Neurology of a Problem
The Pathogenesis of Autism (1)

All that is written about the etiology of autism is also true of congenital disorders of the central nervous system and /or the initial period of life of a newborn baby with motor disorder. This gives rise to an obvious question: how does brain injury give rise to a behavior disorder? Why does the same illness, for instance, viral infection in pregnancy, or perinatal asphyxia encephalopathy from dystocia childbirth, give rise, in some cases, to spastic tetraparesis, and in others, to hyperactivity and stereotypy? Why does the same origin give rise to disorders which, in some cases, do not allow the slightest independent movement by the child, and, in others, to a disorder which leads to hyperactivity, where the child is unable to sit still for one moment? The answers to these questions can be found in the functioning of the brain.

Autism is the consequence of brain injury impacting on sensory perception and hence on the neurological organisation of the brain. There are two biological characteristics of the central nervous system: 1) the central nervous system is in constant reorganisation; 2) this organisation, which occurs mainly in the first few years of life, is possible because of the plasticity of neurons, and this plasticity is retained throughout life.

Neurological Organisation and Sensory Dysfunction

The different perception of sensory stimuli would not enable us to reach a proper understanding of the clinical condition of the child if it were not for the recent recognition of the importance of "*Neurological Organisation"*.

The central nervous system is based on the organisation of neurons and of their axons and dendra forming nerve networks. The central nervous system constantly reorganises itself due its plastic nature, and this plasticity is an important feature carrying out a vital role throughout life.

In the development stage, neurons create neuron maps according to a plan (genetic factors), but each neuron reacts differently to external stimuli to create unique circuits. The development of the human brain is influenced by outside factors, genes provide the basic circuitry, whilst only external stimuli (environmental factors) can form neuron maps.

Hyper or hypo reaction to environmental stimuli due to brain injury causes an anomalous development of neural maps and this in turn means that the brain of an autistic child is organised in an irregular fashion compared to a healthy child. However subject the child to stimuli in such a way that the sensory gathering systems allow neural maps to be created in an organised manner, then the brain can grow in such a way as to enable the child to assume a less dysfunctional

presentation. Environmental stimuli reach the brain through the sensory pathways and the brain organizes itself on the basis of these stimuli.

The "plasticity" of neurons can be expressed as the ability of neurons to change their own metabolism, form and hence function according to the stimulus received (i.e. their use).

This can be said another way: the environment shapes the neurons and regulates their metabolism and use so that they are able to respond to it. The form of the neuron determines its function. As Delacato says: "the function determines the structure" and the structure preserves and protects the function.

The plasticity of neurons is due to a protein in the membrane and, in particular, in the dendra. This protein is called Map-2. In patients with Alzheimer's disease (precocious dementia), this protein is not available in sufficient quantities, causing dementia.

In the case of autism, the plasticity of neurons is not affected (so neurons are able to "recover") but the sensory dysfunction (caused by brain injury) has led to an irregular neurological organization and hence irregular behavior.

The Neurological basis of Organisation by Sensory Integration Therapy

A nerve impulse, which is transmitted from one point of the neuron to another, is the consequence, after suitable stimulation, of the variation in the permeability of the membrane to sodium. After this change in permeability, the inside of the cell changes from negative, to positive, compared to the outside of the cell.

The change, which initiates at the start of the axone membrane, is transmitted throughout to the nerve fibre to the presynaptic end. At this point the neuron cannot pass on the message electrically, because the neurons are not continuous; it must do so chemically and this chemical substance is called a neurotransmitter which binds with specific receptors in the post synaptic membrane.

The link between the neurotransmitter and receptor, either, causes sodium to enter the cell, excitation, by altering the permeability of the membrane, and hence depolarisation, or causes potassium to leave the cell, inhibition, hence hyperpolarisation, making the cell less likely to acquire potential for action. The stimulation is then reconverted into an electrical impulse. The central nervous system has an anatomical component, consisting of neurons and neuroglia, but functions electrically and chemically.

