March / April 2021

An Introduction For Physicians and Patient*
To Modern SPECT Technology
For Identifying Major * Microvascular Brain Pathology,
In both M.E. and Toxic Brain Injury patients
Invisible On CT and MRI Brain Mapping

To my knowledge, when a chronic brain injury does not involve a space-occupying lesion and is at a cellular, microvascular or neuron level, most primary care physicians and neurologists have little or no understanding of how to place the injury in perspective, or in other words, "map" the degree and extent of the injury, even if this is an extensively injured brain.

Nor are many physicians aware of the power, ease, safety and benefits of modern "three-dimensional SPECT brain mapping," in the diagnosis of chronic brain injury resulting from post-infectious, toxic or traumatic injuries. This article is directed to these primary care physicians, internists and neurologists.*

"Brain mapping" is a useful but not a usual Nuclear Medicine term. I borrow the term from my previous work as a geophysicist, to denote creating a readable anatomical and pathophysiological map which will allow the physician to define an accurate physiological interpretation of both brain pathology and physiology.*

The neuronal activity of the brain's network cannot be determined by CT or MRI but appropriate SPECT can demonstrate ***(a)*** *the microvascular competency and* ***(b)*** *rapidity of micro-vascular restoration following any intellectual, motor, emotional or administrative activity. This was clearly demonstrated by Mena and Goldstein in 1987[1]. However, the problem with traditional SPECT* is not whether the technology is capable of doing this, but how open is the older SPECT system to being correctly and easily interpreted by the general medical public. This is no longer a difficulty with modern, "three dimensional" SPECT analysis.*

Correct and Easy Interpretation*: Older SPECT brain mapping has been useful to a certain degree when properly interpreted by nuclear physicians. The problem arises in that most neurologists, internists, primary care physicians and even many expert radiologists rarely are able to interpret older SPECT brain map software correctly. Due to their significant lack of understanding, they have tended to reject SPECT brain mapping and in so doing, tend to miss diagnosing, even major chronic brain injury, particularly post-infectious and toxic chemical injury. *It's notable that most of us are aware of the significant destruction of up to 80-90% of all songbirds and birds of prey since the advent of brain toxic pesticides and herbicides in 1945, but we have little knowledge of*

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[1] Goldstein, J.A. "Chronic Fatigue Syndrome: Limbic encephalopathy in a Dysfunctional neuroimmune network." In B. M. Hyde, J. Goldstein and P. Levine. eds. The Clinical and Scientific Basis of Myalgic Encephalomyelitis & Chronic Fatigue Syndrome. Ottawa, Ontario, Canada: Nightingale Research Foundation Press 19

*the same chemical injuries on the human brain.CT and MRI cannot accomplish what "three dimensional" SPECT can correctly, easily and rapidly diagnose. SPECT can determine * the degree and the specific locations of acquired brain changes, and also measure the recovery cycle giving rise to or causing:*

a. *Cognitive brain injury,*
b. *Administrative brain injury Proprioceptive (POTS – Dysautonomia) injury **
c. *Central motor injuries,*
d. *And potential neuronal death.*

*These missed brain injuries may occur following: **(1)** infections, **(2)** toxic chemical injuries, **(3)** repetitive and even minor head traumas that can occur in sports or motor vehicle or war trauma.*

***The One-Way Window:** Unfortunately, to my knowledge, most nuclear medicine physicians* have little or no understanding of how very unschooled most primary care physicians and neurologists are in the value and safety of SPECT brain mapping. Modern "three-dimensional" SPECT brain mapping is not only an important diagnostic tool by which to measure and interpret significant brain injury, **it is essential,** since diffuse cellular and microvascular injuries are generally invisible with CT and MRI brain imaging. Hopefully, this publication will clarify this lack of understanding of the importance of "three-dimensional SPECT" imaging which persists among many physicians and patients.*

