Electrical Neuro-Modulation and Neurological Disorders

Introduction

Electrical neuro-modulation is a process that couples electrical signals through the skin (transcutaneous) to nerve fibers. The electrical signals penetrate the myelinated nerve sheath and modulate the neurons to improve numerous neurological functions. The effectiveness of this approach to improving neurological performance had been demonstrated anecdotally numerous times, but to date has not been verified by clinical studies.

I was diagnosed with Parkinson's disease in January 2001. My primary symptom was rigidity. My neck movement was severely limited and both of my legs were very tight and would "lock up" with any sudden contraction. The first two years I used the neuro-modulator as prescribed and had modest results, my muscle rigidity was significantly reduced. Since June 2003 I have used the same Synaptic neuro-modulator in a completely different manner that will be described in this paper. The result being that my Parkinson's rigidity is now almost completely controlled and I am no longer taking any Parkinson's medications.

The purpose of this paper is to document my hypothisis of why the neuro-modulator has controlled my Parkinson's and has been able to help many other friends improve their neuro-muscular performance.

1.0 Understanding the Neurology and Motor Control Basics

This section will summarize much of the research that I have conducted over the past 3 years. This research has led me to conclude that <u>most</u> of my Parkinson's symptoms are related to the malfunctions in the <u>Proprioception</u> (position and balance) system and not just a malfunction of the <u>Substantia Nigra</u>, which is typically attributed to causing Parkinson's disease. *Note: Much of the material in this section is from Jeff Radel, Ph.D., University of Kansas Medical Center.*

The Basal Ganglia is a collection of nuclei deep in the white matter of the cerebral cortex. The Substantia Nigra is included in the Basal Ganglia and produces Dopamine, which is critical for normal movement. The Substantia Nigra degenerates in patients with Parkinson's disease. Three symptoms usually associated with Parkinson's disease are tremor, rigidity, and bradykinesia. The tremor is most apparent at rest. Rigidity is the result of simultaneous contraction of flexors and extensors, which tends to "lock up" the limbs. Bradykinesia (slow movement) is a difficulty initiating voluntary movements, as though the brake cannot be released.

2.1 Simplified Description of How the Brain Controls Body Movement

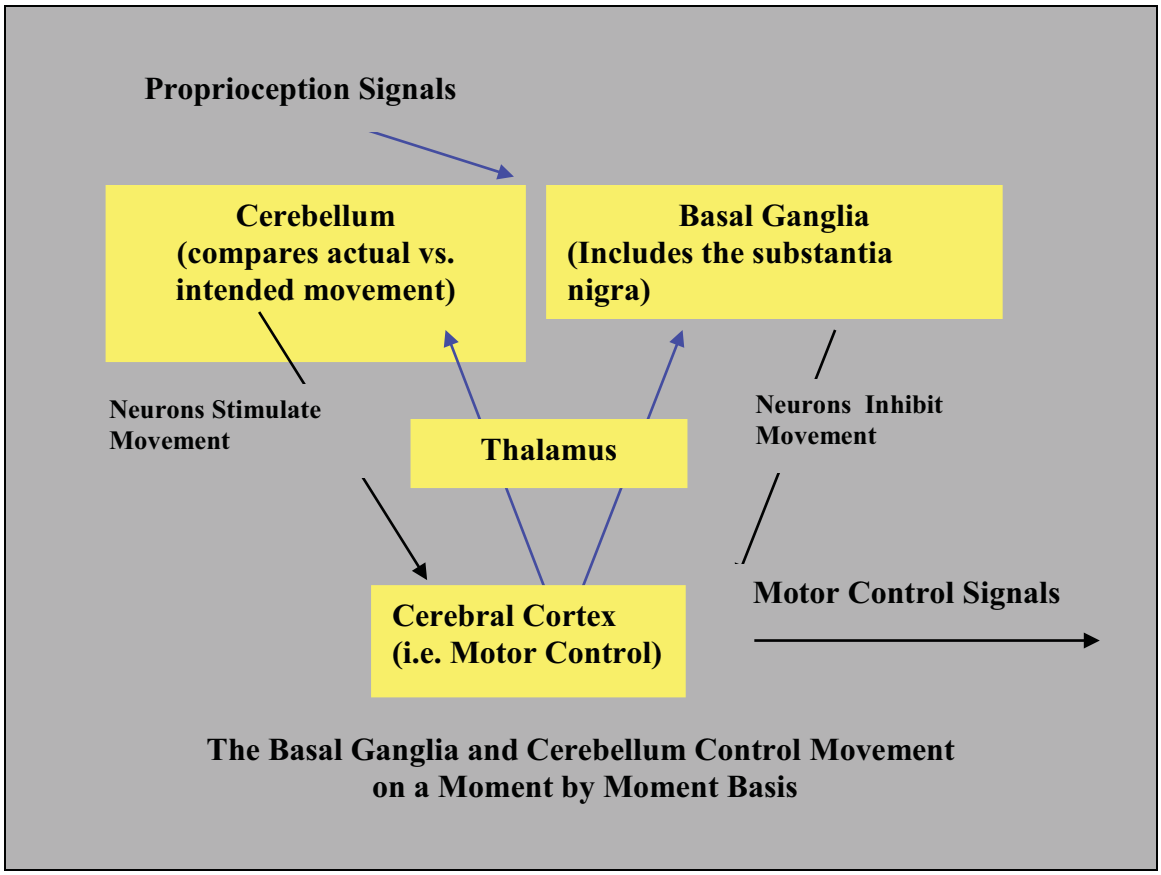


Figure 2.1-1 Motion Processing in the Brain

The Cerebellum is the central computer for controlling movement. It compares what you thought you were going to do (according to the motor cortex) to what is actually happening throughout your body, according to proprioception (position and motion sensor) feedback, and tries to correct the differences in a smooth manner. The Cerebellum also is partly responsible for motor learning, such as properly hitting a golf ball.

