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Does Chemistry Explain the Mind?

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Introduction

Mind has been known to man for more than 10000 years and over the past 5000 years mankind has interested itself in determining the functions and the components of the mind. An enormous amount of knowledge had accumulated over the centuries about the powers and the functions of the mind specially in countries like India and China with long-standing civilisations. In India, our ancient rishis and seers have looked deep into their own mind and mental functioning and had enunciated many methods of mind and body control. Thus while our familiarity with the mind is age-old, our knowledge about the human brain is comparatively very recent. Awareness about the functions of the brain and the important and vital role it plays in body and mental functions was realised only over the past 200 years.

'Mind is Material'

In the last century and in the early half of the 20th century, it was often the fashion to discuss the relationship of mind and the brain and mind and matter. The Indian Philosophers and Psychologists have defined mind as a part of our material existence. Mind as "Manas" is defined as one of the Indriyas (Geetha: Indirayanam Manaschasmi). In Indian Psychology mind is not a single entity but consists of different layers of hierarchy namely the mind or the manas, buddhi or intelligence and ahankara (self awareness). From this it is clear that the Indian psychologists were way ahead of their western counterparts in their concept of the mind and in their understanding of the role of the different aspects of the totality known as the mind. The Indian psychologists also surmised that these mental layers could expand beyond the confines of the individual mind and embrace the "universal mind" but that is another story. There were many philosophers and psychologists in the West who held that the mind was something entirely different and that it had a separate immaterial existence different from the brain, while others tried to correlate the concept 'mind' with the organ "the brain".

Mind is a Concept

The term 'concept' has to be used regarding the mind as this entity is only a concept in the thinking of men. All organs in the body have functions and words have been used to identify such functions e.g. digestion is the function of the alimentary system; breathing

is the function of the lung; movement is the function of the muscle and so on. Similarly the mind or mental functioning is one aspect of the function of the human brain.

The dependence of the mind on the brain is easily clarified. It is obvious that whenever the brain is affected in any manner, the mental function immediately changes. In instances where the brain is seriously affected or damaged the mind ceases to function e.g. after a severe head injury the patient loses consciousness and the mental function ceases. He is not aware of his environment nor is he able to respond to the same. Similarly after the administration or intake of certain drugs the patient may lose consciousness as happens when an anaesthetic drug is given. Changes in the mental functioning like memory intelligence and judgement occur when the oxygen and blood supply to the brain are impaired as may happen in diseases or in old age. Similarly when tumours occur in certain areas of the brain, the patient loses his ability to think coherently, he may lose his memory and in the later stages may become unconscious. It is obvious therefore that proper functioning of the brain is most essential for mental status.

It will be the purpose of this oration to try and define the relationship of the brain and its function namely the mind and to try to present modern knowledge about the electro chemical activities in the brain which determine the mental status and mental powers of the individual.

Neurosciences Research

During the past 200 years there has been an enormous expansion of our knowledge about the functioning of the nervous system and the human brain. The advances have been specially rapid through the past 2 or 3 decades during which time neurosciences have attracted many brilliant intellects. These include not only neurologists, neurophysiologists and neurochemists, but also psychologists, social scientists, computer engineers, electronic experts and mathematicians. Such concentration of effort has yielded a vast amount of data regarding the functioning of the human brain. Still it has to be accepted that what is known is very little and there are many problems to be solved even about the normal functioning of the human brain.

The Marvel of the Human Brain

The human brain, the most marvellous creation, consists of more than 1000 million cells which are termed neurons in addition to having a similar number of supporting cells called glial cells. Each neuron has a long process the axon along which it sends messages and a number of small projections called dendrons through which each neuron receives messages from other cells. There could be anything between 10 to 50 such connections between different cells. One can imagine the number of permutations and combinations that are possible for energy transfer through a system consisting of 1000 million units or more and where each unit can make anything between 10 to 50 connections. The possibilities are really astronomical.

There is an intricate and constant and instantaneous consultation taking place between various parts of the brain and the periphery, between the right and left brain through cross connections, between the frontal, the temporal, the parietal and the occipital portions of the brain on the same side with each other and with their counter parts on the opposite side and with lower concerned levels in the organisation. All this interchange of information occurs within milliseconds and the right answer to help to preserve the integrity of the organism presented in less than a second. This conglomeration of enormous numbers of nerve cells situated inside our head and termed the brain controls every function in the human

body by fibre connections that establish contacts with the skin and with all organs, muscles and all other structures. There is no function performed by the organism from the highest thinking to the basic functions like breathing and heart beat which is not controlled by the brain.