*Until now, when a patient presents with an acute or chronic brain complaint, there is a tendency for physicians to order, and a patient to ask for, a CT and MRI scan of the brain. If this results in a normal or inconsequential finding, most physicians tend to dismiss the seriousness of the patient's CNS complaints. And as mentioned, nor has experience with older SPECT software brain imaging technology given confidence to either neurologists or primary care physicians. Since few physicians understand older SPECT technology, they tend to reject it. *The multiple brain slice images of the older SPECT technology can only be comprehensible by a small group of nuclear radiologists, and consequently, tends to be rejected by most physicians. Physicians like disease and injury to be visible, if they are going to accept it as real.*

*However, over the past 30 years, new SPECT software has both significantly improved * the diagnostic ability of SPECT brain mapping and created an easy-to-read, physician and patient friendly technology. SPECT brain imaging is safe, relatively inexpensive and available in most modern North American hospitals and clinics. In Canada, access to this technology is free. The public health system pays the hospital circa $350 to do this test. If a US patient is examined with this technology in a Canadian hospital, the patient cost is circa $700 US. Cost in the USA may vary greatly.*

Modern SPECT brain mapping makes invisible disease, visible.

*In my experience, the three-dimensional SPECT mapping system, with the best normal age-related database, is the Segami NeuroGam system. If your hospital or clinic does not have Segami software, the DICOM (***D**igital **I**maging and **Com**munications = the electronic copy of the data) *can be sent by mail or email on a CD-ROM or DVD disc to centres that have Segami NeuroGam technology.*

When modern Segami SPECT three-dimensional software is utilized, an entirely new world of diagnostic medicine is revealed. The following explains how I have used diffusion SPECT technology to study major brain dysfunction caused by enteroviral (Myalgic Encephalomyelitis) brain injury as well as injuries caused by other infectious, toxic chemical or traumatic brain injuries.

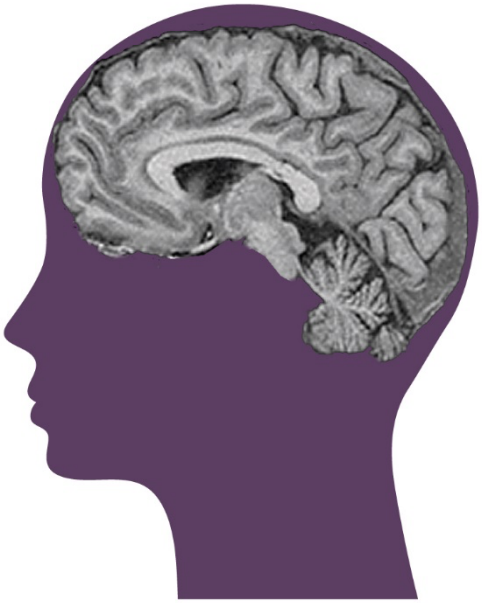
Although many serious brain injuries are invisible on MRI or CT brain scans, physicians can use SPECT to easily, effectively and safely diagnose a patient with significant or minor acute and chronic diffuse* cellular brain injury, such as :

1. Both acute* and gradual *onset chronic post-infectious encephalopathy,
2. Any chronic toxic chemical brain injury,
3. Aerotoxic syndrome from toxic turbine lubricants in pilots or mechanics,
4. Subtle repetitive sports injuries or accident trauma,
5. Suspected head injury not involving an internal CNS bleed,
6. Acute or chronic unexplained memory, proprioceptive or motor dysfunction,
7. Any industrial injury seen frequently in farmers, golf course workers and * golfers exposed to herbicides* and pesticides. Significant brain damage is also seen in military or police utilizing CS or toxic crowd control or radioactive chemicals, who are often misdiagnosed with repetitive strain injury, whereas they may have a missed toxic brain injury.

Rarely will a CT or a standard high-resolution brain MRI resolve the existence of these multiple noted brain injuries. If the CT or MRI brain results appear normal, the ordering physician must not conclude that no significant injury has occurred.

Examples

The following left-lateral view of a **normal-appearing** brain as seen on MRI, can actually hide a seriously dysfunctional, significantly damaged brain. Unfortunately, even if a minor brain injury is indicated on MRI, too often the physician fails to realize the disabling existence of extensive neuronal, cellular and microvascular injury.



