insulin receptor function and lipid metabolism contributing to insulin resistance important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The viroid induced RNA interference can modulate the mRNA concerned with the death receptor pathway producing apoptosis and neuronal degeneration. The RNA viroids can recombine with HERV sequences and get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by RNA viroid binding producing prion disease. Prions and HERV sequences are involved in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Thus the actinidic archaea generated RNA viroids can regulate cell function and produce neuro-immuno-genetic-endocrine-metabolic integration. The RNA viroids and their complementary DNA can serve the purpose of viral speciation. The RNA viroids also contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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Endosymbiotic Actinidic Archaea and Viroids Regulate Cellular Organelle Function, Cell Growth, Cell Differentiation and Cell Death – Role in Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

A hypothesis regarding the role of endosymbiotic actinidic archaea and viroids in the regulation of cell function, cell differentiation, cell proliferation and cell death is presented in this paper. Actinides like rutile producing intracellular magnesium deficiency due to rutile-magnesium exchange sites in the cell membrane has been implicated in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease [1, 2]. Organisms like phytoplasmas and viroids have also been demonstrated to play a role in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease [3-7]. Actinidic archaea and viroids have been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease [2]. The incidence of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease is high in the presence of low level radioactivity of the mineral sands of Kerala[1]. Actinidic archaea and viroids have also been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[2]. Davies has put forward the concept of a shadow biosphere of organisms with alternate biochemistry present in earth itself[8]. An actinide dependent shadow biosphere of archaea and viroids regulating the cell cycle is described in the above mentioned disease states[6]. The endosymbiotic actinidic archaea and viroids can regulate the cell cycle and cellular organelle function.

Materials and Methods

Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The following groups were included in the study: –

neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[9]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids[10-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. The statistical analysis was done by ANOVA.

Results

The parameters checked as indicated above were: – cytochrome F420, free RNA, free DNA, muramic acid, polycyclic aromatic hydrocarbon, hydrogen peroxide, serotonin, pyruvate, ammonia, glutamate, cytochrome C, hexokinase, ATP synthase, HMG CoA reductase, digoxin and bile acids. Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar

results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-7 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on muramic acid and glutamate.*

Group	Muramic acid % (Increase without Doxy)		Muramic acid % (Decrease with Doxy)		Glutamate % (Increase without Doxy)		Glutamate % (Decrease with Doxy)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
AD	23.09	1.81	65.86	4.27	23.66	1.67	65.97	3.36
PD	22.48	2.13	63.12	4.84	23.21	1.74	67.76	3.15
MND	21.94	2.03	64.29	5.35	23.89	1.69	65.09	3.89
Aging	22.93	2.08	63.49	5.01	22.71	1.82	66.13	3.83
F value	348.867		364.999		403.394		680.284	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on free DNA and RNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
PD	22.30	2.19	66.19	4.20	23.16	1.60	64.21	3.43
MND	23.11	2.00	61.52	4.97	23.04	1.66	66.13	3.49
Aging	19.73	2.27	65.49	7.28	19.73	2.27	62.70	3.24
F value	337.577		356.621		427.828		654.453	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 3 *Effect of rutile and antibiotics on HMG CoA reductase and PAH.*

Group	HMG CoA R % change (Increase with Rutile)		HMG CoA R % change (Decrease with Doxy)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.30	0.20	18.35	0.35	4.45	0.14	18.25	0.72
AD	23.43	1.68	61.68	8.32	23.26	1.53	60.91	7.59
PD	22.12	2.27	60.98	8.29	23.63	1.75	62.23	5.43
MND	21.79	1.68	64.51	6.96	23.17	2.02	61.03	5.40
Aging	22.94	2.59	59.19	7.18	22.66	1.96	65.88	5.01
F value	319.332		199.553		391.318		257.996	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 4 *Effect of rutile and antibiotics on digoxin and bile acids.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
AD	0.55	0.03	0.192	0.040	22.12	2.19	62.86	6.28
PD	0.54	0.03	0.193	0.042	23.77	1.40	65.39	4.88
MND	0.53	0.06	0.229	0.051	23.53	1.78	61.61	6.77
Aging	0.56	0.10	0.238	0.049	24.58	1.08	64.20	5.16
F value	135.116		71.706		290.441		203.651	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and hexokinase.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy)		Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
AD	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
PD	21.64	0.67	61.36	8.49	22.95	1.82	64.15	4.62
MND	21.58	0.81	59.11	10.05	23.15	1.78	64.41	4.90
Aging	21.31	2.51	60.42	7.65	23.36	1.78	66.62	4.83
F value	321.255		115.242		292.065		317.966	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and delta amino levulinic acid.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
PD	24.17	1.33	56.09	6.56	23.79	1.58	65.56	4.03
MND	23.58	1.94	57.85	6.63	23.06	1.72	64.82	3.31
Aging	22.27	1.87	61.77	6.79	19.73	2.27	64.78	6.62
F value	380.721		171.228		372.716		556.411	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 7 *Effect of rutile and antibiotics on ATP synthase and cytochrome F 420.*