It is the chemical code, synapse, which makes the brain plastic and unstable, allowing us a whole range of behaviour. In the synaptic space, the impulse can be duplicated, amplified, softened or cancelled. **It is at this level that our brain is remodeled by inputs from the outside world. This continuous remodeling makes the brain extremely dynamic.**

The Brain.

The nervous system comprises two parts, the peripheral nervous system and the central nervous system, the latter comprising spinal cord and encephalus.
The encephalus has two parts, a lower part made up of bulb, bridge, mesencephali and cerebellum, and an upper part including the diencephalus and the two hemispheres.
The bulb, bridge and mesencephalus constitute the encephalic trunk, the pathway for sensory and motor signals, as well as the seat of cranial nerve nuclei. The cerebellum acts as a brake, keeping movements within certain limits.
The thalamus acts as the distribution centre for information received, most signals from the senses cannot reach the cerebral cortex except through the thalamus. The brain cortex is the recipient of sensory signals and the source of motor impulses, and the area of association between sensory input and motor output.

The functioning of the brain

The simplest definition of the functioning of the brain is that it enables interaction with the outside world.
The central nervous system consists of about 100 billion neurons, each having the function of receiving a stimulus, processing, memorising and transmitting a response to other neurons via it's axon collateral fibres.

When reading, the brain receives a stimulus through the visual channel, and on the basis of previous visual experience, the brain is able to memorise and conceptualise the experience, and to impart orders to the muscles keeping you in a seated position, reading. On receipt of another stimulus, for instance through the auditory channel, the ring of a doorbell, the brain memorises the new signal and orders your muscles to move; you get up from the chair. Thus the brain has input from the senses and an output to the muscles: the brain receives sensory stimuli, memorises them, compares them with previous experience and then imparts instructions.

The output- or motor pathway- is also called the common final pathway, since all stimuli converge on this pathway.

The input is sensory, through the five senses (sight, sound, touch, smell and taste). The brain also receives stimulus from the vestibule of the ear, helping to maintain upright posture, and balance.

Between the input and output there are processing centres called interneurons, so-called as they exist between sensory and motor neurons. In the human brain, there are between 10-100,000 interneurons for every sensory and motor neuron. The increase of brain mass over the past few hundred million years is due to the increase of interneurons.

All motor actions are possible due to muscle tone before the action commences (i.e. at rest). Muscle tone is necessary not only for motion, but also just to stay in position (posture). The control of posture is the fundamental function so no other organ except the encephalic trunk can carry it out. Muscle tone is the continuous gentle force exercised by the extensor muscles at rest and for many years it has been known that a lesion to the brain involving the output channel may cause hyper or hypo muscle tone. The outcome of hyper or hypo tone is due to the location of the lesion in the brain.

In the event that a lesion in an area of the cerebral cortex controlling motor functioning occurs, the result is hyper muscle tone i.e. spacticity or rigidity, in the event of the lesion occurring below the cerebral cortex, above the tentorium of the cerebellum, hypo tonality occurs, i.e. flaccidity of the muscles.
Since the central nervous system is an indivisible whole consisting of peripheral receptors, a cerebral cortex and muscle fibre, it can be said that injury (causing hyper or hypo muscle tone) may occur on the output or input side. Hence, just as spastic tetraparesis is a clinical condition causing hyper muscle tone, autism is a clinical condition caused by lesion to one or more of the sensory pathways, causing hyper or hypo activity in that pathway. Just as on the motor side, whether the result is hyper or hypo activity depends on the location of the lesion. All the symptoms of autism are the consequences of the fact that the brain of the autistic child does not perceive sensory stimulation in the same way as the brain of a healthy child.

