

# TITLE: “IMPACT OF ENVIRONMENTAL TRIGGERS ON FUTURE HETEROGENEITY”

## INTRODUCTION:

We are living in a singular moment of history, a moment of crisis in the literal sense of the word. In every branch of our activity, material or spiritual, we seem to have arrived at a critical turning point.

The brain is quite simply the most complicated object known. Issues concerned with its embryological development, anatomical connections, neurochemical heterogeneity, inherited pathologies and co-evolution and physiological interaction of its pre and post synaptic components offer the most extreme challenges to us. It is, of course, possible to examine these issues in terms of basic mechanisms and omit reference to the overt functions which they affect, but these functions are profoundly intriguing to both specialist and non-specialist as we wonder by what means the brain contributes to the ability to perceive, react, move, remember, regulate the internal and external environment, reproduce, reason and speak.

Of all the sciences, brain research raises the most intractable problems of semantics. If the boundaries between perception, action, memory and thought dissolve with the recognition that no biological activity occurs in a vacuum, the issues become even more complex when one acknowledges that these terms have a communicative significance which is entirely determined by the brain itself. Nevertheless, one is obliged to name the phenomenon under study and we all share an understanding of the significance of the general functions considered in this presentation even if, upon investigation, our intuitions seem of to be in dilemma.

## ABSTRACT:

The ultimate level of ability and degree to which a person with an intellectual impairment and learning disability is disadvantage in society, may be strongly influenced by a variety of socially determined factors. The environmental risk factors referred to here are those which has a direct effect (SHUKLAS' SYNDROME) on brain development and thus on the future of intellectuals and emotional development of that person.

As the brain is genetically predisposed to pay attention to human features and this tendency explains many aspects of human conduct where huge population desirably or undesirably lost their normal self-confidence and further surrender to most of the human created circumstance, which ultimately turned into avenues of anti-social and uncivilized deeds. We are obsessed by other people and this anthropocentricity shows throughout the every culture, language, religion, morals, politics and so on.

Many of the major psychiatric disorders aggregate in families. Various theories have been developed to explain how behaviour and personality traits develop and change them but most agree that a combination of genetic and environmental factors are necessary for the expression of many psychiatric disturbances.

These are complex traits which have not shown simple mendelian inheritance patterns, but most are thought to be heterogeneous with genes at several different loci, contributing a susceptibility to them.

There is now little doubt that physical conditions, social interaction, education, professional opportunities and many other environmental factors can produce permanent effects on neuroanatomy, neurochemistry and ideally genomics, effects which have a broader significance than memory storage alone.

## **KEYWORDS:**

SHUKLAS SYNDROME. Detrimental, neurogenetic, Heterogenetic, Probability, environmental triggers, social, political, Government, engineers, Experts, cause& Prones, behaviour, Psychology.

## **BACKGROUND:**

SHUKLAS' Syndrome, the unique observational, experimented research will be of great importance and interest to the genetic engineers, neuropathologists, anatomists, pharmacogenomics, Social - Workers, Governments, Cultures, religions, politicians, Scientists and further every individual to reconsider and reform the expected healthy civilization in broad perception.

The objective of this presentation is to draw worthy attention to the latent truth that in spite of our modern scientific, industrial and social progress, human beings remains isolated from within.

SHUKLAS' Syndrome provides interesting countdowns for a horizon in GENOMICS. Progressive deterioration of intellectual activity leading to SHUKLAS' Syndrome is common with advancing scientific era.

The most important immediate consequences of this young science may, however, be the increasing recognition of the inestimable significance of the natural routes of access to the nervous system that they normally mediate. SHUKLAS' Syndrome is partially a pre and post consequences of depressive state but is indifferent to its natural decisive factors, are definitely shown to have abnormal 'Submissive" OR "Surrender-like" tendency. This syndrome is prevailing throughout the World. The person is losing his distinctive confidence against environment.