The Cerebral Cortex (Motor Cortex) sends information to both the Basal Ganglia and the Cerebellum and both structures send information right back to the cortex through the Thalamus. The motor control signals travel down the spinal chord to control the alpha motor neurons to activate muscles. Sensory signals travel up the spinal chord to report sensor status, such as muscle length and tension.

Inside the spinal column the spinal nerves branch off from the spinal chord in pairs. Each of the nerves has two roots: the one in front is the ventral root and carries only motor

impulses, the one in back is the dorsal root and carries sensory signals. Within the spinal nerve there is two-way traffic, since it carries both sensory and motor signals for the part of the body it serves. At any given time there can be a mixture of different sensory messages being passed along. But once the nerve feeds the signals into the spinal chord, they are sorted and separated into groups of nerve fibers. One tract handles motor impulses from the brain. Other tracts carry sensations of pain, temperature, proprioception, etc.

2.2 Proprioception System Overview

Figure 2.2-1 depicts the mechanism by which the body controls motion and posture. The following describes how this system works.

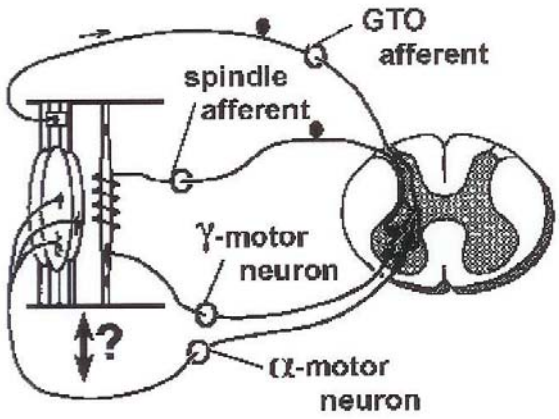


Figure 2.2-1 Example Proprioception System Function

(1) Assume that a load is added to a limb and stretches the muscle. The muscle spindle fires a series of pulses as the muscle is stretched signaling a change in length. Golgi Tendon Organs (GTO) also fire, signaling increased stress on the tendon.
(2) Alpha motor neurons are activated, causing extrafusal fibers of the muscle to contract, shortening the muscle back to its original length. The muscle spindles are no longer stretched, and are therefore inactivated as the muscle shortens. GTOs remain under tension (due to the load and active muscle contraction) and continue to fire, signaling the amount of tension experienced on the tendon.
(3) Gamma motor neurons are activated, causing a contraction of the muscle spindles, in proportion to the change in muscle length. This re-sets the spindles, allowing them to become active in case the shortened muscle changes length. More receptors are recruited as the intensity of the stimulus (stretch or tension) increases to ensure that the signals exceed the threshold required to ensure that muscle damage will not occur. If the tension detected by the GTOs exceeds a safe level, GTO inputs override the inputs of the muscle spindles. This inhibits activity of both the alpha motor neurons and the gamma neurons, and leads to a relaxing (lengthening) of the extrafusal fibers and of the muscle spindles. The muscle tension is reduced to a safe level and the brain is then tasked to determine an alternative approach to handling the load.

In my case, since my muscles were generally tight (contracted), whenever I would swing a golf club too fast: (1) my calf and hamstring muscles would cramp and (2) my other leg muscles would go limp and I would fall down.

2.3 Principles of Muscle Control

2.3.1 Muscle Physics

Figure 2.3-1 depicts the mechanism by which nerves make muscles contract. The left structure represents a relaxed muscle. The right structure represents a contracted muscle.

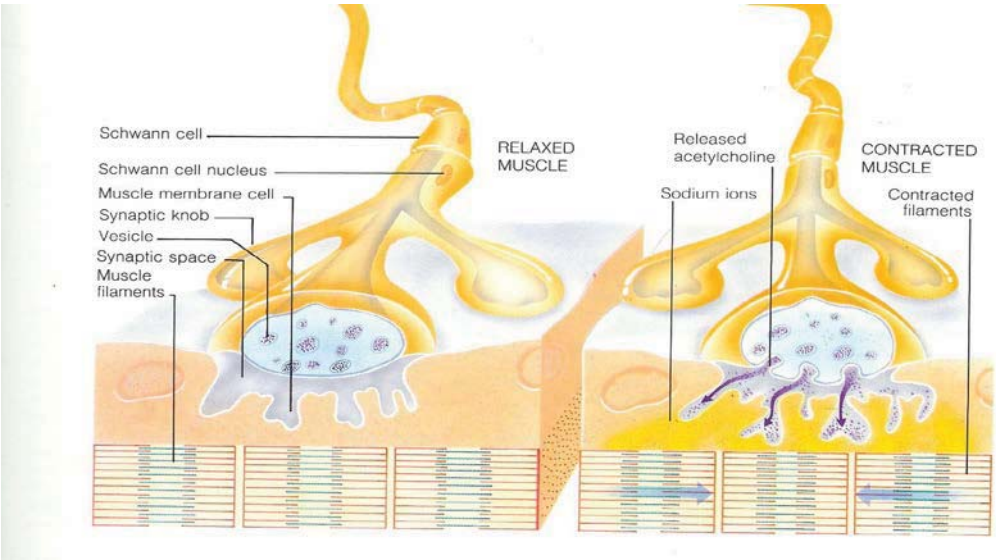


Figure 2.3-1 Muscle Control Mechanisms

The motor control fibers (alpha nerves) directly drive the muscle to which it is connected. A motor endplate terminates in a series of synaptic knobs, which are separated from the muscle tissue by the synaptic space. Within each knob are packets (vesicles) containing the neuro-transmitter acetylcholine. The arrival of a nerve impulse makes the vesicles release acetylcholine into the synaptic space. This in turn, brings about the release of sodium ions, which act on the muscle filaments and make them slide over each other in muscular contraction. Meanwhile, an enzyme acetylcholinesterase breaks down the acetylcholine and makes it inactive. This resets the mechanism in time for the arrival of the next nerve impulse, needed to keep the muscle contracting.

