LIFE is nothing but chemistry! Molecules in every size and shape decide our hereditary destiny, form and shape of our body, our behavior. What is more, there is a continuous chatter between different organs carried on by, who else - the molecules. This chatter has no sound bytes; there are no cell phones either. But cells, there are, billions of them – the neurons being the ‘brainy cells’. The relentless, silent tete-a-tete amongst all these cells is what our day-to-day life is about.

The master organ, the brain, in response to various environmental stimuli shoots off orders on how to behave through chemical messengers called neurotransmitters, produced within the neurons. The brain uses these messengers to tell your heart to beat, lungs to breathe and your stomach to digest. Your moods, your sleep, dreams, concentration, weight and so on – all pay obeisance to these messengers.

How the nervous system is organised and how it works at the cellular and in turn at the chemical level itself makes a very fascinating story. It was all based on a vague inkling of bioelectricity – but how it was generated, they had no clue. Those were the days when technology was in its infancy. It took more than half-a-century to realise that the nervous system is not a giant network but is made of individual cells – the neurons – through a long journey of discoveries such as achromatic microscope, differential staining techniques, electrophysiology/microelectrodes and finally the electron microscope.

Till the turn of the 20th century, there was a general belief among scientists that much of brain communication was electrical. But through very careful and simple staining techniques, a 20 to 40nm gap was discovered between neurons by Ramon y Cajal (1852 – 1934). The presence of such a gap – today known as a synaptic cleft – suggested the involvement of chemicals passing through such a gap. In 1921, a German pharmacologist, Otto Loewi (1873–1961) pursued this idea through a series of experiments involving vagus nerves in frogs.

In his experiment (he dreamt about the experiment), he used two frog hearts; heart #1 was still connected to the vagus nerve and was placed in a beaker filled with saline. (A dissected heart placed in saline does beat for a while). This beaker was connected to a second beaker containing heart #2. Electrical stimulation of the vagus nerve attached to heart #1 caused heart #1 to slow down. Loewi also observed that after a short delay, heart #2 too slowed down. From this experiment, he put forward that electrical stimulation of the vagus nerve released a chemical (that slowed down the heart) into the fluid of beaker #1 that flowed into beaker #2. He called the chemical ‘Vagusstoff’. 
Today we know this chemical as the neurotransmitter acetylcholine – the first neurotransmitter was thus discovered.

Let us hear this story in his own words: "In the night of Easter Saturday, 1921, I awoke, turned on the light, and jotted down a few notes on a tiny slip of paper. Then I fell asleep again. It occurred to me at six o’clock in the morning that during the night I had written down something most important, but I was unable to decipher the scrawl. That Sunday was the most desperate day in my whole scientific life. During the next night, however, I awoke again, at three o’clock, and I remembered what it was. This time I did not take any risk; I got up immediately, went to the laboratory, made the experiment on the frog’s heart, described above, and at five o’clock the chemical transmission of nervous impulse was conclusively proved." (quoted from Loewi, O., From the Workshop of Discoveries, Lawrence: University of Kansas Press, 1953.)

There are about 90 billion neurons in the human brain. Each neuron can be connected through its single axon to dozens of other neurons, and may itself receive input from hundreds of other neurons through its many dendrites. Some neurons communicate using electrical synapses via gap junctions, which allow specific ions to pass through directly from one cell to another.

Neurotransmitters are the brain chemicals that communicate information throughout our brain and body via neurons. Each neurotransmitter is synthesised within the neuron itself, and stored in small granules at the axonic tip.

This is how it happens. Our sensory organs bring in a stimulus, the axon is depolarised, i.e., an action potential arrives at the pre-synaptic button. It releases the content of these granules into the synaptic cleft – a tiny open space between the pre-synaptic axon of one cell and the post-synaptic dendrite of another. The neurotransmitters diffuse across the synapse – (miniature gaps through which they carry impulses via action potentials) – and bind to the receptors on the post-synaptic dendritic tip of the receiving neuron. Only an appropriate receptor will do; if it is right and the receiving cell is another neuron, the incoming signal will act either to help or to curb the release of that neuron’s transmitter leading to another wave of action potential in the next cell. And if it is a muscle, it will contract.