The brain has come upto this present state of complexity over evolution through millions of years by building up from simplest mechanisms and by overlaying of more complex functions on simpler functions, thus building a hierarchy of functional integration. You may be surprised to know that the lower forms of life on earth have perfected many intricate neural and communication responses, like sonar in bats, communication between dolphins, photosignals, mating signals etc.

Complex Electrochemical Conglomerate

The functions of the central nervous system are mediated by chemical processes. Every organism needs for its existence the ability to obtain and to react to information from its environment and from within itself. In the unicellular organisms this is achieved by simple chemical processes, example chemotaxis, an organism is attracted towards its food or repelled from an unsuitable environment. In multi-cellular organisms it was not only important to communicate within the cell and with the environment but information processing became necessary between the cells themselves. As the complexity of the organism became greater, certain cells began to specialise in information transmission and collection, evolved into the highly complicated neurons and established contacts with all the cells in the body and with the periphery. With the increasing complexity of the nervous system resulting from the development of varied and complicated functions in the higher animals and the human beings, it was necessary to have different systems of information transmission and processing; rapid transmission for quick results, slower action for diffused results and much slower action spread over the years. This was achieved by different types and speeds of transmission of neural impulses by adopting different electrochemical mechanisms.

As far as our present knowledge goes, energy generation in the brain is through an electrochemical complex. Shifting of the sodium and potassium ions from the inside and outside of the cells creates an electrical potential which travels down the axons and initiates action in another neuron or in an organ like muscle or gland.

The impulses generated by the neurons influences other neurons through what are known as synaptic junctions. These synapses are junctions between the nerve fibres and the nerve cells through which the electrical impulse coming along with nerve fibres get transmitted. *The synapse is the most important structure in the nervous system* that determines the functioning of the brain.

Chemical Messengers

The modus operandi of this complicated system has been investigated for many decades and recently rapid progress has been made with the discovery of new chemical messengers and mechanisms. These messengers have been termed neurotransmitters, neuromodulators and neurohormones. They are of differing chemical compositions.

Our knowledge of the functioning of neurotransmitters has enlarged because of important technical advances in the methods of selective staining of neurons containing the particular transmitter. These techniques are based on fluorescence or radioactive labelling or on specific antibody techniques and have provided information about the areas of concentration of the individual transmitters in the complex neuronal circuits of the brain. It is found that the transmitters are not distributed diffusely but are precisely localised in specific centres and pathways.

Neurotransmitters

One of the earliest neurotransmitter to be discovered as playing an important part in neuroal function was acetylcholine. This chemical is present in the brain and the central nervous system and also in the periphery at the junction of the nerves and muscles (neuromuscular junction) where it plays a vital part in inducing muscle contraction. Interference with the acetylcholine mechanisms in the peripherry cause a serious disease known as myasthenia gravis. Acetylcholine deficiency in brain may cause premature loss of mental function (presenile dementia).

The other transmitters involved in brain and nerve functioning are noradrenaline, serotonin and dopamine. The noradrenaline system has a reciprocal relationship with the acetylcholine system with opposite functions. When one system acts like an accelerator, the other system acts like a brake. The noradrenaline system is necessary for defence mechanisms in the body. When an animal is threatened, it has to defend itself by fighting or running away (fight or flight). For this purpose, large amounts of energy stores have to be released urgently and the noradrenaline system is most essential for this; to get more oxygen and blood to the tissues, to make the heart pump blood faster, to provide the necessary glucose for muscles to act etc. The hypothalamus in the brain is the chief main centre for this functional mobilisation.

In ordinary circumstances the noradrenaline is utilised by the fight or flight mechanism. But in modern society, problems are not solved by a simple solution of fight or flight. In many situations when anger arises one is forced to remain silent. This leads to frustration and the unused noradrenaline leads to psychomomatic illnesses like peptic ulcer, blood pressure, headaches, neck and back pain insomnia etc. These are the diseases of fashion and frustration. The advice 'not to get angry at all' is good. If one gets angry it is better to do some physical activity to vent out the anger rather than suppress it. No wonder husbands went on long walks when there were domestic quarrels. How about the wives? They made pots and pans fly.

The dopamine and serotonin systems are inside the central nervous system. The dopamine systems control mental process as well as muscle movements. In schizophrenia, the dopamine system is disturbed. Serotonin systems are involved in functions like alertness, sleep, temperature regulations etc. Serotonin excess or deficiency may cause certain problems and one of the well known problems is migranious headache.