2.3.2 Normal Muscle Control

Muscles are present in opposing groups, as illustrated by the biceps and triceps of the upper arm. Contraction of the biceps bends the elbow, while contraction of the triceps straightens it. When a muscle is being intentionally stimulated to contract, it is called an agonist. Opposing muscles are called antagonists. For instance, when you flex your biceps, it is the agonist, while the triceps is the antagonist. Note that any given muscle will be an agonist in one situation, but an antagonist in another. Also note that *when an agonist contracts, the antagonist naturally gets stretched.* The response to this stretching is what goes wrong in spasticity.

This natural stretching of antagonist muscles is necessary for movement, but too much stretching can damage the muscle. Two related signaling pathways help prevent too much, and too little, stretch of the antagonist. First, while an agonist is contracting, the spinal cord sends inhibitory signals to the antagonist to prevent it from contracting while it is being stretched out. Second, the antagonist sends sensory signals back to the spinal cord to indicate how much it is being stretched. When the antagonist is stretched too far or too fast, these sensory signals override the inhibitory signals, and set off protective contractions in the antagonist to prevent muscle damage. These two antagonist-regulating pathways help to insure that the intended movement can occur, but cannot damage surrounding muscles.

Spasticity occurs when these two antagonist-regulating pathways are improperly controlled, usually due to upper motor neuron damage. First, the pathway that normally inhibits antagonist contraction becomes less active than normal, leading to unwanted co-contraction of antagonists during movement of an agonist. This prevents smooth movement and full range of motion in the agonist. Second, the stretch reflex becomes hyperactive, so that the antagonist is likely to contract even when stretched only slightly. As a result of loss of inhibition and hyperactive stretch reflexes, movement becomes difficult to control, and muscles may remain stiff and contracted for long periods of time.

2.4 Description of How Nerve Impulses are Created and Transported

2.4.1 Nerve Structure Overview

Figure 2.4-1 shows the elements of nerve fibers. Each nerve fiber has a cell body

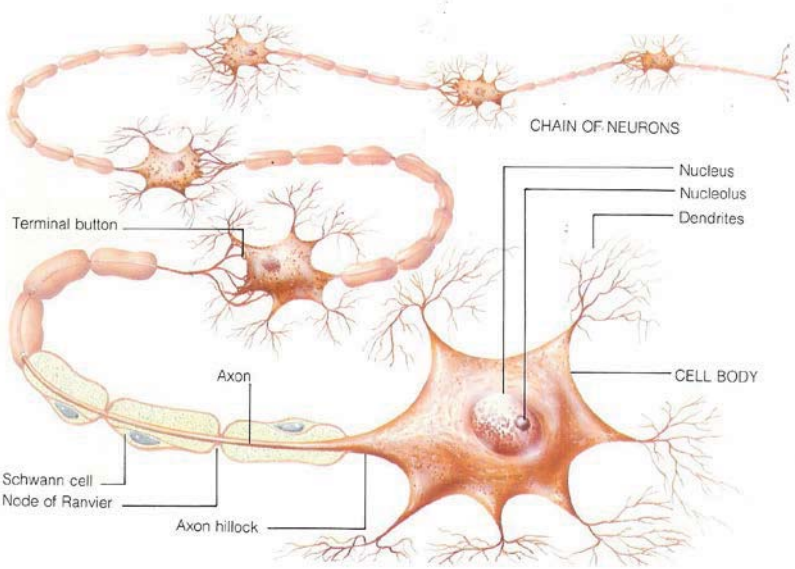


Figure 2.4-1 Nerve Fiber Structure

containing a nucleus bearing root like dendrites. An axon extends from a "hillock" on the cell body, and is wrapped with myelin sheath (a chain of Schwann cells separated by gaps at the nodes of Ranvier). Terminal buttons at the end of the axon link to other nerve cells.

Most nerve cells have a single axon and a large number of dendrites. The dendrites are approximately 1.3 mm (.05 in.) long and terminate in thousands of smaller dendrite spines. Electrical impulses arrive from other nerve cells through these dendrites. All the electrical messages (series of impulses) are integrated in the cell body. The cell body creates a new series of impulses containing the appropriate information and passes it along the axon.
An axon diameter (in humans) is approximately 10 μm. The axon length may be as short as 100 μm and as long a 1-1.5meters. The nerve sheath acts as an electrical insulator that limits ion leakage, but also reduces electrical interaction between nerve fibers. The rate of propagation for myelinated sensory neurons is about 60 – 120 meters/second. Non-myelinated nerve fibers propagate only at 7-25 meters/second because of ion leakage.