Once their function is over, these messengers should be removed from the site (or they would rebind to the receptors) – this is achieved by diffusion (drift away from the synaptic cleft), enzymatic degradation, glial cells remove them from the cleft or reuptake by the axon terminal that had released it.

Individual neurons normally have receptors – proteins embedded in the membranes of the neurons – for a wide range of different neurotransmitters at the tips of their dendrites. A given neuron can thus be influenced by many different types of other neurons to which its dendrites are connected.
If I’m moody...

...blame it on My neurotransmitters

It is because of this organised release and uptake of varying kinds of neurotransmitters between and among cells communication in the brain is possible. The action of a given neuron will depend on the sum of the chemical inputs it is receiving at any given time from other neurons.

There are two kinds of neurotransmitters – Excitatory and Inhibitory. Excitatory neurotransmitters are not necessarily exciting – they stimulate the brain. Those that calm the brain and help create a balance are called inhibitory. Inhibitory neurotransmitters balance mood and are easily depleted when the excitatory neurotransmitters are overactive.

When glutamate is released it helps in opening of sodium channels within the post-synaptic membrane allowing sodium ions to enter the membrane and causing depolarisation. Therefore, glutamate makes it easier for the cell to reach its depolarisation threshold and generate an action potential. Due to this, glutamate is classified as an excitatory neurotransmitter. Acetylcholine is another example of excitatory while dopamine acts both as excitatory as well as inhibitory.

When GABA (gamma-aminobutyric acid) is released it results in the opening of chloride ion channels within the post-synaptic membrane resulting in the membrane becoming hyperpolarised. The cytosolic side of the membrane becomes more negative. Therefore GABA makes it more difficult for the cell to reach its depolarisation threshold to generate an action potential, thus classified as inhibitory. Glycine is another such messenger. Glycine is present in the spinal cord and is crucial for limb movement; in particular the motor function associated with limb reflexes.

Dopamine can be both excitatory and inhibitory. Dopamine is responsible for our drive or desire to get things done – or motivation as well as a ‘feel-good-factor. When dopamine is either elevated or low we can have focus issues such as not remembering where we put our keys, forgetting what a paragraph said when we just finished reading it or simply daydreaming and not being able to stay on a task. Stimulants such as medications and caffeine cause dopamine to be pushed into the synapse so that focus is improved. Unfortunately, stimulating dopamine consistently can cause a depletion of dopamine over time.

Everything known about human behaviour suggests it is regulated entirely by the human brain. One place to look for a role of genes in human behaviour is the genes controlling neurotransmitters and their receptors. Subtle changes in either of these molecules could have profound effects on behavior, and indeed scientists are beginning to correlate specific mutations in these genes with behavioral alterations.

All neurotransmitters are the end products of enzymatic pathways present in the cells that produce them. Different alleles of the genes governing production of these enzymes could lead to differing rates of neurotransmitter production in different individuals. There is already some evidence that the gene for a key enzyme involved in serotonin production, tyrosine hydroxylase, is present in multiple alleles in humans.

The evidence that allelic differences in neurotransmitter-related genes can cause behavioral differences is accumulating rapidly. Changes in the underlying genes and their interactions with one another and with the environment, all leading to behavioral patterns will be key in any final understanding of the genetic basis of behaviour.

Knowledge of the pathways involved in neurotransmitter function has allowed development of drugs that modulate these pathways up or down. Glutamate and its receptor are critical in learning and memory. A class of drugs called SSRIs (Prozac; Zoloft) can regulate the flow of serotonin throughout the brain, affecting disorders such as depression and impulsivity.

A cautionary note: Neurotransmitter levels can be depleted in many ways. Stress, poor diet, neurotoxins, genetic predisposition, drugs (prescription and recreational), alcohol and caffeine usage can cause these levels to be out of optimal range. This brings us to choosing the right lifestyle habits – your behaviour and your well-being is in your own hands.

So, these messengers do leave a message behind – that of striking a balance. A little conscious effort on your part will create the right stimulus and through appropriate messengers, culminate in proper action. We can thus complete the good old grandma’s adage – you ARE not only what you EAT but also how you BEHAVE!

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