SHUKLAS' Syndrome is prevailing throughout the world but more prominent where people are prone to blind beliefs, myths, superstitions, child labour, unstable Government policy, unhealthy socio-economic conditions, corruption, orthodox and expensive religious processions, unsafe industrial conditions, discrimination, injustice, social insecurity, dowry system, long tenured inflation, unhygienic living standards, usage of synthetic fertilizers (which has toxic effects), uneducation,

deprivation of fundamental human rights, recreational drugs, fear of wars and many more.

Millions of people are embraced to this distinguish characteristic of SHUKLAS' Syndrome. The whole World is living under chronic stressful conditions. Living with SHUKLAS' Syndrome in wider perception, leads to many neurophysiological disease like, high or low blood pressure, diabetes mellitus, paralysis, arthritis, dementias, amnesia, cancer, AIDS and avenues of others.

An environmental trigger or influence is considered to play a major role in resultant expression. Variable penetrance within families as well as inconsistent and changing expression of the disorder among affected individuals makes the identification of patient a challenge.

Interestingly multiple genetic alterations which combine with environmental factors do increase susceptibility to SHUKLAS' Syndrome.

To procure temporary relief or adopt permanent profession from this syndrome, huge victims turned to alcoholism, theft, Corruption, prostitutional activity, robbery, suicides, murders, illegal migration, hijacking, terrorism, political asylum and many more.

Defining the phenotype for the genetic study presents a number of problems for the major psychoses. First, diagnoses which depend on the identification and assessment of diverse groups of clinical symptoms may not define discrete phenotypes in the genetic sense, and what is considered a clinically homogenous entity may in fact represent several disorders of distinct etiology as like Shuklas' Syndrome. Indeed, in the case of schizophrenia, a number of subtypes have been proposed which, if valid, are likely to differ in the extent to which genetic and environmental factors contribute to their etiology.

A candidate gene is one for which there is some a priori reason to suspect its involvement in the etiology of the disorder in question.

## **DISCUSSION:**

Candidate genes may be studied directly, their structure and function compared between patients and controls. Functional abnormalities may occur anywhere from transcription of the gene into RNA, through processing of that RNA, to translation into protein. The function of a gene is studied by examination of messenger RNA (mRNA). The relative site of action of the gene in the brain and the abundance of its expression is determined using in situ hybridization with cloned segments of transcribed gene. It is important to note, however, that the function of a set of genes may be disturbed as a secondary consequence of abnormality elsewhere.

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The concept of the 'social brain' attempts to account for the neural apparatus required for such interactions, in particular for the extent to which primate brain evaluation has been dependent upon the development of a capacity for recognizing and communicating with nonspecific.

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## **OBSERVATION:**

### [PRE AND POST FACTORS AND CONSEQUENCES BORNE OUT OF SHUKLAS' SYNDROME]

The pendulum of our beautiful and varied culture and the modern civilization has changed its movements in notorious way. Let us unzip the reality of human life, though it's a bitter, but the latent truth, which we have to realize. The realization of motives and objectives, the hopes of millions, presently crushed under the debris of variety of powers and judgments but not justice. We have to modify avenues of related factors involved, whatsoever, biological, genetic and environmental in a broad perception. Of course, we are well advance in modern mathematics but we are failed to calculate human values manifested in perfectly harmonious trend.

Here I am prescribing some of the factors involved and the consequences borne out of SHUKLAS' SYNDROME. (Cause and Prone) :

1. Nearly half a million illegal abortions are done every year
2. Throughout the World: Age Group observed: 15 - 19 years.
3. More than half a million rape cases are reported every year throughout the World.
4. Suicides other than psychic disorders. (Depression and Maniac)
5. Hijacking: Human, Airplane, Car etc.
6. Recreational Drug (Drug abuse)
7. Murders and Assassinations.
8. Political Asylum under the umbrella of anti-Social deeds.
9. High ratio of unemployment to the educated population.
- 10.. High inflation ratio for long tenure.