2.4.2 Electrical Impulse (Action Potential)

Transmission of nervous systems signals is carried out using electrical impulses. Figure 2.4-2 shows the shape and duration of the electrical impulse (action potential). The amplitude and shape of this action potential is universal throughout the body. This action potential is generated in a nerve cell as follows:

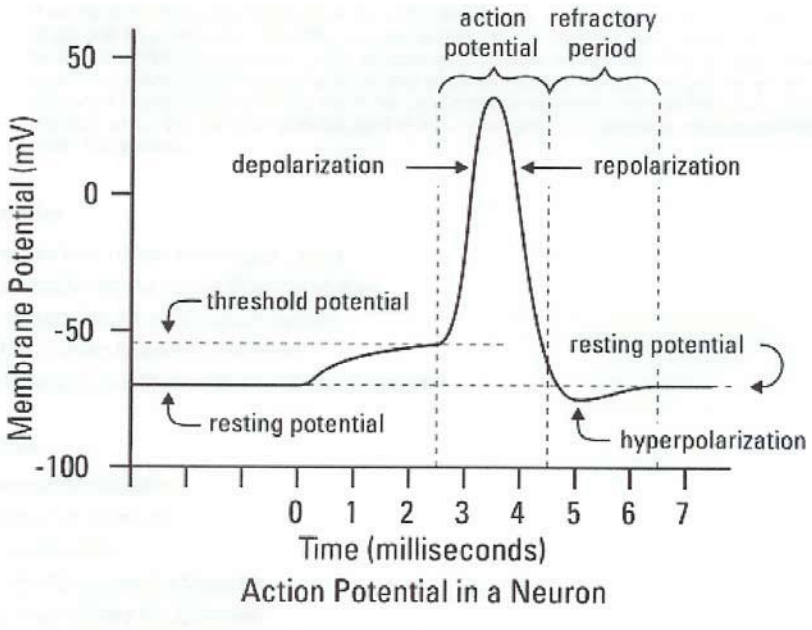


Figure 2.4-2 Impulse Shape and Duration

(1) The resting potential to start the action potential is approximately –70mV.
(2) An action potential begins when the neuron is polarized by about 20mV to its threshold potential. Sodium permeability is triggered and the action potential is initiated. The neural membrane is depolarized to about 40mV, where sodium permeability ceases.
(3) Potassium permeability increases, and the new influx of cations re-polarize the membrane to a negative potential.

(4) The Potassium influx temporarily overcompensates by hyperpolarizing the membrane below its resting potential. After the under-shoot, the resting potential is restored.

Cell membranes surround neurons just as any other cell in the body has a membrane. When a healthy neuron is at rest the electric charge on the outside of the membrane is positive while the electric charge on the inside of the membrane is negative. The outside of the cell contains excess sodium (Na) ions; the inside of the cell contains excess potassium (K) ions. The resting potential is approximately 70 mV. When a healthy resting neuron is stimulated by a pulse whose amplitude exceeds the threshold potential (about 50 mV), the cell will fire and an action potential will be generated. The action potential duration is approximately 1.2 ms. The cell that generated the action potential must reset before it can fire again. This takes approximately 1.4 to 2ms. Therefore a cell is limited to a firing rate of approximately 300 to 400 pulses per second.

It is important to note that if a cell does not have a sufficiently polarized resting potential, the cell's potential is always at a Voltage above threshold and the cell will not generate an action potential. The associated nerve will not conduct and the cell is generally called "dead". Also note that if the cell's resting potential is approximately 50 mV, spurious signals will cause the nerve to "fire". The associated nerve will transmit false messages.

2.4.3 Neural Messaging by Spike Trains

The nerve pulses passing along the axon of a particular neuron are constant amplitude sent in bursts coded in the form of pulse frequency modulation. The intensity of the stimulation is generally proportional to the number of pulses generated. However, since many synapses generally fire at once, the encoding is usually described in a statistical manner. The number of pulses generated, the pulse spacing and the burst duration are determined by the arrival of the action potentials from the many activated synapses. The nature and method of encoding and decoding these signals is a recent area of research. So far the research has shown that proprioception sensors send spike trains with an average burst rate of 11 bursts per second. Some other data indicate the following:

(1) A constant stimulus often produces a constant spike frequency, at least in the beginning.
(2) All of the spikes have about the same amplitude
(3) All of the spikes have the same duration (about 1.8 ms).
(4) The spike frequency varies according to the nature, timing, and intensity of the stimulus and to the neuron's intrinsic dynamics.

Any normal nerve fiber or terminal can't produce spontaneous "firing" unless it is stimulated. After a nerve injury, tiny mechanical or chemical changes in or out of the neuron can often cause violent firing from the injured site or cell body. Neuropathic pain and other sensation abnormalities such as tingling and numbness are induced by axon injury and by peripheral nerve inflammation. Often when the cell is depolarized (either by drugs or electrical stimulation) the normal nerve transmission is restored. Also it should be noted the nerves try to re-generate and repair themselves.

2.4.4 Synaptic Transmission

Transmission of impulses between nerve fibers is carried out using both electrical and chemical signals. Figure 2.4-3 illustrates the synapse. When a cell is activated and creates the electrical impulse it transfers the message down the axon into the dendrite through the synaptic process. When the electrical impulse reaches the synapse it causes a flow of calcium ions. When the calcium ions rush in, a chemical called a neuro-transmitter is released into the synapse. The neuro-transmitter moves across the synapse and binds to proteins on the neuron membrane that is about to receive the impulse. The proteins serve as the receptors for several neuro-transmitters which each have specific receptors. After the neuro-transmitter produces its effect, the receptor releases the excess neuro-transmitter back into the synapse.