Neurons

The central nervous system of human beings consists in about one hundred billion neurons; about 30% of them are locate in the cerebral cortex.
Neurons are the **FUNCTIONAL UNITS** of the central nervous system. Although there are many other cells in the nerve center (neuroglia)[1], only neurons generate and carry nerve impulses; neurons make contact between themselves by means of the membranes forming synapses (a term first used by Sherrington derived from the Greek meaning solid connection). A neuron in the cerebral cortex may be contacted by between 50 and 100,000 synapses.

Neurons are **ANATOMICAL UNITS** in that each cell is separate (they are separated by membranes) from all other surrounding cells (be they neurons or glial cells). Neurons have a cell body containing the cell nucleus, and dendrons, which may expand, increasing the total surface area of the neuron, and a single neurite, axial cylinder or axone. The axone is always singular and may be as long as one meter (for example the sciatic nerve) and is covered with a sheath, forming the nerve fibre.

Neurons have different forms according to their function, Pyramid cells in the cerebral cortex, Purkinje cells in the cerebellum, motor nerve cells in the spinal chord.

Neurons are also **GENETIC UNITS** since they are derived from single neuroblasts[2] by process of differentiation. The nerve tissue of the embryo has a faster growth rate than even the most malign tumor.

One of the most important areas of research for neuroscientists these days is to establish how neurons differentiate themselves for their different functions, i.e. how they become specialists in one function or another, since they are all created from a neuroblast. When we see something we are able to recognize it because of the specialist neurons in the visual cortex.

They have a different function to tactile neurons which enable us to recognize objects by touch, with our eyes closed. How did one become a vision neuron and the other a touch neuron, given that they both have the same origin? It used to be thought that as neurons specialized they received less and less information from the original genetic input (DNA), i.e. the parent cell. Now it is known that all information in the two gametes are transferred from one cell to another, but that an increasing quantity of this information is no longer "read". In the following pages we will see what role the environment plays in terms of sensorial input in establishing what part of the DNA input is read.

The first evolutionary step leading to cells similar to neurons took place about 1,500 million years ago with unicellular organisms complete with channels sensitive to voltage and permeable by ions such as calcium ions (Ca++). About 700 million years, following mutation, cells appeared which were permeable to sodium ions (Na+). Since sodium is less toxic than calcium for cells, and since the channels permeated with sodium were able to generate more power than those permeated with calcium, this mutation was rewarded, and further rewarded with the appearance of glias, allowing quicker conduction of the nerve impulse.

In his introduction to "The Modular Brain" Richard Restak wonders if a tree falling in a desert makes any noise. He says the answer to this question can be provided by an understanding of the relationship between the ear and brain, starting with the tympanic membrane along the hearing pathways, towards the medial geniculate body of the mesencephalus, and thence to the primary hearing area of the temporal lobe, and finally to the area of hearing association where the sound is recognized and identified.

If the sound waves provoked by the falling of the tree do not excite the tympanic membrane or if, for some reason, that message does not reach the brain then there is no sound, because a sound - by definition - requires an ear and brain. If they are not present, there are only sound waves at a certain frequency.
One of the functions of cell membranes is to separate the cytoplasm (cell body) from intercellular liquids. Intercellular liquids should be thought of as watery solutions containing sodium, chlorine (Cl-), potassium (K+) and calcium, i.e. salts in brokendown form. Potassium prevails inside the cell, sodium outside it. Since the cell membrane allows these substances (ions) in at different rates, the concentrations are different inside, and outside the cells, so there is also a difference in electrical potential inside and outside the cell, given by the difference in positive ions (Na+, Ca++, K+), and negative ions (membrane proteins and Cl-) either side of the cell membrane.

In many cases the cell membrane responds to an electrical or chemical stimulus by varying its permeability selectively for one or more ions. When the difference in potential on the two sides of the cell membrane increases, this is called hyperpolarization; when it diminishes it is called depolarization. The membranes of some cells (nerve cells, heart cells and muscular cells) are able to invert the polarization of the membrane, hence they are called electrogenic. If the cell membrane did not prevent the free exchange between ions in the cytoplasm and the intercellular liquid there would be no differences in ionic concentrations.
The membrane therefore has no pores, which, opening and closing, allow the ions to enter or prevent them from entering; instead, the protein membrane and energy establish the permeability of the cell and hence enable the cell to store up energy. All living cells are able to store up energy at rest. The ability to release energy (i.e. electrical energy) in order to carryout activities and functions is one shared only by nerve, heart and muscle cells.