Inhibition or Suppression in the Brain

It was for many years assumed that the nerve cells in the brain show only a positive response i.e. a stimulus results in a discernible or a measurable reaction. However it was found that there were instances where such a reaction was absent and also some instances where a stimulus resulted in an effect being slowed down or stopped. This led to further investigations of the functioning of these neurons and it was discovered that there were many cells in the nervous system that inhibit or slow down reactions rather than start or speed up a process. Such inhibitory cells are known to be present throughout the nervous system and the important role they play in protecting the nervous system and in making it function optimally has been fully recognised.

Such inhibitory groups of cells act as 'gates' that allow or do not allow impulses to pass through. This should have been expected, as otherwise, millions of stimuli bombard the human brain every moment and it will be virtually impossible for the brain to function without such protective devices. We can see many instances in every day life where such protective or inhibitory

mechanism are used e.g. one can work and concentrate in the middle of disturbances. If one is sufficiently interested, one can study or write in spite of a distracting loudspeaker noise on the street—a common phenomenon in our country.

How is the brain protected from such disturbances and allowed to work? The inhibitory cells are placed from the most peripheral parts of the nervous system to the very centre. Inhibitory or gate mechanisms are seen in the skin and organ surfaces, in the peripheral nerves, in the ganglia near the spinal cord, in the spinal cord itself, in the lower levels of the brain known as the brain-stem, in the cerebellum and also distributed throughout the cerebral cortex. These cells make it possible for the brain to function in spite of bombardment by innumerable stimuli. The inhibitory transmitter involved is gamma amino butyric acid (GABA). This inhibitory transmitter is manufactured exclusively in the brain and the spinal cord. GABA mechanisms are involved in most of the activities of the brain. More than a third of the synapses in the brain employ GABA as a transmitter. Recently GABA has been implicated as a probable target for the actions of drugs like Diazepam.

Neurohormones—Slow Actors

The chemical mechanisms that we have talked about are used by the nervous system to produce immediate and instantaneous action in the periphery, the time scale being in millionseconds. The brain also has to function at a slower speed in certain situations and also at a very slow speed spreading over many months and years in certain areas: e.g. in sexual maturation and growth of the organism, the brain plays its part by very slow acting mechanisms and achieves its aims through glands situated in various parts of the body known as the endocrine glands and the chemical messengers are neurohormones. The brain controls the hypothalamus which in turn controls the pituitary gland, the adrenals, the ovaries and the testes. Such neurohormonal systems also control the time clock mechanism situated in the hypothalamus that determines when a child becomes a sexually matured person and also determines the growth in height. Ofcourse there are also short and swift acting endocrine mechanisms in this system which are essential for sexual function and also for the growth and preservation of the life of the fetus inside the mother.

Synaptic Transmission

Precise biochemical events are involved in synaptic transmission and when such events are interfered with either by injury, disease process or toxic substances, the mechanisms in the brain get altered resulting in drowsiness, excitement psychosis etc. Drugs are now available that selectively enhance, inhibit or block specific steps of synaptic transmission. This has given us good knowledge about the mechanisms of action of drugs used in mental diseases and also an idea of how some neurological and mental disorders might be related to specific defects in the mechanisms of synaptic transmission.

A number of steps are involved in the process of chemical synaptic transmission. Synthesis, storage, release, reaction with the receptor, termination of action and reabsorption or destruction.

The molecules of the transmitters are manufactured by a series of enzyme reactions in the body of the nerve cell from the constituents circulating in the blood stream. At the end of the axon (long nerve projection) they are stored in small quantities in tiny sacs called synaptic vesciles. When the nerve impulse arrives at the axon terminal, large numbers of transmitter molecule are discharged into the synaptic space and travel rapidly across this space to interact with specific receptor sites on the other side of the synapse called the post-synaptic

membrane. Once the interaction has taken place, the excess of transmitter molecules are destroyed by an enzyme or reabsorbed into the axon terminal.

The receptors for the neurotransmitters are large protein molecules embedded in the cell membrane with parts sticking out like projections. These projections are precisely tailored to match the configuration of the neurotransmitter molecule so that the two molecules fit into each other with precision. This interaction may cause a neuron to become excited or inhibited, a muscle cell to contract or a gland cell to secrete a hormone. Some reactions take place within a fraction of a second while others like secretion of hormones may take minutes or hours.

Psychoactive Drugs (Drugs Used in Mental Illness)

Modern psychoactive drugs act by interfering with the mechanisms of synaptic transmission. They may enhance or inhibit the release of a particular neurotransmitter. Amphetamine (Dexedrine) increase the release of dopamine in the nerve terminals in the brain and enhances arousal and a feeling of well being. Excess of amphetamine leads to hallucinations and delusions, resulting probably from a derangement of dopamine systems. Drugs like chlorpromazine and haloperidol bind tightly to dopamine receptors in the brain, thus preventing the action of natural transmitters on the receptors. These two observations on the mechanisms of action of amphetamine and chlorpromazine has led to the suggestion that scizophrenia could be due to disturbance of dopamine systems.