Group	ATP synthase % (Increase with Rutile)		ATP synthase % (Decrease with Doxy)		CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.40	0.11	18.78	0.11	4.48	0.15	18.24	0.66
AD	23.58	2.08	66.21	3.69	23.12	2.00	56.90	6.94
PD	23.86	1.86	65.93	3.95	22.32	2.17	57.31	9.22
MND	23.75	1.81	66.49	4.11	22.76	2.20	61.60	8.74
Aging	23.19	1.74	65.68	4.06	22.09	1.38	61.42	7.26
F value	449.503		673.081		306.749		130.054	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaea can synthesize and use cholesterol as a carbon and energy source[14, 15]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[16]. There was

also an increase in archaeal HMG CoA reductase activity indicating increased cholesterol synthesis by the archaeal mevalonate pathway. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[7]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[15]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH, serotonin and dopamine was also detected[17]. The archaeal glycolytic hexokinase activity and archaeal extracellular ATP synthase activity were increased. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[18]. This can lead to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The archaeal digoxin is the master conductor regulating and coordinating cellular organelle function. Digoxin can produce sodium-potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis. The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains. The digoxin induced lipid microdomain modulation can regulate the GPCR couple, neurotransmitter-glutamate, dopamine, and serotonin, GPCR coupled endocrine receptors-adrenaline, noradrenaline, glucagon and neuropeptide receptors and protein tyrosine kinase linked insulin receptor. The digoxin mediated inhibition of nuclear membrane sodium-potassium ATPase can modulate nuclear membrane lipid microdomains and steroidal/thyroxine DNA receptor function. Thus endogenous digoxin can modulate all the neurotransmitter and endocrine receptors by regulating lipid microdomains. Digoxin induced sodium potassium ATPase inhibition can

increase intracellular calcium and reduce intracellular magnesium. Digoxin by increasing intracellular calcium can produce mitochondrial PT pore dysfunction. There is intracellular magnesium deficiency producing ATP synthase defect. Digoxin can thus modulate mitochondrial function. Decreased intracellular magnesium can lead to altered glycoconjugate synthesis and a protein processing dysfunction and lysosomal dysfunction. Digoxin induced redox stress can produce histone deacetylase inhibition and modulate gene expression. Digoxin can modulate mRNA splicing and RNA function. Digoxin can thus modulate mitochondrial, cell membrane, golgi body, lysosomal and nuclear functions. It can integrate the function of cell organelle[2]. Archaeal bile acids can modulate mitochondrial function. Bile acids can produce uncoupling of oxidative phosphorylation and produce mitochondrial hibernation. Archaeal pyruvate is a HDAC inhibitor and modulates gene expression. Archaeal ammonia can activate membrane sodium potassium ATPase and produce mitochondrial PT pore dysfunction. Archaeal butyrate functions as a HDAC inhibitor modulating gene expression. Butyrate can also modulate protein conformation and folding. Butyrate can thus regulate protein structure and function. Butyrate is used in the treatment of the unfolded protein response. Archaeal PAH can combine with the cell membrane, proteins and nucleic acids modulating their structure and function. Thus the archaeal cholesterol catabolites can regulate function of multiple cellular organelle and produce integration of cellular organelle function[2]. This can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The actinidic archaea and viroids can modulate DNA and RNA function and regulate the cell cycle. There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides modulate RNA folding and catalyse its ribozymal action. Digoxin can

cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[19]. Archaeal pyruvate can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[20]. The noncoding DNA is lengthened by integrating RNA viroidal complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[21]. The integrated viroids and archaea can undergo vertical transmission and can exist as genomic parasites[20, 21]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters[22]. The viroidal complementary DNA can function as jumping genes producing a dynamic genome modulating gene expression. The RNA viroids can regulate mRNA function by RNA interference[19]. The phenomena of RNA interference can modulate T cell and B cell function, cell differentiation, cell growth and euchromatin/heterochromatin expression. RNA viroidal mRNA interference can modulate the cell cycle producing malignant transformation. The phenomenon of RNA interference and the RNA viroidal complementary DNA related jumping genes can lead onto proof reading errors and generation of trinucleotide repeats contributing to the pathogenesis of huntington's disease. The phenomena of viroidal RNA induced RNA interference can modulate the cell death pathways producing neuronal and cell degeneration. This can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The presence of muramic acid, HMG CoA reductase and cholesterol oxidase activity inhibited by antibiotics indicates the presence of bacteria with mevalonate pathway. The bacterial with mevalonate pathway include streptococcus, staphylococcus, actinomycetes, listeria, coxiella and borrelia[23]. The bacteria and archaea with mevalonate pathway and cholesterol catabolism had a evolutionarily advantage and constitutes the isoprenoidal clade organism with the archaea evolving into mevalonate pathway gram positive and gram negative organism through horizontal gene transfer of viroidal and virus genes[24]. The isoprenoidal clade prokaryotes develop into other groups of prokaryotes via viroidal/virus as well as eukaryotic horizontal gene transfer producing bacterial speciation[25]. The RNA viroids and its complementary DNA developed into cholesterol enveloped RNA and DNA viruses like herpes, retrovirus, influenza virus, borna virus, cytomegalo virus and ebstein barr virus by recombining with eukaryotic and human genes resulting in viral speciation. Bacterial and viral species are ill defined and fuzzy with all of them forming one common genetic pool with frequent horizontal gene transfer and recombination. Thus the multi and unicellular eukaryote with its genes serves the purpose of prokaryotic and viral speciation. The multicellular eukaryote developed so that their endosymbiotic archaeal colonies could survive and forage better. The multicellular eukaryotes are like bacterial biofilms. The archaea and bacteria with a mevalonate pathway uses the extracellular RNA viroids and DNA viroids for quorum sensing and in the generation of symbiotic biofilm like structures which develop into multicellular eukaryotes[26, 27]. The endosymbiotic archaea and bacteria with mevalonate pathway still uses the RNA viroids and DNA viroids for the regulation of multicellular eukaryote. Pollution is induced by the primitive nanoarchaea and mevalonate pathway bacteria synthesized PAH and methane leading on to redox stress. Redox stress leads to sodium potassium ATPase inhibition, inward movement of plasma membrane cholesterol, defective SREBP