11. Adverse medicinal reactions : as more people died from adverse effects of modern medicines then in second World war. For example chemotherapy which has more than 60% failure ratio but for so called pompy dignity it is being utilized. (inspite of undue adverse effects)  
(Science Reporter, Nov. - 2000)
12. Myths, superstitions and blind beliefs, which is more prominent in Underdeveloped and developing countries, derived from their so-called culture - but curse for the individual and the society.  
(Due to uneducation but some times educated people are also Involved)
14. Poor and inefficient educational opportunities for talented. (May cause severe depression on intelligent or talented individuals looking themselves as a "smart Idiots" !)
15. Frequent changes in Government policies (Unstable Policies).
16. **Child Labour**
17. Unhygienic Life - Style.
18. Poor Socio - economic strategy.
19. Unsafe and unsecured industrial conditions by whatsoever reason.
20. Alcoholism, chewing tobacco, excess smoking habits.
21. Dowry System : e.g. thousands of women suicides for the same as it may not be fulfilled by a poor or a middle class family - torturing for dowry leads to suicides.
22. Religious procession with extravaganza has impact on others.
23. Constant war threats: Atomic weapons.
24. Pollution: Water, environmental and others.
25. Natural Calamities : Flood, earthquakes, Volcano, shortage of potable water resources.
26. Accidents due to carelessness, physical trauma, endocrinal changes with nutritional and socio-environments factors.
27. Terrorism.
28. Forceful migrations due to environmental factors.

29. Loss of dignity due to unfair Government policies.
30. Corruption - Bribery.
31. Unhealthy, unjustified and inefficient administration in all level of Governments.
32. Unhealthy psychic effects of many movies and TV serials - e.g. a student shoots his teacher when seen in movies / TV serial of that kind.
33. Smuggling: Human Resources and Commodities.
34. Discrimination: e.g. Reservation policy for backward classes for long tenure has impact on deserving and talented.
35. Injustice & late justice
36. Communism - Riots (Puppets in the hands of few who has wasted interest)
37. Fake currency
38. Prostitutional activities. (Normally socio-economic conditions)
39. Students' unrest
40. Gambling - played under stress and despair.
41. Theft and Robbery.
42. All violence's including religious related.
43. War Mongers / War maniacs. (Some times egoistic instincts)
44. HIV / AIDS/ STD's.-Every 14 Seconds new case of HIV in the World.
45. Many Neurological disorders like Dementia, Alzheimer's' Disease, Amnesia, Phobia and so on.
46. Misuse of education / Artificial intelligence)
47. Immunity Disorders.
48. Many genetic disorders as like juvenile diabetes and muscular Dystrophy.
49. **Breast Cancer (Most of them acquired from fertilizers, environmental factors and radiation). \* Reference: EXHIBIT: C : (Next page)**
50. Susceptibility to retarded progeny.
51. Obesity
52. As observed and experienced that terrorists are produced by the politicians and police (In many Countries)
53. **Every 40 seconds one suicide in the World.**
54. **Nuclear Plants (undue toxic effects of radiation). \* Reference:**



The various systems of nomenclature in current usage in neuroscience reflect not only the heterogeneity of traditions but also the major problems of addressing the functional issues. If the boundaries between perception, action, memory and thoughts dissolve with the recognition that no biological activity occurs in a vacuum, the issues become even more complex when one acknowledges that these terms have a communicate significance which is entirely determined by the brain itself. It is now little doubt that physical conditional opportunities can produce permanent effects which have a broader significance than memory storage alone'. (G.S. Stent (1969) the coming of the golden age: A view of the end of progress the nature History press, New York)

With the cruising events, we have discovered avenues of psychosomatic diseases, as some coupled with genetic predisposition and some are from the environmental factors in broad sense. We have many names to stick on the discovered symptoms with reasons and further its clinical features, epidemiology, aetiology, management, prognosis and counseling. We have developed sophisticated instruments to assess each and every phenomena and further many treatments for the variety of psychic ailments.