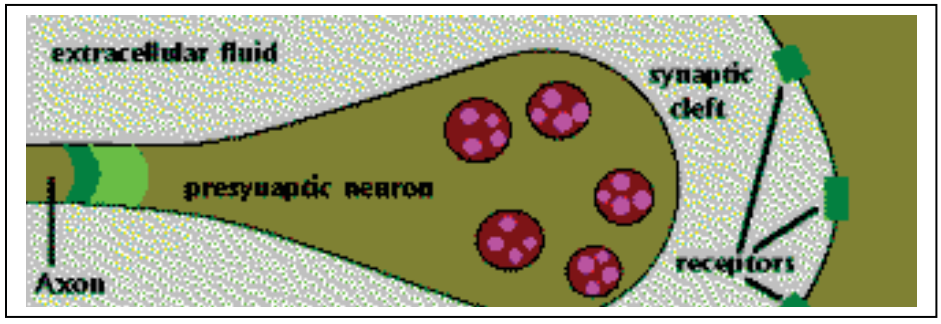


Figure 2.4-3 Synaptic Transmission

The synaptic neurotransmitter process is as follows:

Step1. The neurotransmitter is manufactured by the neuron and stored in vesicles at the axon terminal.

Step 2. When the action potential reaches the axon terminal, it causes the vesicles to release the neurotransmitter molecules into the synaptic cleft.

Step 3. The neurotransmitter diffuses across the cleft and binds to receptors on the post-synaptic cell.

Step 4. The activated receptors cause changes in the activity of the post synaptic neuron (the next dendrite).

Step 5. The neurotransmitter molecules are released from the receptors and diffuse back into the synaptic cleft.

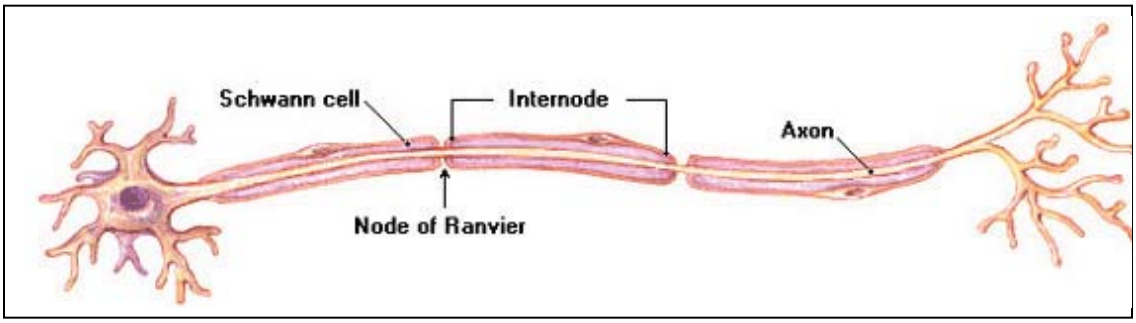
Step 6. The remaining (unused) neurotransmitter is reabsorbed by the post synaptic neuron. This process is called reuptake.

2.4.5 Role of Neurotransmitters

Research scientists are attempting to learn how neurotransmitters are synthesized, how they are released and how they activate receptors in the post-synaptic membrane. But, we do know that neurotransmitters play a very important role in how our body functions and how we feel. **Beta-endorphins and Enkephalins** are powerful natural opiates that combat pain as well as make one feel good. **Serotonin** is a neurotransmitter, produced in the brain, that plays a significant role in both vasoconstriction and vasodialation of blood vessels. Reduced Serotonin levels lower pain thresholds, cause depression, increase appetite and decrease sleep quality. **Dopamine** is a neurotransmitter that is somehow related to Parkinson's disease.

2.4.6 Propagation of Electric Impulses in Myelinated Axons

Figure 2.4-4 shows a single myelinated nerve fiber. Most of the nerve fibers that carry signals in the body (except in the brain) are myelinated. Nerve impulses travel along a myelinated nerve fiber chain by a process called "saltatory" conduction, not through the synaptic process used to connect nerve fibers together. The essential aspect of this whole process is the rapid conversion of chemical potential energy to electrical potential energy.



<u>Figure 2.4-4</u> Myelinated Nerve Fiber Diagram

These myelinated fibers have small (1 μm long) interruptions in the sheath every 2 mm. These interruptions are called "Nodes of Ranvier", and are the sole places where ion transfer takes place. Typical values of propagation times quoted for myelinated axons are 6 to 9 meters/second per micron diameter. A 10μm diameter myelinated fiber will propagate an action potential impulse at between 60 and 90 meters/second. Myelinated nerve diameters are typically between 5 and 20 microns.

The propagation of a nerve impulse along an axon begins when the synapse receives neurotransmitters from nerve endings nearby. The neuron then increases its internal potential, setting off a chain of events which is repeated for each Node of Ranvier as the nerve impulse "jumps" down the axon (this is known as "saltatory" conduction).

1. Voltage gated Na channels open when the membrane potential raises about 20 mV above the rest potential; this potential is called the "threshold". Na ions rush in for about 1 ms; positive feedback (the membrane potential continues to rise above the threshold) keeps the channels open until the cell interior becomes positively charged to approximately 30 mV before the Na channels close. About 2000 ions enter per channel during the Na influx. <u>Note that until the membrane potential drops below the threshold, the neuron cannot react to further stimulus</u>.
2. The Na ions migrate a small distance away from the node, and additional Na ions move toward the node within the interstitial fluid. The increased positive ion concentration inside the node increases the membrane potential at both neighboring nodes (with very minute effects further down the axon on both sides). The "downstream" node reaches threshold and the process continues there. The "upstream" node reaches threshold as well, but its threshold has been raised high enough by its firing that it does not fire again. In this way, the nerve impulse

propagates down the axon, maintaining its intensity until it causes the release of neurotransmitters at the nerve endings.