sensing, increased cholesterol synthesis and nanoarchaeal/mevalonate pathway bacterial growth[28]. Redox stress leads on to viroidal and archaeal multiplication. Redox stress can also lead to HERV reverse transcriptase and integrase expression. The noncoding DNA is formed of integrating RNA viroidal complementary DNA and archaea with the integration going on as a continuing event. The archaeal pox like dsDNA virus forms evolutionarily the nucleus. The integrated viroidal, archaeal and mevalonate pathway bacterial sequences can undergo vertical transmission and can exist as genomic parasites. The genomic integrated archaea, mevalonate pathway bacteria and viroids form a genomic reserve of bacteria and viruses which can recombine with human and eukaryotic genes producing bacterial and viral speciation. This can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The change in the length and grammar of the noncoding region produces eukaryotic speciation and individuality[33]. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue This results in a new neuronal, metabolic, immune and tissue phenotype leading to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The microchimeras formed can lead to polyploidy and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea, viroids and digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[35]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis,

inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics. The increased glycolysis and induction of Warburg phenotype results in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol and lipid synthesis[35]. Cholesterol oxidase activity, increased glycolysis related NADPH oxidase activity and mitochondrial dysfunction generates free radicals important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis leading to metabolic channeling to the mevalonate pathway. This leads to increased synthesis of digoxin. Hyperdigoxinemia is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signaling can activate NFKB producing chronic immune activation[2, 36]. The archaea and viroid induced chronic immune activation and generation of superantigens. Autoimmunity is important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaea and viroids can regulate the nervous system including the NMDA synaptic transmission[2]. NMDA can be activated by digoxin induced calcium oscillations, PAH and viroid induced RNA interference[2]. The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate. NMDA excitotoxicity can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The higher degree of integration of the archaea

into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance[2]. Right hemispheric dominance can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease as reported previously from this laboratory. Archaeal PAH can thus induce neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[37]. The archaeal bile acids can bind GPCR and modulate D2 regulating the conversion of T4 to T3. T3 activates uncoupling proteins reducing redox stress. Bile acids can also activate NRF ½ inducing NQO1, GST, HOI reducing redox stress. The archaeal bile acids can bind VDR, the vitamin D receptor resulting in inhibition of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[38, 39]. Thus the actinide, viroid and mevalonate pathway bacteria induced metabolic, genetic, immune and neuronal transmission changes can lead on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The actinidic archaea and viroids can modulate cell death and neuronal degeneration. Bacteria and viruses have been related to the pathogenesis of motor neuron disease, alzheimer's disease and parkinson's disease. Chlamydia, mycoplasma, cyanobacteria, actinomycetes and borrelia have been reported to be involved in the pathogenesis of alzheimer's disease. Helicobactor pylori, nocardia, streptococcus and corona viruses have been implicated in parkinson's disease. Mycoplasma, borrelia, retroviruses and enteroviruses have been related to the pathogenesis of MND[40-46]. The change in the length and grammar of the noncoding region[33]. The integration of nanoarchaea, mevalonate pathway prokaryotes and viroids in to the eukaryotic and human genome produces a chimera which can multiply producing biofilm like multicellular structures having a mixed archaeal, viroidal, prokaryotic and eukaryotic characters which is a regression from the multicellular eukaryotic tissue. This results in a new

neuronal, metabolic, immune and tissue phenotype leading to human diseases like neuronal degeneration. The microchimeras formed can lead to polyploidy which has been implicated in degenerations like alzheimer's disease. Microchimeras can lead onto autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The actinidic archaea and viroids can regulate the NMDA transmission leading onto cell death[2]. As discussed before NMDA receptors can be activated by digoxin induced calcium oscillations, PAH increasing NMDA activity as well as viroid induced RNA interference[2]. The cholesterol ring oxidase generated pyruvate can be converted by the GABA shunt pathway to glutamate contributing to NMDA excitotoxicity. The archaea can regulate dopaminergic transmission with archaeal cholesterol aromatase/ring oxidase generated dopamine[16]. The increased dopamine synthesis can generate increased free radicals consequent to its catabolism. Cholesterol oxidase can generate free radical hydrogen peroxide. Free radicals can produce neuronal degeneration. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left hemispheric dominance[2]. Previous studies by the authors have related right hemispheric chemical dominance to neuronal degeneration. Archaea and RNA viroid can bind the TLR receptor induce NFKB producing immune activation and cytokine TNF alpha secretion. The archaeal DXP and mevalonate pathway metabolites can bind γδ TCR and digoxin induced calcium signaling can activate NFKB producing chronic immune activation[2, 36]. The archaea and viroid induced chronic immune activation and generation of superantigens can lead on to autoimmune disease. Immune activation and autoantibodies have been related to neuronal degeneration. Immune activation and free radicals induce neutral sphingomyelinase generating ceramide. Ceramide acts upon the mitochondrial PT pore producing cell death. Archaea, viroids and digoxin can induce the host

AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[35]. The increased glycolytic hexokinase activity, decrease in blood ATP, leakage of cytochrome C, increase in serum pyruvate and decrease in acetyl CoA indicates the generation of the Warburg phenotype. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics. Mitochondrial dysfunction has been related to neuronal degeneration. The increased glycolysis results in increased generation of the enzyme glyceraldehyde 3 phosphate dehydrogenase (GAPD). GAPD can undergo polyadenylation via free radical activated PARP enzyme. The polyadenylated GAPD can undergo nuclear translocation producing nuclear cell death. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis[35]. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. Ammonia can produce NMDA excitotoxicity and cell death. Ammonia can activate sodium potassium ATPase producing increased neuronal requirement of ATP leading onto mitochondrial transmembrane potential changes and cell death. The increased cholesterol substrate leads to increased archaeal growth and digoxin synthesis leading to metabolic channelling to the mevalonate pathway. Digoxin can produce sodium potassium ATPase inhibition and increase in intracellular calcium producing mitochondrial PT pore dysfunction and cell death[2]. The archaeal cholesterol catabolism generated PAH can produce NMDA excitotoxicity and cell death. The archaeal and mevalonate pathway bacteria cholesterol catabolism can deprive cholesterol from neuronal cell membrane and organelle membranes like mitochondrial, ER and lysosomal membranes producing cellular and organelle dysfunction and death. Cholesterol metabolic defect has been described in huntington's disease. Thus, the shadow biosphere of actinide dependent archaea, viroids and mevalonate pathway bacteria can lead

onto neuronal degenerations like alzheimer's disease, huntington's disease, parkinson's disease and motor neuron disease.