Lateral MRI image of **an apparently normal** brain

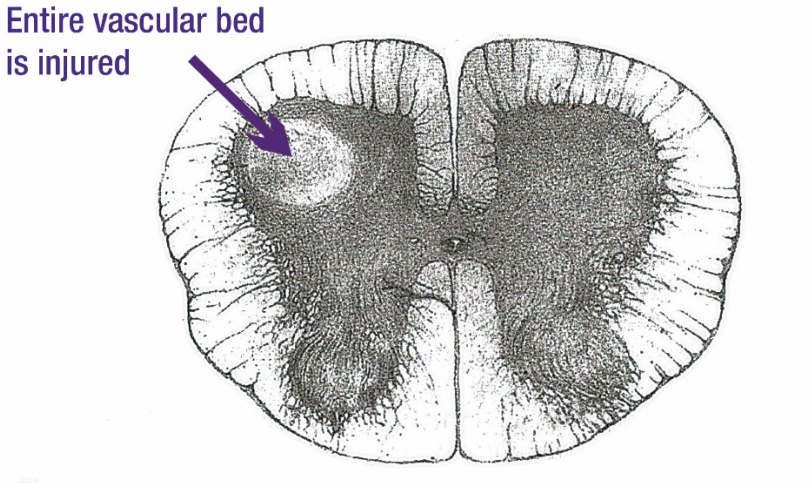
Midline view

The above MRI brain image would appear to be perfectly normal because there is **no solid, or visible space-occupying brain injury or lesion**. A physician ordering a CT or MRI brain can readily appreciate and visualize injury caused by a solid space occupying lesion such as seen in **(1) M**ultiple **S**clerosis myeloid changes, **(2)** primary brain or metastatic malignancy, **(3)** gross vascular injury as in a CVA or a bleed, **(4)** a significant contre-coup injury following fractures, or **(5)** a brain containing * a bullet, shrapnel or large brain parasite.

If a new brain MRI* were to be completed years later, left/right brain shift might be diagnosed due to a significant, regional brain injury caused by an injury years earlier. Only years later might brain atrophy be detected due to previous microvascular or cellular injury which would * potentially have been diagnosed with brain SPECT. Unfortunately, such a late identification would neither assist* the patient nor the original physician in making a correct diagnosis or instituting a timely treatment.

There is a tendency to forget the human brain represents a complex computer system build upon a susceptible **(1) microvascular-supplied (2) neuron network,** in which the major brain injury is

not visible when examined on the most powerful MRI brain imaging system. I believe* that the primary neurological injury to both spinal neurons (anterior horn cells) seen traditionally in paralytic Polio and * following infectious and chemical injury, is secondary * to a microvascular bed injury, as first seen below in 1871, extending around the entire area of the neurons of the anterior horn cells.



Cross-Section of spinal cord, showing the anterior and posterior horns of the grey matter.
The left anterior horn (top left in the image) contains a lesion ultimately causing poliomyelitis.
Reproduced from Roger, H., Recherches anatomo-pathologiques sur la paralysie de l'enfance, Paris.
Adrien Delahaye (1871) © Bibliothèque Interuniversitaire Santé, Paris

As physicians* we must remember, a toxic or post- infectious microvascular brain injury can be quite massive yet appear as normal on the best MRI or CT scan.

Injury to the integrity of the microvascular neuron bed in the human brain is potentially capable of inflicting major organizational change including:

1. short and long-term memory dysfunction,
2. motor dysfunction or rapid exhaustion due to cortical or basal ganglia injury,
3. hormonal deregulation,
4. autoimmune deregulation, affecting ability to control infection,
5. proprioceptive or vasopressor dysfunction as in POTS
6. CNS administrative functional defects, affecting ability to regulate cardiac, hormonal, immune, gastro-intestinal or other body systems

None of these six major brain injuries is usually seen with either CT or MRI technology, yet these, often massive, vascular bed injuries can provoke major changes in the manner in which the entire human vascular, nervous, muscular, hormonal and organ systems function. Modern, easy-to-read,

"three dimensional" SPECT mapping technology can point the way to better understanding, a better diagnosis, and possibly a timely treatment.

Making brain pathology visible can be easily accomplished with appropriate modern perfusion* brain SPECT software. I have employed this technology since first meeting Ismael Mena at the U. of California in 1987. Since then, I have ordered approximately 2,000 SPECT brain evaluations with not a single patient adverse reaction.