3. The Na channels close when the voltage peaks, and K channels open and let K into the interstitial fluid. They remain open for about 1.5 ms, until the membrane potential overshoots its initial value slightly. During this time, the neuron's "firing" threshold is much higher than normal.
4. Finally, Na pumps restore the concentrations that existed before firing.

2.5 Neural Pathways Not Just Nerves

2.5.1 Neural Network Disorders

Networks of nerves (the nervous system) direct and monitor every body system and cell, governing all movement, sensation, thought, and emotion. These many networks function properly in a healthy body. However, whenever the flow of neurons is disrupted a change in the body's function occurs. The most drastic examples involve injury to the spinal chord that either puts pressure on, or completely severs the nerve. Other cases involve inflammation of the nerve, or nerves, which may be caused by some kind of general poisoning (lead, arsenic, alcohol) or a virus.

Many neurologic impairments are caused by degenerative diseases such as Alzheimer's, Parkinson's, Multiple Sclerosis, etc. These diseases are generally attributed to degeneration of specific cells in the brain. Alzheimer's is attributed to slowly progressive neural atrophy of the cerebral cortex; Parkinson's disease is attributed to slowly progressive degeneration of the substantia nigra and corpus striatum, with a dopamine deficiency; Multiple Sclerosis is attributed to patchy de-myelination of the white matter in the brain and spinal chord, marked by unpredictable exacerbations and remissions. These diseases are currently managed by drugs but are deemed incurable. **There seems to be little effort to mitigate these brain-induced symptoms through attempts to restore neurologic function throughout the many related neural networks and neural-muscular systems**.

Neurologic disorders are the realm of neurologists and are generally treated by judicious use of medicines. Often, Chiropractors are able to relieve pressure on the nerves. Also, acupressure and electric stimulation are often effective in reducing pain. In many cases neurologic function is restored. **My experience in using Neuromodulation to restore neurologic function has provided hope for managing some neurologic disorders but does not attempt to address cell degradation in the brain. Consequently, Neuromodulation Stimulation only provides a partial solution**.

2.5.2 Comparison of Asian and Western Nervous System Descriptions

Historical evidence reveals that the ancient Chinese physicians knew that acupuncture was physiologically based, affecting blood and vital air (breath) circulation as well as nerve function. Neuroanatomic acupuncture correlates traditionally described points and channels with neurologic pathways and influences as understood today. In the 1980's,

investigators related the effects of acupuncture to the stimulation of at least 10 neural structures. Evidence also shows that complete denervation obliterates the effects of acupuncture.

Figure 2.5-1 shows the distribution of the nerves in the arm and shoulder. The picture on the right is from Grey's anatomy (Western Medicine). The figure on the left is an acupuncture chart (Asian Medicine). Note that many of the acupuncture points and meridians follow the anatomical nerve structure. Figure 2.5-2 shows the distribution of the nerves in back of the leg. The picture on the right is from Grey's anatomy. The figure on the left is an acupuncture chart. Again, many of the acupuncture points and meridians follow the anatomical nerve structure. This relationship is central to my use of Neuromodulation to restore neurologic function. It is important that the neural messages can be conducted throughout the neural paths as intended.