At the end of the eighteenth century Galvani proved that living organisms store electrical energy. In a cell at rest there is a different electrical potential between the inside and outside due to the different concentration of ions either side of the membrane. If we look at two positive ions (cations), such as potassium and calcium, and two negatively charged ions (anions) such as chlorine and protein anions, inside the cell potassium and protein anions prevail, whilst outside calcium and chlorine prevail.

All substances for which the membrane is permeable would tend to reach the same concentration by simply moving from high to low concentration. So let us look at how a cell maintains its high potassium concentration. When potassium leaves the cell, this should be balanced by the simultaneous departure of protein ions (A-), but these cannot move. The area around the cell therefore acquires a positive charge since potassium is permeable and moves out of the membrane but the protein ions are held in by the membrane. This also explains why chlorine remains outside the cell (passive phenomenon) since the inside of the cell has a larger negative charge).

These passive mechanisms are not in play in the case of sodium, which is abundant outside the cell. Since the concentration of sodium ions outside the cell is higher than inside, sodium "tries to" enter the cell. If this happened we would have a balance, but this does not occur.

Hence active systems must be at work, call them a pumping system, preventing sodium from entering the cell. The presence of potassium around a cell generally indicates that the "pump is on". The different concentration of ions inside and outside the cells is the form in which the cell stores electrical energy. The use of this energy is related to the ability of cells to change polarity (depolarization) by altering the ion content inside the cell. At the moment the potential for action begins, the permeability of the membrane to sodium increases by five hundred times whilst the permeability to potassium remains the same. This causes a massive input of sodium to the cell of the nerve fibre, and positive polarity inside the cell. This forces potassium out of the cell (by electrical and chemical action, due to charge and concentration) so that charges around the cell (polarization) tend to-wards normal (inside the cell: positive, outside: negative), but the

chemical state is not normal. At this point the cell expels sodium and reabsorbs potassium.

If we give the right electrical stimulus to a nerve or muscle fibre we create a potential for action (inversion of the distribution of charges either side of the membrane) throughout the length of the fibre. This occurs by a kind of "chain-reaction" by which each cell passes on its own change of state to the neighboring cell. The potential action is transmitted by transmitting a change of state inside the cell (amount of sodium). A local anaesthetic works by blocking this mechanism so that the chain is broken and the transmission of "data" is stopped. All cell membranes are able to block the free flow of ions but only nerve, heart and muscle fibres are able to transmit energy in this way. This is what is called a nerve impulse - an electric signal which is transmitted from one point to another of a nerve fibre.

The synapse

We have therefore explained that a nerve impulse is the depolarization of the cell membrane and the mechanisms by which the impulse is transmitted through the nerve fibre by self-excitation of the points of neighboring membranes. But a further question needs to be clarified: neurons, apart from being functional units that generate and conduct nerve impulses to other cells, are also anatomic units, i.e. each cell is separated from other cells by a membrane. So how is it possible for them to carry out this function? How is information transferred from one cell to another, given that cells are isolated units? The existence of what Sherrington called the synapse is the consequence of the morphological individuality of a neuron and another cell (another neuron or, for example, muscle fibre).