Other psychoactive drugs may act by mimicking the natural transmitters. The hallucinogenic drug mescaline is similar to dopamine and norepinephrine, and LSD is related to serotonin. Drugs like caffeine and theophylline act by increasing the amount of cyclic AMP that is produced in response to a stimulus, thus exerting a general mild stimulant action on brain. Other drugs inhibit the enzyme monoamine oxidase (MAO) which degrades norepinephrine. Thus MAO inhibitors act as antidepressants. Tricyclic antidepressants like imipramine and amitriptaline act by blocking the reuptake of NE and serotonin from the synapse. Cocaine also acts by a similar mechanism. It is thus clear that by manipulating the synaptic transmission mechanisms in the brain, *it is possible to alter mood, behaviour, thought processes, sleep, attention etc;*

Neuropeptides

In recent years our knowledge of the number of chemical messenger systems known to function in the brain has expanded dramatically with the discovery of neuro-peptides. These are short chains of amino acids that are widely but precisely distributed in the central peripheral and the autonomic nervous systems. The occurrence of neuropeptides in specific cell groups strongly suggests that they influence and control specific neural functions. Approximately 50 neuropeptides have been identified in intervertebrates and are found to control behaviour in these organisms. There is no doubt that neuropeptides form a basic mode of communication and control in the nervous system. Neuropeptides found active in the highly evolved human brain are also seen in the lowest forms of life, *thus emphasising the fundamental nature of the biochemical processes involved in neural control.*

Neuropeptides may function as neurotransmitters in the classical sense like acetyl choline and dopamine. Others may act to modulate the action of another neurotransmitter. They also produce diffuse changes in many groups of neurones, thus influencing complex behavioural patterns. The chemical sequence of amino acids in each neuropeptide has been identified and by the use of immuno cytochemical and radio

immuno assays their site of production and action have been determined. Some of these neuropeptides originally found outside the nervous system have recently been identified as occurring also in the brain.

The first group of peptides to be discovered were the substances that act on the smooth muscles of the blood vessels, or the viscera; the second group are the hypothalamic releasing peptides and the newest group are the encephalines and endorphins.

Substance P

Substance P is intimately concerned with pain transmission and perception and is found concentrated in the sensory neurones in the periphery and in certain specific nuclei in the brain and the spinal cord. Though the existence of substance P was first described in the extract of brain and intestine as early as 1931, its chemical composition and precise action could be determined only when better bioassay systems became available. SP has been implicated in the sustained pain which persists long after the application of a painful stimulus.

Angiotensin

Angiotensin is widely distributed in the brain. This neuropeptide has a striking effect on drinking behaviour and seems to be involved directly and indirectly with the maintenance of extracellular fluid volume and the electrolyte balance.

Hypothalamic Releasing Factors (Hypophysiotrophic neuropeptides)

These substance originally described as releasing factors for pituitary hormones are now known to belong to the group of neuropeptides. The amino acids sequence for some of these neuropeptides has now been determined. They are (1) Thyrotrophine releasing hormone (TRH) (2) Luteinizing hormone-releasing horome (LHRH) (releasing both the leutinizing and follicle stimulating hormone) and (3) somatostatin (SOM) which suppresses the release of somatotrophin (the pituitary growth hormone).

The surprising fact about TRH LHRH and SOM is that they are found all over the nervous system and not confined to the hypothalamic regions. Apart from its action through the pituitary, LHRH has a specific activating effect on sexual behaviour which is mediated via the nervous system.

Somastatin has a depressant action on the central nervous system; it enhances barbiturate anaesthesia and induces hypothermia (lowered temperatue) SOM has also been found in the gastro intestinal tract and the pancreas.

Encephalins and Endorphins (Opioid Peptides)

The most exciting and the newest of the neuropeptides are the encephalins and endorphins — chemicals occuring naturally in the brain that bear a surprising similarity to morphine. The discovery of these neuropeptides stemmed from the obsrvations that certain regions of the brain were found to bind opiate drugs with high affinity. The opiate receptors are found concentrated in the areas that are involved in the perception and integration of *pain and emotional experience.*

Encephalins

In 1975, two naturally occurring peptides were discovered that bound tightly to the opiate receptors in the brain and were named encephalins. Both the encephalins are chains of five aminoacids. The terminal aminoacid is methionine in one peptide and leucine in the other — hence they are termed Met. Encephalin and Leuencephalin. Both mimic morphine and related opiates by binding to the same highly specific receptor sites. Most of these receptors are related to pain while some are not. It was soon realised that encephalins must have many other actions unrelated to pain as they were found concentrated in areas not concerned with pain mechanism.