Note: Excellent brain mapping can be achieved with Positron Emission Tomography (PET) technology, but access tends to be significantly limited due to PET's much higher cost and lack of availability for brain mapping in many centres.

Measuring the brain's level of injury from a normal to a severe dysfunctional injury level

The measurements in the Segami "three dimensional" views of the brain are given in **standard deviations from normal**. In my book Understanding Myalgic Encephalomyelitis there are **two different colour codes** which the examining physician may encounter. This is unfortunate, and is due to the fact that much of my work has been done in Dr. Mena's clinics who employed his own variation.

1. The routinely used original Segami's colour code which was developed by Dr. Philippe Briandet,
2. Dr. Ismael Mena's altered colour code used, I believe, exclusively by his clinic,

It doesn't matter which code is used, since the Segami SPECT brain map comes with the appropriate colour code. In my book, Understanding Myalgic Encephalomyelitis, I have employed both the original Segami colour code and Dr. Mena's system. The appropriate standard deviation colour code images are always attached to the Segami brain image.

A Radical and Improved Change in Understanding Brain Function

Until Dr Briandet developed the rainbow hued colour system utilized in Segami NeuroGam SPECT software to measure both normal brain function and hyper and hypo brain dysfunction, all brain imaging whether in CT, MRI, or previous SPECT was based upon an interpretation of Normal VS Abnormal Brain. Brain Technology was limited to whether there was a structural change to the brain or not.

What Drs. Briandet and Mena succeeded in doing, working together, was not only developing a totally new brain mapping system but * coupling this technology with the best age-related **normal database**. Subsequently, many countries no longer allow studies on a normal healthy population.

Understanding the Rainbow Colour Codes

The SPECT colour code originated with Dr Philippe Briandet circa 1974 following the progression of colours in the rainbow from high to low frequencies. The middle colour scales for normal circulation was replaced by gray. The black at the lowest level of the colour bar in the -5 standard deviation is actually very dark blue.

The upper part of the stick code demonstrates increased brain microvascular circulation and consequently increased neuron activity. We may see this increased activity in patients taking certain pharmaceuticals, natural chemicals or possibly associated with the use of street drugs. However, these changes may also occur in localized areas due to what might be termed* brain messaging kinetics.

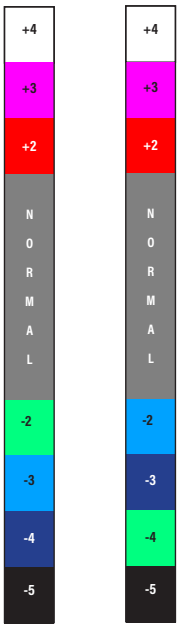
I always recall a charming woman whose brain scan I ordered who was a twenty-year constant user of LSD and street drugs and her brain SPECT was lit up like a Christmas tree. Increased standard deviation may also be associated with anxiety or at times improper SPECT technique. Fortunately, addiction and street drug changes are not a brain area that I have studied in any great depth.

As mentioned, elevated brain SPECT activity can be due to other internal causes. **Example:** With significant memory dysfunction and decreased circulation associated with the left anterior temporal lobe, particularly Brodmann 38, there tends to be an associated marked elevation of limbic system activity in the posterior cingulate gyrus. When this occurs, it is often associated in turn with a marked **increased** basal ganglia activity, which I assume* may be the overactivity of the basal ganglia trying, with difficulty, to retrieve administrative commands from the hypo-functioning cingulate gyrus. It is as though the brain * has encountered certain "*highway transporting difficulties"* and the basal ganglia are overworking to recover this information.

To make it obvious to the non-nuclear physician reader, I have labeled the normal gray area of the standard deviation code bars, **normal**.