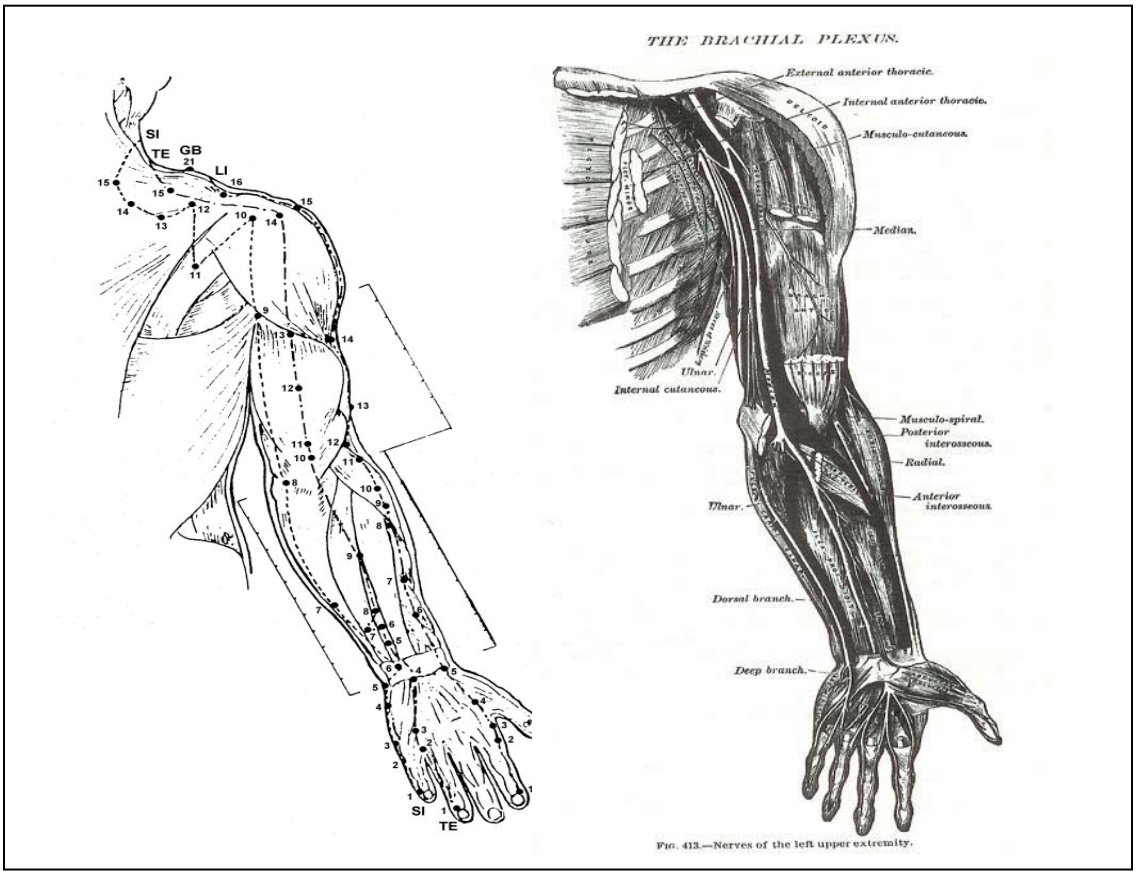


Figure 2.5-1 Comparison of Western Nerve Anatomy and Asian Acupressure Paths of the Arm & Shoulder

One fundamental difference between Western and Asian medicine is in the manner that the nervous system is described. Western medicine defines the nervous system as a

system of interrelated systems. Some are physically separate, others differ only in function. The brain and spinal chord make up the Central Nervous System (CNS). The rest of the system is called the peripheral Nervous System (PNS). It is impossible to obtain a broad picture of how this complex and sophisticated nervous network controls our every thought, feeling and movement. However, Asian medicine attempts to do this by making an analogy to repetitive and circulatory functions such as blood flow and breathing. Asian medicine relates overall function of the stomach, gall bladder, intestines, etc., to acupressure points and energy (Qi) channels. Additionally Asian medicine seems to account for turbulent flow within these channels.

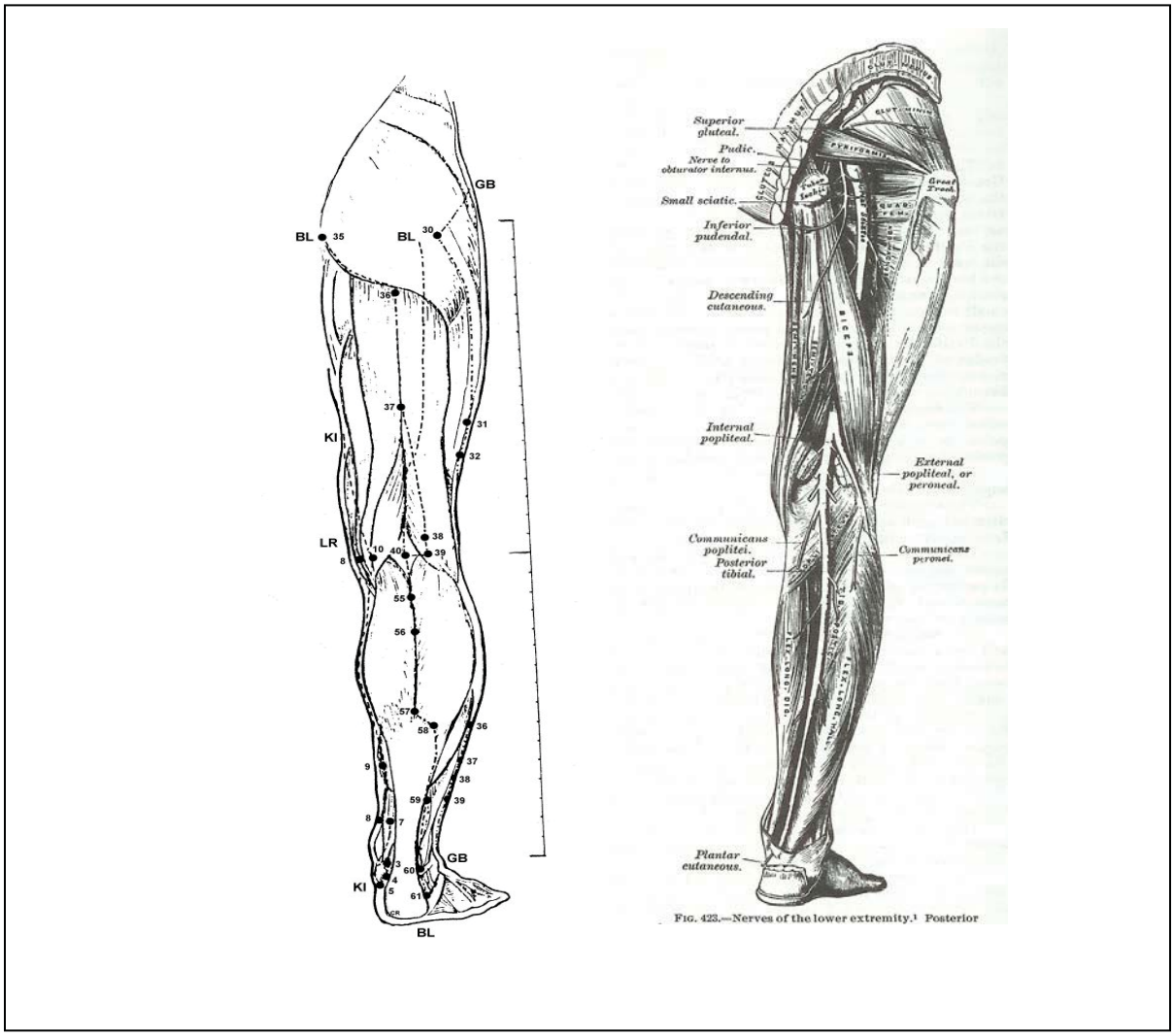


Figure 2.5-2 Comparison of Western Nerve Anatomy and Asian Acupressure Paths of the Arm & Shoulder Paths of the Leg and Hip

To date there seems to be no one-to-one correlation but there are many physical points where nerves and acupressure paths are essentially the same. I have used this apparent correlation to electrically stimulate neural paths and re-establish neural conduction. For example; one can place one electrode on the left ankle's instep and a second electrode on the palm of the left hand and conduct electrical impulses at approximately the same voltage level as for normal local stimulation. This will be discussed in more detail later in this paper.