Beta lipoprotein, a large peptide found in the pituitary contains metencephalin. Some of the large frangements of beta lipoprotein from the pituitary gland are found to interact specifically with opiate receptors and have been termed endorphins.

Encephalins are also found in the dorsal horn of the spinal cord at the same sites as substance P. If substance P is an activator of pain impulses, encephalins are suppressors of pain at the same sites.

Prostaglandins

Amongst other chemicals that appear to play a modulatory role in the brain, the prostaglandins are found widely distributed and are present at high levels in the brain tissue. They elicit a variety of excitatory and inhibitory effects on the neurons, depending on the precise molecular structure of the prostaglandin and the nature of the target cell. The prostaglandins effects long term shifts in membrane polarisation and modulate the effect of neurotransmitters.

Global Chemical Coding

The neuropeptides are chemical messengers of a nature different from that of the previously identified transmitters. They appear to represent a global means of chemical coding for patterns of brain activity associated with particular functions like sexual behaviour, pain or pleasure, fluid balance etc. Biologically active peptides originally found in the G.I. tract such as gastrin, substance P vaso active intestinal polypeptide (VIP) and cholecystokinin are also present in the central nervous system. Some peptides originally found in the brain have now been found to occur in the intestinal tract e.g. encephalins, somatostatin, neurotensin. The fact that many of the neuropeptides are found outside the central nervous system (e.g. the gastro intestinal tract) shows that neuropeptides serve a multiplicity of roles acting as local hormones in the gastro-intestinal system and as *global transmitters in the brain.*

For a long time it was not possible to correlate some of the slow processes that occur in the central nervous system, with the rapidity of the electrical process of nerve conduction. With the discovery of the neuropeptides and the elucidation of their mechanisms, specially in the field of neuro endocrinology and behaviour responses, this is better understood.

Vigorous research is going on all over the world in the field of mental functioning, mental life and in psychiatric disorders, to understand the physical and chemical basis and some amount of success has been achieved. In our own country and elsewhere, chemical changes occurring in the brain and in the cerebrospinal fluid have been demonstrated during mind control, mental concentration and yogic states. Chemical changes have also been shown to occur during biofeedback techniques and operant conditioning. In other words there are many nonchemical processes and techniques which can alter the chemical basis of mental functioning and thus influence the mental status of an individual, yoga and other Eastern techniques of mind control being the best of them. It is also conjunctured that the electrochemical potential of the human brain is so vast and enormous that the brain is capable of much more effort and achievement than has been obvious so far during human development.

Conclusion

We have so far seen that the brain is a conglomeration of millions of neurons that functions and controls itself and the entire human organism through its electro chemical activity. This function is mediated by numerous chemical messengers acting in various precise and specific locations in the brain. It appears as if some of these chemical mesengers act in one specific area, others have a more diffuse function while certain others assume a global role.

In the time scale of action, some messengers are responsible for swift action, some for slow action and others for very slow long lasting effects. It has also been indicated that throughout the brain, there are mechanisms and messengers which act as brakes or inhibitors of neutral function. It is this marvellous organisation with millions of neurons throbbing with activity, with controls and feed back at every stage and every step, mediated by complicated electrochemical mechanisms, that determines all the known functions of the brain.

While the mechanisms of gross lower functions like self preservation, feeding, sex and reproduction are clearly known, the complex mechanisms responsible for the higher levels of response as in memory, behaviour and intelligence are only vaguely understood. Of course it has been clearly indicated in the preceding paragraphs how chemicals influence varieties of brain functions like consciousness, attention, mood, drive etc. and also the precise mechanisms of such action. But in many areas of higher human development like intelligence, altruism, unselfish love, generosity, kindness, sympathy, sacrifice for others etc, we have no concept at all of how the brain functions either physically, chemically, electrically or otherwise.

Are these qualities inbuilt in the brain and genetically determined. Are the chemical processes in brains different between a criminal a cruel sadist or a kind person.

From the knowledge so far available, can we correlate changes in cell functioning with changes in our mental function? Today the answer is clearly a 'no' as our knowledge is very incomplete. From neurons to brain, from brain to mind and mind to intellect still seems a long way, but the human mind in its enthusiastic quest will enlarge in the near future our knowledge about its own functioning.

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