## NEUROGENETIC CONCEPT

### [Justification - SHUKLAS' SYNDROME]

Here, one should distinguish between the appropriate logic for the interpretation of scientific result and the natural form of scientific ambition. Thus, not only our reason fails us in the discovery of the ultimate connection of causes and effects but even after our experience has informed us of their *constant conjunction*, it is impossible for us to satisfy ourselves by our reason, why we should extend that experience beyond those particular instances which have fallen under our observation.

**" As animals and human do seek to explain events in their Worlds in terms of presumed causality, and they develop skill in interpreting and are content to accept, the man who can explain a phenomena understands it, in the sense that he can predict it and utilize it more than other man" (Craik,1943).**

A scientist with faith in absolute determinism need not feel compelled to pursue every phenomenon into its roots of atomic causality in order to satisfy himself that he has arrived at an explanation. A reliable account of relationship that has predictive power within a single domain of discourse can be an intellectually satisfying form of explanation for the pragmatist.

Hence, SHUKLAS' Syndrome in wiser sense will be lighthouse to many intellectuals to assess and modify crucial life events and further heterogeneity.

Some observation indicates that altered response of enzyme which is an enduring trait marker. As enzyme is composed of two subunits, a large catalytic and a smaller glycoprotein subunit. The catalytic subunit is encoded by at least three separate genes. All of these are potential candidate gene.

The hypothesis is that gene families are group of genes showing sequence homology and presumably derived from a common ancestor. Most families are dispersed across many chromosomes but some like HLA and the globins are clustered. As nucleotide and amino acid sequence data accumulate it is becoming possible to link most genes into families and superfamilies.

Gene clusters are group of structurally related genes lying together on a chromosome. They are likely arisen by gene duplication. Examples are the HLA and globin clusters and the genes for visual pigments on the X chromosome. Pseudogenes may occur within clustered gene families e.g. there is a  $\beta$ -globin pseudogene within the  $\beta$ -globin gene cluster, or in unrelated chromosome locations e.g. the functional dihydrofolate reductase gene in on chromosome 5 and pseudogenes are on chromosomes 3,6 and 18.

## Tables and captions

<b>Transcription</b>	RNA polymerase II makes the primary transcript using the DNA template. The choice of sequence to be transcribed is controlled by interactions between specific protein factors and DNA sequences near each gene.
<b>RNA Processing</b>	capping: addition of a modified nucleotide to the 5' end splicing: introns are cut out and discarded, and

	the end rejoined polyadenylation: addition of typically 200 A's at the AATAAA polyadenylation site at the 3' end
<b>Translation</b>	Ribosomes read the mRNA and assemble the polypeptide, controlled by specific initiation and elongation factors
<b>Modification</b>	may involve: cleavage to remove parts of the chain modification of amino acids e.g. hydroxylation of proline and lysine glycosylation
<b>Transport</b>	within or beyond the cell

*As with balanced reciprocal translocations, carriers are at risk of conceiving chromosomally abnormal offspring. In this case the abnormality is complete trisomy or complete monosomy.*

*Crossing over in a pericentric inversion loop produces chromosomes with terminal duplications and deficiencies, which may result in abnormal offspring.*

*. Today, protein coding nuclear genes from the Oxphos system complexes or those responsible for their assembly are beginning to be assessed (Shuklas' syndrome).*

This syndrome is characterized by neurogenic muscular weakness, ataxia and pigment retinitis. It usually involves dementia, convulsions and axonal sensory neuropathy, is inherited maternally and has been associated with a specific mutation, T8993G, in the ATPase subunit 6 genes. The mutation normally appears in heteroplasmic form and in all the tissues studied: leucocytes, fibroblasts, muscle, kidney and brain. A high correlation exists between the proportion of mutated DNA and the severity of the disease

## SHUKLAS' SYNDROME (HETEROGENEITY PROBABILITY)

It will be interesting to assess following critical factors for the research and development of suitable drug therapy as well as neurogenetic concept in context with the SHUKLAS' Syndrome.