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Endosymbiotic Actinidic Archaeal Cholesterol Catabolic Syndrome – Hypocholesterolemia and Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinidic archaea have been implicated in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-9]. Actinide based primitive organism like archaea have a mevalonate pathway and cholesterol catabolism. Cholesterol catabolism by actinidic archaea can lead to cholesterol depletion and a hypocholesterolemic state contributing to the pathogenesis of these disorders[10-17].

Archaea can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low cholesterol values in populations have been related to high mortality. The archaeal cholesterol catabolising enzymes were studied and the results in presented in this paper. This can be described as the endosymbiotic actinidic archaeal cholesterol catabolic syndrome[10-17].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was

prepared as described by Richmond[18]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, polycyclic aromatic hydrocarbon, digoxin, bile acid, cholesterol oxidase activity measured by hydrogen peroxide liberation, pyruvate, butyrate and propionate were estimated[19-21]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-4 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
PD	23.46	1.87	59.27	8.86	22.67	2.29	57.69	5.29
AD	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
MND	22.70	1.87	60.46	8.06	23.73	1.38	65.20	6.20
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on butyrate and propionate generation from cholesterol.*

Group	Butyrate % change (Increase with Rutile)		Butyrate % change (Decrease with Doxy+Cipro)		Propionate % change (Increase with Rutile)		Propionate % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
PD	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MND	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and bile acids.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		Bile acids % change (Increase with Rutile)		Bile acids % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.29	0.18	18.15	0.58
PD	0.51	0.05	0.199	0.027	22.61	2.22	66.62	4.99
AD	0.55	0.03	0.192	0.040	22.12	2.19	62.86	6.28
MND	0.51	0.05	0.213	0.033	23.41	1.41	58.70	7.34
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 290.441 P value < 0.001		F value 203.651 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on pyruvate and hydrogen peroxide.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**
Normal	4.34	0.21	18.43	0.82	4.43	0.19	18.13	0.63
PD	20.94	1.54	62.76	8.52	23.81	1.19	61.08	7.38
AD	22.63	0.88	56.40	8.59	22.65	2.48	60.19	6.98
MND	22.29	2.05	62.37	5.05	23.29	1.67	60.52	5.38
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 380.721 P value < 0.001		F value 171.228 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[22-24]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[22-24]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis and archaeal cholesterol hydroxylase activity indicating bile acid synthesis were increased[22-24]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[22-24]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The archaeal aromatization of cholesterol generating PAH was also detected[22-24]. This indicates archaeal cholesterol aromatase activity. The archaeal cholesterol side chain oxidase activity generates butyrate and propionate. Thus archaeal cholesterol oxidase, cholesterol aromatase, cholesterol side chain oxidase, cholesterol hydroxylase and beta hydroxyl steroid dehydrogenase activity were detected in high levels in the patient population of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron

disease. The archaeal cholesterol catabolising enzymes were actinide dependent. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[25]. This leads to a cholesterol depleted state and hypocholesterolemic syndrome in patients with neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Low cholesterol has been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Cholesterol is required for the formation of synaptic connectivity in neuronal cultures. Depletion of cholesterol from the brain results in loss of synaptic connectivity in multiple neuronal circuits contributing to neuronal degeneration. Low cholesterol has been related to autoimmunity important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[10-17].

The gut endotoxins and lipopolysaccharides are absorbed along with fat producing the syndrome of metabolic endotoxaemia. The endotoxins and lipopolysaccharides can combine with lipoproteins and are detoxified. Metabolic endotoxaemia produces chronic immune activation and generation of superantigens. This has been related to the genesis of autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Metabolic endotoxaemia results in immune activation and generation of TNF alpha which modulates the insulin receptor producing insulin resistance. Insulin resistance is related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Metabolic endotoxaemia has been related to neuronal degenerations like Alzheimer's disease and Parkinson's disease. Metabolic endotoxaemia related chronic immune activation drives the retroviral state. Endogenous retroviruses are related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Thus hypocholesterolemia leads to non-detoxification of endotoxins and

lipopolysaccharides resulting in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[10-17].

Infections have been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. H. pylori infection and nocardiosis has been related to Parkinson's disease. Chlamydial infection and actinomycosis has been related to Alzheimer's disease. Clostridial infection has been related to motor neuron disease. Gut bacteria with increase in gut firmicutes and decrease in bacteroides have been related to insulin resistance important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Low cholesterol leads to lack of lipoprotein binding to endotoxins[10-17]. The endotoxins and lipopolysaccharides are not detoxified.

Viral diseases have been related to the pathogenesis of neuronal degeneration. The virus binds to lipid microdomains in the cell membrane. Cholesterol depletion leads to alteration in lipid microdomains and increased entry of virus in the cell. Entero virus infection has been associated with motor neuron disease. Corona virus infection predisposes to Parkinson's disease. Herpes virus infection is implicated in Alzheimer's disease. Retroviral infection-exogenous and endogenous have been related to neuronal degeneration. Prion disease has been related to alterations in cholesterol metabolism. Prion proteins are important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Thus a cholesterol depleted state can lead to increased predilection to viral infection and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[10-17].