3.0 Procedure for Using the Synaptic Neuromodulator to Treat Several Neurological Disorders

Treatment of neurological disorders is based upon 2 principles; (1) use of the neuromodulator in the central location will stimulate the central nervous system and cause an increase in neurotransmitter production; (2) reactivation of nerves in the proprioception system. Often the nerves that send signals back to the central nervous system become inactive. This may be caused by normal nerve failure with age; the effects of an injury or scar tissue in a critical sensory feedback path; or inflammation of the nerve.

Apparently the damaged nerve cell or a section of a myelinated nerve fiber loses its negative charge. Once this happens the cell can no longer pass an action potential (nerve message) on to the next cell. Electrical stimulation appears to recharge the inactive cell (cells) and normal neural conduction is restored. When there is an underlying disease the nerve cells seem to need to be reactivated approximately once a week.

3.1 Use of the Synaptic Neuromodulator

The Synaptic Neuromodulator (shown in Figure 3-1) is used in the procedure discussed in this paper. The neuromodulator has two identical channels that are activated by the black buttons that unfortunately look like they are only labels. The output is controlled by the attached hand controller (just out of view in Figure 3-1). The slide control must be pulled all of the way down when the modulator is turned "on" by a toggle switch on the upper back of the modulator. If the slide control is not all of the way down the modulator display will show a series of letters instead of sequencing through a series of numbers. When the number sequence has stopped the display will go blank. Push the black buttons (that look like labels) and the modulator display should show zeros in all four columns.

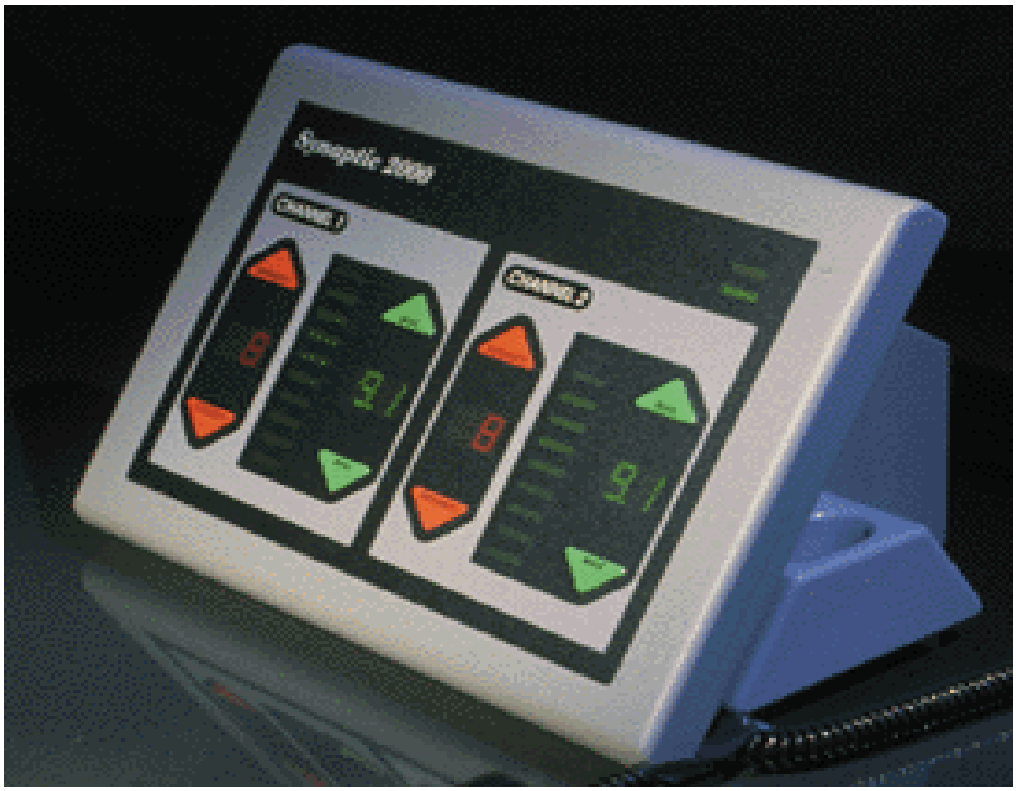


Figure 3-1 The Synaptic Neuromodulator

As the slide control is pushed up, the green display will increase from 0 to a maximum of 9.9. When the display is at "0" the modulator output is approximately 40 KHz. As the numbers increase the frequency decreases until it is approximately 400 Hz at "9.9". While the Red display is at "0" the output voltage is at its minimum value. Note that if the slide is advanced too quickly the neuromodulator will go into a "Safe mode" and a series of letters will be displayed. When this happens the neuromodulator must be turned "off" at the back toggle switch and the startup procedure repeated. Always slide the control slowly and smoothly to avoid this annoying safety feature.
When the slide control is slid back down to "0", after previously reaching 9.9, the output voltage will increment up one level. Initially this is from "0" to "1". The maximum output level is "9.9".

3.2 Basic Use For Stimulating Neurotransmitter production

This paper will begin by discussing use of the neuromodulator in the manner intended for pain management and stimulation of neurotransmitters. Later the more advanced methods will be described to relieve Parkinson's symptoms and other neurological disorders.