- (A) The hypothalamus - pituitary - adrenal axis (HPA) versus petrochemical systems should be observed as there is growing evidence that one of the protective functions of the HPA axis is considered the homeostasis of euthymia, through the effects of its hormones on neurochemical systems which contribute to behavior.
- (B) Hippocampus appears to have a significant role in the fast-feed back control of the HPA. Within the hippocampus they influence serotonin (5HT) turnover and 5HT receptor capacity, binding at 5HT<sub>1A</sub> and 5HT<sub>1B</sub> receptors, the electrophysiological response to serotonin and other monoamines, GABA uptake and Beta-adrenergic receptor binding. This cause neuronal damage vice versa.
- (C) Several cytokines produced by stimulated immune cells are able to stimulate the HPA axis. Secondly, to predict that immunological competency may be impaired in SHUKLAS' Syndrome, providing a potential link between SHUKLAS' Syndrome and increased risk of immune related diseases such as infections, autoimmune disorders and Cancer. It is highly speculated that natural killer cells activity is altered.
- (D) It is noteworthy that the Na<sup>+</sup>/K<sup>+</sup>-ATPase isomer present in brain appears to have higher affinity for ouabain than that present in the erythrocyte. Finally, it is further interesting to speculate on the role of the interaction of a humoral agent determined by the neuroendocrine environment with a potentially

genetically determined trait abnormality of  $\text{Na}^+/\text{K}^+$ -ATPase in the pathogenesis of SHUKLAS' Syndrome

- (E) Molecular genetic techniques may be applied to identify a point of mutation.
- (F) Chromosomal abnormalities may be identified with a patient of SHUKLAS' syndrome. There is enough evidence that of maldevelopment of the cerebellum and portion of limbic system and it appears as if the later stages of CNS development are arrested.
- (G) Brain MAO enzyme may be observed for its molecular weight. Further, certain methodology is also necessary to assess in connection with the SHUKLAS' syndrome. Concentration of total tryptophan in plasma should also be observed.
- (H) Denervation led to hypersensitivity of pathways and the tachyphylaxis to drugs in the CNS meant that a similar but reverse mechanism of hyposensitivity applied in the brain.
- (I) Heterogeneity.
- (J) Cytogenetic Assessment.
- (K) Pharmacogenomics.
- (L) Heteroplasmic intervention
- (M) mt. chondrial DNA replication
- (N) rRNA, tRNA and DNA – Mutation
- (O) Nuclear Genes

The brain is the basis for all mental activity. If its development is impaired or abnormal, there an exists the potential for abnormalities of normal cognitive and mental abilities and emotional experience. Genes and/or their controlling DNA sequences may be absent or have point mutation. There may be failure of the normal

differentiation and folding of the neural tube. Neuronal cell division may be abnormal or delayed, thus affecting brain growth. Finally, if the development of different parts of the CNS is dependent upon patterns of neuronal activity, then a fault in one system may affect the development of another.

The development of the nervous System does not take place in isolation but within the context of the developing organism as a whole and therefore is both influenced by and influences developing sensory and motor systems. In addition there is a changing metabolic and hormonal environment. It is difficult to disentangle, on the other hand, the direct effect of gene expression itself on this process to, on the other, the influence of the intra and extracellular environment then created, on subsequent gene expression and in turn, on the growth and differentiation of the neurones and glial cells which make up the functioning of nervous system.

At least three categories of influence at this early stage are thought to be important. These include the instructions contained within the nucleus, ie genes and other DNA, the influence of cytoplasmic structures and proteins which effect gene expression, and instructions arising from other developing cells and the extracellular environment, e.g. cell adhesion molecules, trophic factors and neuronal activity itself. The interaction between these broad categories of influence also changes over time with, for example, the switching on and off of gene expression and with the increasing sophistication of the neuronal environment.

Unhealthy and poor life-style due to socio-economic conditions are also responsible for many physical restraints and diseases, e.g. Alzheimer's' disease coupled with SHUKLAS' Syndrome are observed in many underdeveloped and developing countries. For example, usage of aluminum utensils is very common nowadays. As it is the established fact, though neglected at first instance, but aluminum silicates are concentrated in the centre of senile plaques and neurofibrillary tangles and further serum aluminum concentration have been shown in many cases. As once in the cells, aluminum can cause toxic effects by a number of mechanisms including the disruption of phosphatidylinositol, the second messenger systems; causing neuronal

dysfunction and eventually cell death and interference with microtubule assembly leading to neurofibrillary tangles.