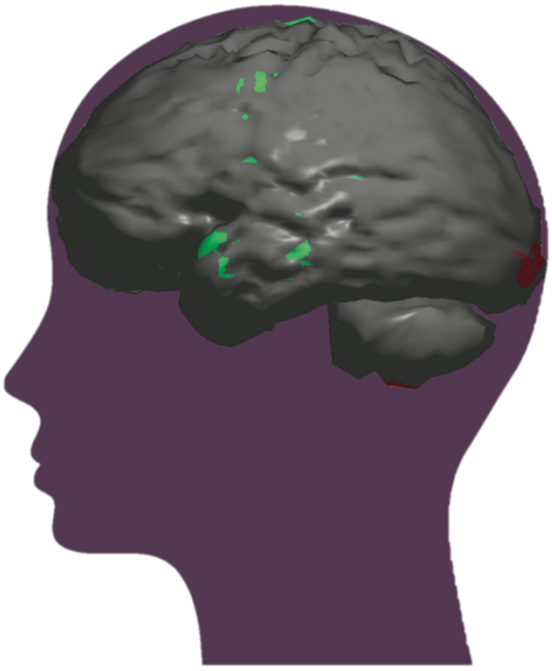
The lower part of the stick code indicates where brain circulation and neuron activity is progressively decreased to various levels of physiological dysfunction and recovery. Black *(-5)* is seen in profound circulatory brain injury or even brain death. Drs. Ismael Mena and Jay Goldstein also demonstrated that physical, mental or other activity in a brain-injured patient can not only decrease circulation, but also alter normal brain function for an extended period. They demonstrated circulatory dysfunction provokes an unusually slow recovery of brain function, lasting as long as a week after any intellectual, physical or emotional activity.

Standard Deviation is a scientific/mathematical term used in this bar code, which* signifies how far any change varies from normal activity.



Standard Deviations from Normal

A Normal Segami NeuroGam Brain SPECT Map Left lateral view



Above* is a left lateral view of a normal brain utilizing a Segami NeuroGam brain SPECT. The small green areas represent minor inconsequential **+2** standard deviation brain changes in a Segami

company brain image. These may be minor changes acquired over several years of the patient's life. These scattered changes in (a) the anterior left temporal region and (b) the motor cortex in the posterior frontal lobe are of little or no consequence. What is important are the large gray areas which represents a massively normal brain activity of both microvascular and neuron function. Compare this normal brain function with the major injuries in the brain of a severe post-infectious M.E. patient, to follow.

SPECT Images of Severe Brain Injuries

In Patient Study

*The following SPECT images are taken from a **post-enteroviral** infected patient's brain with severe, chronic Myalgic Encephalomyelitis. I have coloured the perimeters of the various lobes to make discussion easier. Unlike the normal brain SPECT demonstrated previously, you will notice in this brain, the loss of large areas of normal brain function.*

While working as a summer student at a Kingston Ontario Hospital, this honours M.A. Queens University student fell acutely ill during an enteroviral epidemic. Due to her encephalitic injuries, she was never able to return to University. She developed an enteroviral encephalopathy correctly diagnosed as Myalgic Encephalomyelitis. She became largely bedridden, due to her extreme muscular weakness following even modest activity. This has been a chronic change. She became incapable of continuing academic work due to major post-infectious cognitive dysfunction. Although her brain MRI was anatomically normal, as illustrated in the previous brain image, she failed to recover normal or appropriate cognitive or motor abilities. Many partial system failures also occurred. A number of physicians whom she consulted failed to diagnose any injury. The reasons they failed to diagnose her multiple resulting injuries were (1) the physicians failed to order appropriate examinations and tests, (2) they failed to dig deeper and only ordered superficial tests, (3) above all, they failed to do SPECT perfusion brain scans.

How to Order and Read a Segami Three-dimensional, SPECT Perfusion Brain Map

Finding a SPECT Brain Scanner: Many thousands of SPECT scanners exist and are usually located in hospitals in every state and province so it is not difficult for a physician to find a centre which is close by and which performs this test. Some private clinics also have SPECT machines but may charge considerably more than hospitals. In most countries, SPECT brain mapping is part of the insured private or public health services.

Note: I use HMPAO to make the brain scans. This is a short life radiotracer consisting of technetium -99m linked to hexa-methyl-propylene-amine oxime. I have ordered over 2000 HMPAO SPECT brain maps over the past 35 years with no patient ill effects. It is very safe. (The fact this radiotracer may be marginally more expensive should not be used to negate its usefulness.)