The actinidic archaea uses cholesterol catabolism to generate energy. The cholesterol catabolising enzymes of the archaea are dependent on actinides. The archaeal cholesterol catabolism leads to a cholesterol depleted state and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron

disease. Cholesterol depleted state have been related to high mortality. This can be described as the endosymbiotic actinidic archaeal cholesterol catabolic syndrome[10-17]. This can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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10

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Endosymbiotic Actinidic Archaeal Mediated Warburg Phenotype Mediates Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinides like rutile as well as organisms like phytoplasmas and viroids have been implicated in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-4]. The Warburg phenotype has been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[4]. The possibility of Warburg phenotype induced by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered in this paper[5-8]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[7, 9].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420 and hexokinase[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm

and emission wavelength 520 nm). Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.70	1.87	60.46	8.06
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on hexokinase.*

Group	Hexokinase % change (Increase with Rutile)		Hexokinase % change (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.21	0.16	18.56	0.76
PD	23.33	1.79	62.50	5.56
AD	22.96	2.12	65.11	5.91
MND	21.66	1.94	67.03	5.97
F value	292.065		317.966	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15, 16]. The archaeal glycolytic hexokinase activity were increased. The part of the increased glycolytic hexokinase activity detected is human. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. This can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Archaea can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[18]. The increased glycolytic hexokinase activity indicates the generation of the Warburg phenotype. The generation of the Warburg phenotype is due to activation of HIF alpha. This stimulates anaerobic glycolysis, inhibits pyruvate dehydrogenase, inhibits mitochondrial oxidative phosphorylation, stimulates heme oxygenase, stimulates

VEGF and activates nitric oxide synthase. This can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and insulin resistance. Insulin resistance is important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The archaea and viroid generated cytokines can lead to TNF alpha induced insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increase in glycolysis can activate glyceraldehyde 3 phosphate dehydrogenase which gets translocated to the nucleus after polyadenylation. The PARP enzyme is activated by glycolysis mediated redox stress. This can produce nuclear cell death and neuronal degeneration. The increase in the glycolytic enzyme fructose 1, 6 diphosphatase increases the pentose phosphate pathway. This generates NADPH which activates NOX. NOX activation is related to NMDA activation and glutamate excitotoxicity. This leads onto neuronal degeneration[18].

The increase in glycolysis activates the enzyme fructose 1, 6 diphosphatase which activates the pentose phosphate pathway liberating NADPH. This increases NOX activity generating free radical stress and H_2O_2. Free radical stress is related to insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Free radicals can activate NFKB producing immune activation and autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Free radicals can open the mitochondrial PT pore, produce release of cyto C and activate the caspase cascade. This produces cell death and neuronal degeneration. The free radicals can activate NMDA receptor. Increased NMDA excitotoxicity can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Free radicals can produce HDAC inhibition and HERV generation. The encapsulation of HERV particles in phospholipids

vesicles can mediate the generation of the acquired immunodeficiency syndrome. HERV particles can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[18].

The lymphocytes depend on glycolysis for its energy needs. The increase in glycolysis owing to the induction of Warburg phenotype can lead to immune activation. Immune activation can lead to autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. TNF alpha can activate the NMDA receptor leading to glutamate excitotoxicity and neuronal degeneration. TNF alpha activating NMDA receptor can contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. TNF alpha can induce expression of HERV particles contributing to pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. TNF alpha can also act upon the insulin receptor producing insulin resistance important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. NOX activation consequent to the generation of the Warburg phenotype also activates the insulin receptor. Thus there is a hyperinsulinemic state leading on to insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[18].

Thus the induction of the Warburg phenotype can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The Warburg phenotype leads to inhibition of pyruvate dehydrogenase and accumulation of pyruvate. The accumulated pyruvate enters the GABA shunt pathway and is converted to citrate which is acted upon by citrate lyase and converted to acetyl CoA, used for cholesterol synthesis. The pyruvate can be converted to glutamate and ammonia which is oxidised by archaea for energy needs. The increased cholesterol substrate leads to increased archaeal growth and

further induction of the Warburg phenotype[18]. The Warburg phenotype is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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11

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Endosymbiotic Actinidic Archaeal Synthesis of Digoxin From Cholesterol Regulates Cellular Function and Contributes to Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinides like rutile, endogenous digoxin as well as organisms like phytoplasmas and viroids have been implicated in the etiology of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-4]. Endogenous digoxin has been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[4]. The possibility of endogenous digoxin synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered[5-8]. An actinide dependent shadow biosphere of archaea in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease is described[7, 9].

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – cytochrome F420 and digoxin[11-13]. Cytochrome F420 was estimated

flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-2 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time.

Table 1 *Effect of rutile and antibiotics on cytochrome F420.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)	
	Mean	**± SD**	**Mean**	**± SD**
Normal	4.48	0.15	18.24	0.66
PD	23.46	1.87	59.27	8.86
AD	23.12	2.00	56.90	6.94
MND	22.70	1.87	60.46	8.06
F value	306.749		130.054	
P value	< 0.001		< 0.001	

Table 2 *Effect of rutile and antibiotics on digoxin.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003
PD	0.51	0.05	0.199	0.027
AD	0.55	0.03	0.192	0.040
MND	0.51	0.05	0.213	0.033
F value	135.116		71.706	
P value	< 0.001		< 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15, 16]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis was increased[8]. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[17]. This is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Archaeal digoxin induced redox stress can produce histone deacetylase inhibition resulting in endogenous retroviral (HERV) reverse transcriptase and integrase expression. Digoxin can cut and paste the HERV RNA by modulating RNA splicing generating RNA viroidal diversity[18]. This can also integrate the HERV RNA complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase[19]. The noncoding DNA is lengthened by