Constant humiliating or insulting behavior or exposure also responsible for SHUKLAS' Syndrome. For example, India, along with many underdeveloped countries are the best models to expose or manifest. As reservation policy for many schedule caste and tribes are enjoying privilege to have avenues of undue benefits, even after and over half a century !! This is empathetically harmful to the educated and talented individuals when lasting for long time. The overall scenario of such a policy is only political dilemma.

Under such policy, they are being provided special incentives without deserving capability. They are being provided Government jobs, Bank Jobs, College and school jobs besides cash incentives. Some special laws are imposed for such a policy even other distinctive and talented candidates are awaiting the opportunity. They are entitled for medical and engineering faculty even if they are not having deserving candidacy. In such a long tenure, brilliant / intellectuals has to work under fools, considering themselves as a "smart Idiots" ! This off course affects the career and slowly embracing to 'Submissive tendency' which in vice versa, SHUKLAS' Syndrome. For their bread and butter they accept jobs without interest and feel surrendered to circumstances as it is definitely humiliating their deserving dignity. On the other hand, it cannot be considered as a depressive state or neglecting attitude as such illness can be precipitated not only by traumatic psychological events but also by physical factors such as drug, viral infections and some endocrine upsets. Deprivation of fundamental rights will cause SHUKLAS' Syndrome in whatsoever Governments' legitimate policy even if such a policy made available for "Vote Banks" under the umbrella of 'restructuring" dilemma!!

### **Breast Cancer & Synthetic Fertilizers:**

Now it is well established that breast cancer is a produce out of toxic chemicals, mostly from foods (Synthetic fertilizers, radiation and environmental).

Really it is obvious that how we befools others and ourselves. We made synthetic fertilizers to produce more food-grains and than we opened our eyes and found the

reality those synthetic fertilizers have undue toxic effects! We have also find out the principal cause of breast cancer and feel happy that we have established fact of breast cancer!

Further pitiable mockery is that we are now after 'organic foods' which was in the use before many many years back! Many other toxic effects are in queue and we will find out more in future to satisfy ourselves that we have done scientific progress to establish our own legitimacy!

I have also observed arthritis, Sexual debility, Lethargy, memory disorientation, Students' unrest, pornographic usage and many other symptoms in youngsters. We have many reasons to find out the causes.

Neurogenetic factors in SHUKLAS' Syndrome plays an important role and, attention should be focused on genes involved and how DNA mutations might interact with the environment to produce the constellation of symptoms now known as SHUKLAS' Syndrome, in which 'Submissive' / 'Surrender' tendency is prominent. Millions of people are suffering from this syndrome throughout the World.

We have unique experience in the advance of medical practice, a period of empirical understanding in which the regular combination of a certain constellation of symptoms is recognized as an entity of disease for which certain treatments are reliably effective, precedes a full level of explanation in which those symptoms can be assigned on organic cause a degenerative process etc. and the cures can be understood in terms of their actions on this causal sequence. In any case, as many philosophers have pointed out, uncertainty need not imply indeterminacy but might merely compromise observers' powers of ultimate prediction.



## CONCLUSION

*Further complexity is added to these issues by evidence indicating that a deficit in a particular function also result in the extraordinary development of another. In its broad perception, the condition of the nervous system is the most significant factor in determining the quality of human life.*

The ultimate goal of this hypothesis highlights two major aspects:

1. Environmental factors which affects heterogeneity complex.
2. To modify social, economical and educational structures in broad perception.

Now it is time for the Governments, politicians, religion, culture, neuropathologists, anatomists, social workers, intellectuals, genetic engineers, scientists and every individual who is responsible and respected citizen of all the countries throughout the World to assess and accept Shuklas' Syndrome and eliminate the causes and care for the huge victims..

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