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Endosymbiotic Actinidic Archaeal Synthesis of Neurotransmitters by Cholesterol Catabolism Regulates Brain Function

Introduction

Endomyocardial fibrosis (EMF) along with the root wilt disease of coconut is endemic to Kerala with its radioactive actinide beach sands. Actinides like rutile as well as organisms like phytoplasmas and viroids have been implicated in the etiology of EMF.¹⁻⁴ Bacterial synthesis of neurotransmitters plays a role in quorum sensing and motility. The possibility of endogenous neurotransmitter synthesis by actinide based primitive organism like archaea with a mevalonate pathway and cholesterol catabolism was considered in EMF and systemic diseases like neuronal degeneration, psychiatric disease, metabolic syndrome x, autoimmune disease and malignancy.⁵⁻⁸ An actinide dependent shadow biosphere of archaea in the above mentioned disease states is described.^{7,9}

Materials and Methods

The following groups were included in the study: - endomyocardial fibrosis, Alzheimer's disease, multiple sclerosis, non-Hodgkin's lymphoma, metabolic syndrome x with cerebrovascular thrombosis and coronary artery disease, schizophrenia, autism, seizure disorder, Creutzfeldt Jakob's disease and acquired immunodeficiency syndrome. 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+ciprofloxacin 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withdrawn at zero time immediately after mixing and after incubation at 37 °C for 1 hour. The following estimations were carried out: - Cytochrome F420, dopamine, serotonin, noradrenaline, acetyl choline and glutamate.¹¹⁻¹³ Cytochrome F420 was estimated fluorimetrically (excitation wavelength 420 nm and emission wavelength 520 nm). 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 rutil increased their levels. The addition of antibiotics to the patient's plasma caused a decrease in all the parameters while addition of rutil increased their levels but the extent of change was more in patient's sera as compared to controls. The results are expressed in tables 1-3 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 glutamate.*

Group	CYT F420 % (Increase with Rutile)		CYT F420 % (Decrease with Doxy+Cipro)		Glutamate% change (Increase with Rutile)		Glutamate% change (Decrease with Doxy+Cipro)	
	Mean	±SD	Mean	±SD	Mean	±SD	Mean	±SD
Normal	4.48	0.15	18.24	0.66	4.34	0.21	18.43	0.82
Schizo	23.24	2.01	58.72	7.08	20.99	1.46	61.23	9.73
Seizure	23.46	1.87	59.27	8.86	20.94	1.54	62.76	8.52
AD	23.12	2.00	56.90	6.94	22.63	0.88	56.40	8.59
MS	22.12	1.81	61.33	9.82	21.59	1.23	60.28	9.22
NHL	22.79	2.13	55.90	7.29	21.19	1.61	58.57	7.47
DM	22.59	1.86	57.05	8.45	20.67	1.38	58.75	8.12
AIDS	22.29	1.66	59.02	7.50	21.21	2.36	58.73	8.10
CJD	22.06	1.61	57.81	6.04	21.07	1.79	63.90	7.13
Autism	21.68	1.90	57.93	9.64	21.91	1.71	58.45	6.66
EMF	22.70	1.87	60.46	8.06	22.29	2.05	62.37	5.05
F value	306.749		130.054		321.255		115.242	
P value	< 0.001		< 0.001		< 0.001		< 0.001	

Table 2. *Effect of rutile and antibiotics on noradrenaline and acetyl choline.*

Group	Noradrenaline % (Increase with Rutile)		Noradrenaline % (Decrease with Doxy+Cipro)		Acetyl choline % (Increase with Rutile)		Acetyl choline % (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
Seizure	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
MS	21.14	1.20	60.53	4.70	22.38	1.79	67.10	3.82
NHL	23.35	1.76	59.17	3.33	23.34	1.75	66.80	3.43
DM	23.27	1.53	58.91	6.09	22.87	1.84	66.31	3.68
AIDS	23.32	1.71	63.15	7.62	23.45	1.79	66.32	3.63
CJD	22.86	1.91	63.66	6.88	23.17	1.88	68.53	2.65
Autism	23.52	1.49	63.24	7.36	23.20	1.57	66.65	4.26
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	

Table 3. *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
Schizo	21.88	1.19	66.28	3.60	23.02	1.65	67.61	2.77
Seizure	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
MS	22.92	2.14	67.54	3.65	21.93	2.29	63.70	5.63
NHL	23.81	1.90	66.95	3.67	23.12	1.71	65.12	5.58
DM	24.10	1.61	65.78	4.43	22.73	2.46	65.87	4.35
AIDS	23.43	1.57	66.30	3.57	22.98	1.50	65.13	4.87
CJD	23.70	1.75	68.06	3.52	23.81	1.49	64.89	6.01
Autism	22.76	2.20	67.63	3.52	22.79	2.20	64.26	6.02
EMF	22.28	1.52	64.05	2.79	22.82	1.56	64.61	4.95
F value	403.394		680.284		348.867		364.999	
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.^{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 cholesterol oxidase activity results in generation of pyruvate.¹⁴ The pyruvate gets converted to glutamate and GABA by the GABA shunt pathway. The pyruvate generated by cholesterol oxidase activity can also get converted to acetyl CoA and acetyl choline. The archaeal aromatization of cholesterol generating norepinephrine,

serotonin and dopamine was also detected.¹⁶ The archaea can undergo magnetite and calcium carbonate mineralization and can exist as calcified nanoforms.¹⁷

The archaea and viroids can regulate the nervous system including the NMDA/GABA thalamo-cortico-thalamic pathway mediating conscious perception.^{4, 18} NMDA/GABA receptors can be modulated by cholesterol catabolism generated glutamate and GABA. The archaea can regulate limbic lobe transmission with archaeal cholesterol aromatase/ring oxidase generated norepinephrine, dopamine, serotonin and acetyl choline.¹⁶ The increased integration of archaea into the neuronal genome can produce increased cholesterol oxidase and aromatase mediated monoamine and NMDA transmission producing schizophrenia and autism. The archaeal cholesterol catabolism generated glutamate can produce NMDA excitotoxicity producing neuronal degeneration. The archaeal glutamate and GABA synthesis can play a role in neurodegeneration, autism and schizophrenia.

Archaeal cholesterol catabolism generated glutamate and serotonin can produce immune activation and acetyl choline can produce immunosuppression. The balance between the two sets of immunostimulatory and immunosuppressive neurotransmitters can contribute to autoimmune disease. Parasympathetic neuropathy and vagal blockade can lead to autoimmune disease. Immunity is regulated by the vagal reflex. Archaeal cholesterol catabolism generated glutamate and GABA can regulate insulin secretion from the pancreatic beta cells contributing to metabolic syndrome x. Metabolic syndrome x has been attributed to alteration in the sympathetic/parasympathetic balance. There is vagal suppression and sympathetic overactivity. This produces hyperinsulinism, immune activation and metabolic syndrome x. Sympathetic overactivity and vagal blockade can lead to vasospasm, microangiopathy and vascular disease. Sympathetic overactivity and parasympathetic blockade can

produce malignant cell proliferation. The Warburg phenotype can be induced by vagal blockade induced immune activation.¹⁹ Thus the archaeal synthesis of acetyl choline and catecholamines can regulate the sympathetic and parasympathetic nervous system contributing to metabolic syndrome x, autoimmune disease and malignancy.

The archaeal neurotransmitters may control the human nervous system regulating visceral functions and consciousness.

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