integrating HERV RNA complementary DNA with the integration going on as a continuing event. The archaea genome can also get integrated into human genome using integrase as has been described for trypanosomes[20]. The integrated archaea can undergo vertical transmission and can exist as genomic parasites[19, 20]. This increases the length and alters the grammar of the noncoding region producing memes or memory of acquired characters as well as eukaryotic speciation and individuality[21]. The HERV RNA complementary DNA can function as jumping genes producing a dynamic genome important in storage of synaptic information, HLA gene expression and developmental gene expression. The HERV RNA can regulate mRNA function by RNA interference[18]. The phenomena of RNA interference can modulate T cell and B cell function, insulin signaling lipid metabolism, cell growth and differentiation, apoptosis, neuronal transmission and euchromatin/ heterochromatin expression. This is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The archaeal digoxin can regulate the nervous system including the NMDA receptor[4, 22]. NMDA can be modulated by digoxin induced calcium oscillations resulting NMDA induction[4]. NMDA excitotoxicity can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The dipolar PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state[22] inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world[4, 22]. This can lead to perception of low level EMF contributing to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The higher degree of integration of the archaea into the genome produces increased digoxin synthesis producing right hemispheric dominance and lesser degree producing left

hemispheric dominance[4]. Right hemispheric dominance is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The increased integration of archaea into the neuronal genome can produce increased digoxin mediated NMDA transmission producing neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Digoxin induced calcium oscillations can activate NFKB producing immune activation and cytokine secretion. The archaeal digoxin induced chronic immune activation can lead on to autoimmunity important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[23]. Archaeal digoxin can induce the host AKT PI3K, AMPK, HIF alpha and NFKB producing the Warburg metabolic phenotype[24]. There is induction of glycolysis, inhibition of PDH activity and mitochondrial dysfunction resulting in inefficient energetics and insulin resistance. The archaeal digoxin generated cytokines can lead to TNF alpha induced insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Digoxin induced sodium potassium ATPase inhibition can lead to increase in HMG CoA reductase activity and increased cholesterol synthesis. The increased cholesterol substrate also leads to increased archaeal growth and digoxin synthesis due to metabolic channeling to the mevalonate pathway. Digoxin can produce sodium potassium ATPase inhibition and inward movement of plasma membrane cholesterol. This produces defective SREBP sensing, increased HMG CoA reductase activity and cholesterol synthesis. The digoxin induced inward movement of plasma membrane cholesterol can alter membrane cholesterol/sphingomyelin ratio producing modified lipid microdomains. The digoxin induced lipid microdomain modulation can regulate the GPCR couple adrenaline, noradrenaline, glucagon and neuropeptide receptors as well as protein tyrosine kinase linked insulin receptor. The digoxin mediated inhibition of nuclear membrane sodium-potassium ATPase can modulate nuclear membrane

lipid microdomains and steroidal/thyroxine DNA receptor function. Thus endogenous digoxin can modulate all the endocrine receptors by regulating lipid microdomains. Hyperdigoxinemia by producing defective neuro-immuno-endocrine integration is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Digoxin induced sodium potassium ATPase inhibition results in an ATP sparing effect. Eighty percent of the ATP generated is used to run the sodium potassium ATPase pump. The digoxin inhibition of the sodium-potassium ATPase spares this ATP which is then used for lipid synthesis. Thus endogenous digoxin and the shadow biosphere generated Warburg phenotype can produce increased lipid synthesis and insulin resistance important in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Fat fuels insulin resistance by binding to the toll receptor and producing immune activation and immune infiltration of the adipose tissue. The archaeal digoxin induced insulin resistance leads to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The digoxin induced increased intracellular calcium can lead to PT pore dysfunction, cell death and neuronal degeneration[4]. The digoxin mediated transcribed HERV RNA can get encapsulated in microvesicles contributing to the retroviral state. The prion protein conformation is modulated by HERV RNA binding producing prion disease. HERV sequences and prions can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[4]. Thus the archaeal digoxin can produce neuro-immune-metabolic-endocrine-genetic integration. The increased archaeal cholesterol catabolism and digoxin secretion can lead to diverse pathological states of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

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19

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Archaeal Porphyrins, Regulation of Cell Function and Neuro–Immuno–Endocrine Integration – Role in Pathogenesis of Neurodegenerations – Alzheimer's Disease, Parkinson's Disease and Motor Neuron Disease

Introduction

Actinidic archaea have been related to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[1-8]. An actinide dependent shadow biosphere of archaea and viroids in the above mentioned disease states is described[7, 9]. Actinidic archaea have a mevalonate pathway and are cholesterol catabolising. They can use cholesterol as a carbon and energy source. Archaeal cholesterol catabolism can generate porphyrins via the cholesterol ring oxidase generated pyruvate and GABA shunt pathway. Porphyrins have been related to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The role of archaeal porphyrins in regulation of cell functions and neuro-immuno-endocrine integration is discussed.

Materials and Methods

The following groups were included in the study: – neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. There were 10 patients in each group and each patient had an age and sex matched healthy control selected randomly from the general population. The blood samples were drawn in the fasting state before treatment was initiated. Plasma from fasting heparinised blood was used and the experimental protocol was as follows (I) Plasma+phosphate buffered saline, (II) same as I+cholesterol substrate, (III) same as II+rutile 0.1 mg/ml, (IV) same as II+ciprofloxacine and doxycycline each in a concentration of 1 mg/ml. Cholesterol substrate was prepared as described by Richmond[10]. Aliquots were withdrawn at zero time immediately after mixing and after incubation at 37 ℃ for 1 hour. The following estimations were carried out: – Cytochrome F420, free RNA, free DNA,

polycyclic aromatic hydrocarbon, hydrogen peroxide, pyruvate, ammonia, glutamate, delta aminolevulinic acid, succinate, glycine and digoxin[11-13]. Cytochrome F420 was estimated flourimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). Polycyclic aromatic hydrocarbon was estimated by measuring hydrogen peroxide liberated by using glucose reagent. Informed consent of the subjects and the approval of the ethics committee were obtained for the study. The statistical analysis was done by ANOVA.

Results

Plasma of control subjects showed increased levels of the above mentioned parameters with after incubation for 1 hour and addition of cholesterol substrate resulted in still further significant increase in these parameters. The plasma of patients showed similar results but the extent of increase was more. The addition of antibiotics to the control plasma caused a decrease in all the parameters while addition of rutile increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutile increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-6 as percentage change in the parameters after 1 hour incubation as compared to the values at zero time. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase.