Segami Three-Dimensional SPECT Software: I use Segami NeuroGam because it is easy to read and explain to both physicians and patients. Older SPECT software requires an experienced nuclear physician reader who is able to do the mental gymnastics to convert multiple different

brain slices, to conceive of a three-dimensional brain image. Most nuclear radiologists can do this to various degrees. However, very few radiologists are capable of this task and I doubt if any physicians or patients are able to perform this complex brain gymnastic accurately.

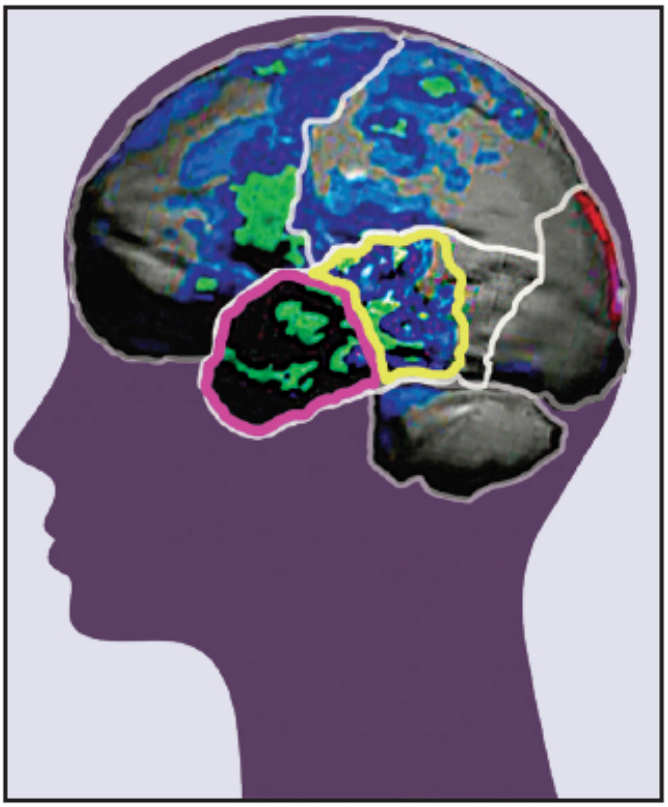
Brain function or lack of function is based upon cerebral blood flow in SPECT. Blood flow is closely linked to neuronal (brain) activity, lack of activity and recovery after any CNS activity. Distribution of the HMPAO reflects neuronal activity levels in different areas of the brain. As noted above, two types of change may be observed. Decreased uptake of tracer indicates decreased or lack of function of a specific brain area. Increased uptake indicates increased function.

Normal Brain: The normal, healthy brain uptake is coloured in gray whereas the area of microcellular (neuron & microvascular) brain abnormality is measured in colour coded standard deviations as mentioned above.

Degree of Brain Function Injury:

Although the brain MRI was found to be anatomically normal, repeat HMPAO * Segami NeuroGam SPECT brain maps revealed multiple brain perfusion abnormalities as shown. I have outlined the appropriate brain lobes demonstrating how readily any physician can read what turned out to be her persisting pathophysiological brain abnormalities.

In the following three Segami NeuroGam Brain maps[i] the gray brain areas represent normal, uninjured brain tissue and accordingly normal brain function. The various coloured sections represent degrees of decreased function in terms of standard deviations from normal as observed in the bar to the right of the images. *(**Note:** I have circled the brain lobes in the three following images to identify the injured lobes. These colours are not part of the Segami colour codes.)*