A synapse is formed when a message is transmitted from one cell to another. The lack of contact between the two cell membranes as they lengthen and the short circuiting carried out by the synaptic fissures (space between the two membranes) means that no electric signal can be transmitted, so that when the message reaches the extended part of the transmission neuron (presynaptic membrane), chemical substances must be released for the message to carry. When these substances reach their destination (post-synaptic membrane) the cell is either depolarized (by the entrance of sodium into the cell: excitation) or hyperpolarized (by the exit of potassium) by the strengthening of the positive charge outside the membrane (inhibition). When a nerve impulse is transmitted by a nerve fibre to a muscle fibre (neuro-muscular synapse) the effect on the muscle fibre is always one of depolarization creating potential for action which leads to the contraction of the excited muscle. At the level of synapses between two neurons (central synapse) one impulse rarely produces a potential for action at the post-synaptic neuron.

This explains why, at the level of the cortex, a neuron has between 50-100,000 synapses; whilst the message from a nerve fibre to a muscle fibre is always sufficient to provoke muscle contraction, the message from neuron to neuron may excite (i.e. sodium enters the second neuron), or inhibit (i.e. potassium leaves the second neuron, creating higher polarity). The neuron is therefore able to influence neighbouring neurons, and to transmit a potential for action to the post-synaptic neuron, which in turn may pass this on to other neurons.

Synapses may be formed between the axone of neuron A (presynaptic-membrane) and the dendron ends of neuron B (postsynaptic membrane). In this case communication is uni-directional and can go only from A to B. These synapses form the macrocircuitry.
Synapses can also be formed between the axone ends of two neurons in synaptic contact; in this case communication is bi-directional. These synapses form the microcircuitry.
The number of microcircuits in the most developed mammals is very high with an important impact, on the ability of neurons to store data (or memorize).

Neurotransmitters

A neurotransmitter[3] (NT) is the chemical substance which is released from the presynaptic ends into the synaptic space when the electrical impulse reaches the presynaptic membrane, and reaches its specific receptor on the postsynaptic membrane. The neurotransmitter binds with the receptor and this modifies the postsynaptic cell membrane, changing the permeability to sodium and potassium, so that the inside of the cell takes on positive polarity compared to the outside (excitation) or becomes even more negative compared to the outside (inhibition). A cell membrane is presynaptic if it contains the neurotransmitter and is postsynaptic if it contains the receptor.

Our brain contains a few dozen neurotransmitters. Millions of neurons use the same neurotransmitter. There are three groups:

1) First type NTs consisting of amino acids which can excite (glutammic acid) or inhibit (GABA): this is the most common

2) Second type NTs consisting of aminic substances (serotonin, acetylcholine, and catecholamine) involved in mood, behavior and cognitive processes; generally they function as modulators.

3) Third type NTs consisting of neuropeptides which, like aminic substances, are used for synaptic modulation; they govern functions such as eating and drinking, physical properties before and after copulation, and general sensations of uneasiness or wellbeing.

One of the differences between,on the one hand, first and second type transmitters and, on the other, third type NTs, is that whilst the first two are produced in the presynaptic ends, and, then released into the synaptic space when stimulated, the third type are proteins, and therefore are produced in the cell body, and, then taken (axoplasmatic flow) to the presynaptic ends. This explains why third type neurotransmitters are not always available at the presynaptic ends. Clinically this can be seen in the familiar phenomenon that immediately after trauma there is often an almost total lack of feeling, followed at a later stage by acute pain. This is caused by the fact that analgesic endorphins and other neuropeptides in the presynaptic ends have run out.

[1] Neuroglia consists of ependymal cells, astrocytes, oligodendrocytes and Del Rio Hostage cells.The neuroglia has the same function in the central nervous system as other connecting systems for organs: it acts as the frame supporting the encephalus and spinal column, and accompanies nerves along their pathways. It also has a number of functions in the case of swelling of the neurons, although this process is not yet well understood.

[2] Neuroblasts are the cells generating neurons. They appear during the second month of pregnancy and have no extensions. As they change form (process of differentiation) they generate nerve cells (neurons) which always have extensions.

[3] The British scientist T.R. Elliot was the first to use the expression, in 1904; he was also the first to investigate the idea that neurons communicate with each other and with other cells chemically and not electrically.

(1) Based on the publication “Children who do not look you in the eye”
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