Table 1 *Effect of rutile and antibiotics on cytochrome F420 and PAH.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		PAH % change (Increase with Rutile)		PAH % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.48	0.15	18.24	0.66	4.45	0.14	18.25	0.72
PD	23.46	1.87	59.27	8.86	22.67	2.29	57.69	5.29
AD	23.12	2.00	56.90	6.94	23.26	1.53	60.91	7.59
MND	22.70	1.87	60.46	8.06	23.73	1.38	65.20	6.20
	F value 306.749 P value < 0.001		F value 130.054 P value < 0.001		F value 391.318 P value < 0.001		F value 257.996 P value < 0.001	

Table 2 *Effect of rutile and antibiotics on free RNA and DNA.*

Group	DNA % change (Increase with Rutile)		DNA % change (Decrease with Doxy+Cipro)		RNA % change (Increase with Rutile)		RNA % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.37	0.15	18.39	0.38	4.37	0.13	18.38	0.48
PD	23.40	1.51	63.68	4.66	23.08	1.87	65.09	3.48
AD	23.52	1.65	64.15	4.60	23.29	1.92	65.39	3.95
MND	22.29	2.05	58.70	7.34	22.29	2.05	67.03	5.97
	F value 337.577 P value < 0.001		F value 356.621 P value < 0.001		F value 427.828 P value < 0.001		F value 654.453 P value < 0.001	

Table 3 *Effect of rutile and antibiotics on digoxin and delta aminolevulinic acid.*

Group	Digoxin (ng/ml) (Increase with Rutile)		Digoxin (ng/ml) (Decrease with Doxy+Cipro)		ALA % (Increase with Rutile)		ALA % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	0.11	0.00	0.054	0.003	4.40	0.10	18.48	0.39
PD	0.51	0.05	0.199	0.027	22.83	1.90	67.23	3.45
AD	0.55	0.03	0.192	0.040	23.67	1.68	66.50	3.58
MND	0.51	0.05	0.213	0.033	22.29	2.05	61.91	7.56
	F value 135.116 P value < 0.001		F value 71.706 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Table 4 *Effect of rutile and antibiotics on succinate and glycine.*

Group	Succinate % (Increase with Rutile)		Succinate % (Decrease with Doxy+Cipro)		Glycine % change (Increase with Rutile)		Glycine % change (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.41	0.15	18.63	0.12	4.34	0.15	18.24	0.37
PD	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
AD	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
MND	22.29	1.33	65.38	3.62	22.13	2.14	66.26	3.93
	F value 403.394 P value < 0.001		F value 680.284 P value < 0.001		F value 348.867 P value < 0.001		F value 364.999 P value < 0.001	

Table 5 *Effect of rutile and antibiotics on pyruvate and Glutamate.*

Group	Pyruvate % change (Increase with Rutile)		Pyruvate % change (Decrease with Doxy+Cipro)		Glutamate (Increase with Rutile)		Glutamate (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.34	0.21	18.43	0.82	4.21	0.16	18.56	0.76
PD	20.94	1.54	62.76	8.52	23.33	1.79	62.50	5.56
AD	22.63	0.88	56.40	8.59	22.96	2.12	65.11	5.91
MND	22.29	2.05	62.37	5.05	21.66	1.94	67.03	5.97
	F value 321.255 P value < 0.001		F value 115.242 P value < 0.001		F value 292.065 P value < 0.001		F value 317.966 P value < 0.001	

Table 6 *Effect of rutile and antibiotics on hydrogen peroxide and ammonia.*

Group	H_2O_2 % (Increase with Rutile)		H_2O_2 % (Decrease with Doxy+Cipro)		Ammonia % (Increase with Rutile)		Ammonia % (Decrease with Doxy+Cipro)	
	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Normal	4.43	0.19	18.13	0.63	4.40	0.10	18.48	0.39
PD	23.81	1.19	61.08	7.38	22.83	1.90	67.23	3.45
AD	22.65	2.48	60.19	6.98	23.67	1.68	66.50	3.58
MND	23.29	1.67	60.52	5.38	22.29	2.05	61.91	7.56
	F value 380.721 P value < 0.001		F value 171.228 P value < 0.001		F value 372.716 P value < 0.001		F value 556.411 P value < 0.001	

Discussion

There was increase in cytochrome F420 indicating archaeal growth. The archaea can synthesize and use cholesterol as a carbon and energy source[6, 14]. The archaeal origin of the enzyme activities was indicated by antibiotic induced suppression. The study indicates the presence of actinide based archaea with an alternate actinide based enzymes or metalloenzymes in the system as indicated by rutile induced increase in enzyme activities[15]. The archaeal beta hydroxyl steroid dehydrogenase activity indicating digoxin synthesis[8]. The archaeal cholesterol oxidase activity was increased resulting in generation of pyruvate and hydrogen peroxide[14]. The pyruvate gets converted to glutamate and ammonia by the GABA shunt pathway. The pyruvate is converted to glutamate by serum glutamate pyruvate transaminase. The glutamate gets acted upon by glutamate dehydrogenase to generate alpha ketoglutarate and ammonia. Alanine is most commonly produced by the reductive amination of pyruvate via alanine transaminase. This reversible reaction involves the interconversion of alanine and pyruvate, coupled to the interconversion of alpha-ketoglutarate (2-oxoglutarate) and glutamate. Alanine can contribute to glycine. Glutamate is acted upon by Glutamic acid decarboxylase to generate GABA. GABA is converted to succinic semialdehyde by GABA transaminase. Succinic semialdehyde is converted to succinic acid by succinic semialdehyde dehydrogenase. Glycine combines with succinyl CoA to generate delta aminolevulinic acid catalysed by the enzyme ALA synthase. There was upregulated archaeal porphyrin synthesis in the patient population which was archaeal in origin as indicated by actinide catalysis of the reactions. The cholesterol oxidase pathway generated pyruvate which entered the GABA shunt pathway. This resulted in synthesis of succinate and glycine which are substrates for ALA synthase. The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms[16, 17]. This can

contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

There was an increase in free RNA indicating self replicating RNA viroids and free DNA indicating generation of viroid complementary DNA strands by archaeal reverse transcriptase activity. The actinides and porphyrins modulate RNA folding and catalyse its ribozymal action. Digoxin can cut and paste the viroidal strands by modulating RNA splicing generating RNA viroidal diversity. The viroids are evolutionarily escaped archaeal group I introns which have retrotransposition and self splicing qualities[18]. Archaeal pyruvate producing histone deacetylase inhibition and porphyrins intercalating with DNA can produce endogenous retroviral (HERV) reverse transcriptase and integrase expression. This can integrate the RNA viroidal complementary DNA into the noncoding region of eukaryotic non coding DNA using HERV integrase as has been described for borna and ebola viruses[19]. The archaea and viroids can also induce cellular porphyrin synthesis. Bacterial and viral infections can precipitate porphyria[20-23]. This can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The porphyrins can undergo photooxidation generating free radicals. The archaeal porphyrins can produce free radical injury. The porphyrins can complex and intercalate with the cell membrane producing sodium potassium ATPase inhibition adding on to digoxin mediated inhibition. Porphyrins can complex with proteins and nucleic acid producing biophoton emission. Porphyrins complexing with proteins can modulate protein structure and function. Porphyrins complexing with DNA and RNA can modulate transcription and translation. The porphyrin especially protoporphyrins can bind to peripheral benzodiazepine receptors in the mitochondria and modulate its function, mitochondrial cholesterol transport and steroidogenesis. Peripheral benzodiazepine receptor modulation by protoporphy-

rins can regulate cell death, cell proliferation, immunity and neural functions. The porphyrin photo-oxidation generates free radicals which can modulate enzyme function. Redox stress modulated enzymes include pyruvate dehydrogenase, nitric oxide synthase, cystathione beta synthase and heme oxygenase. Free radicals can modulate mitochondrial PT pore function. Free radicals can modulate cell membrane function and inhibit sodium potassium ATPase activity. Thus the porphyrins are key regulatory molecules modulating all aspects of cell function[20-23]. This regulatory role of porphyrins is important in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

The archaea and viroids can regulate the nervous system including the NMDA receptor[4, 22]. Porphyrin photo-oxidation can generate free radicals which can modulate NMDA transmission. Free radicals can increase NMDA transmission. Free radicals can induce NMDA excitotoxicity and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The dipolar porphyrins, PAH and archaeal magnetite in the setting of digoxin induced sodium potassium ATPase inhibition can produce a pumped phonon system mediated Frohlich model superconducting state[22] inducing quantal perception with nanoarchaeal sensed gravity producing the orchestrated reduction of the quantal possibilities to the macroscopic world[4, 22]. The increased perception of low level EMF can lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Thus the porphyrins can mediate quantal perception of low level EMF leading to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyrins binding to proteins, nucleic acids and cell membranes can produce biophoton emission. Biophotons can mediate quantal perception. Cellular porphyrins photo-oxidation are involved in sensing of earth magnetic fields and low level biomagnetic fields. Thus prophyrins can mediate extrasensory perception. The increase in archaeal

porphyrins can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyria can thus lead to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Altered porphyrin metabolism has been described in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Porphyrin induced increased NMDA transmission and free radical injury can contribute to neuronal degeneration. Free radicals can produce mitochondrial PT pore dysfunction. This can lead to cyto C leak and activation of the caspase cascade leading to apoptosis and cell death. Altered porphyrin metabolism has been described in Alzheimer's disease. The increased porphyrin photo-oxidation generated free radicals mediated NMDA transmission can also contribute to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The protoporphyrins binding to mitochondrial benzodiazepine receptors can regulate brain function and cell death[20-23].

The porphyrin photo-oxidation can generate free radicals which can activate NFKB. This can produce immune activation and cytokine mediated injury. The increase in archaeal porphyrins can lead to autoimmunity in neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate immune function[20-23].

The porphyrin photo-oxidation mediated free radical injury can lead to insulin resistance and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Glucose has got a negative effect upon ALA synthase activity. Therefore hyperglycemia may be reactive protective mechanism to increased archaeal porphyrin synthesis. The protoporphyrins binding to mitochondrial benzodiazepine receptors can modulate mitochondrial steroidogenesis and metabolism. Altered porphyrin metabolism has been

described in insulin resistance states. Porphyrias can thus lead on to neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The porphyrin photo-oxidation can generate free radicals inducing HIF alpha and neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease[20-23].

The porphyrin can combine with prion proteins modulating their conformation. This leads to abnormal prion protein conformation and degradation. Archaeal porphyrins can contribute to prion disease. Prions are implicated in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. The porphyrins can intercalate with DNA producing HERV expression. The HERV particles generated can contribute to the retroviral state[20-23]. HERV particles are involved in the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease.

Thus the archaeal porphyrins can contribute to the pathogenesis of neurodegenerations-alzheimer's disease, parkinson's disease and motor neuron disease. Archaeal porphyrin synthesis is crucial in the pathogenesis of these disorders. Porphyrins may serve as regulatory molecules modulating immune, neural, endocrine, metabolic and genetic systems. The porphyrins photo-oxidation generated free radicals can produce immune activation, produce cell death, activate cell proliferation, produce insulin resistance and modulate conscious/quantal perception. The archaeal porphyrins functions as key regulatory molecules with mitochondrial benzodiazepine receptors playing an important role[20-23].

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