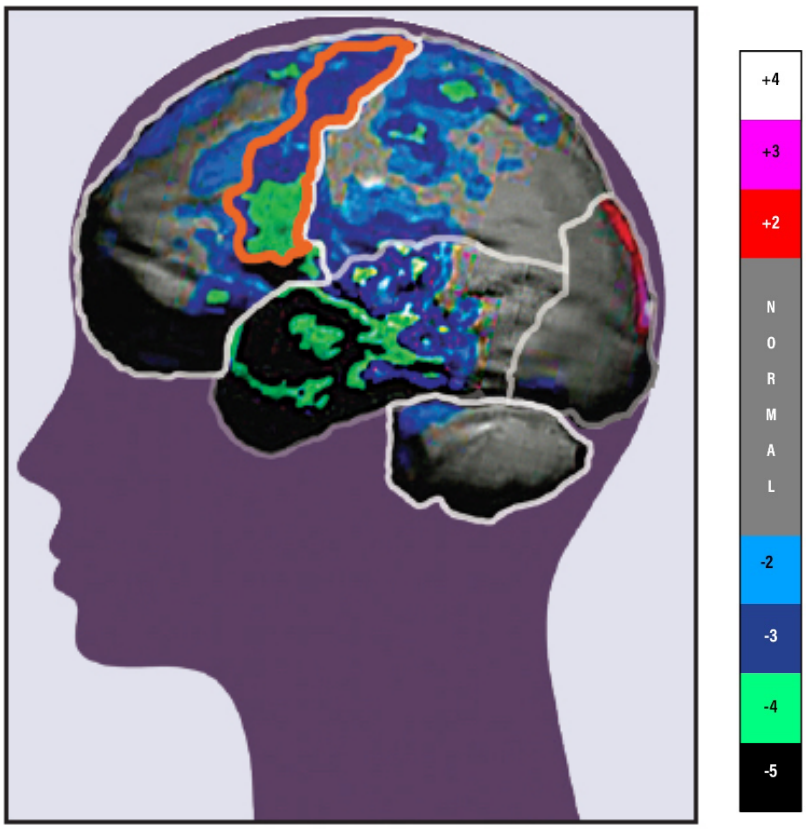


Memory Cortex Injury

The anterior left temporal lobe, encircled in pink, includes the region designated as **Brodmann 38.** This is the major memory and cognition cortical area for receiving stored data from the various brain areas, particularly the parietal and occipital lobes. The black colour indicates the most severely injured area in terms of standard deviation function loss. You will notice there is **NO** normal functioning brain tissure in the anterior temporal memory lobe.

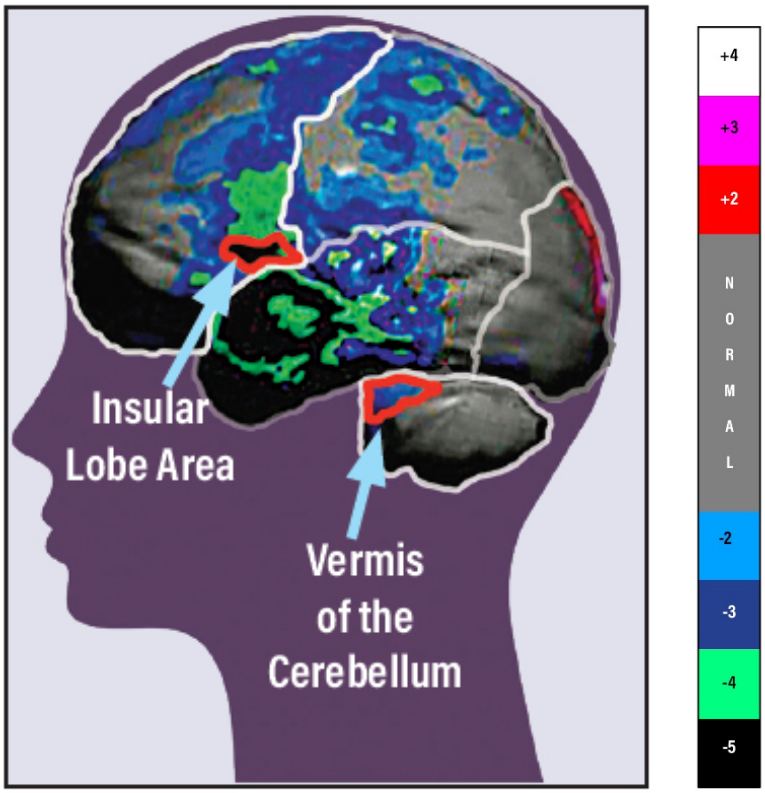
Brodmann 38 is also the area responible for forwarding collected data to the cingulate gyrus of the limbic system, from which the **executive brain functions** activate the body messaging system. In Betrayal by the Brain, Dr. Jay Goldstein[ii] defined M.E. as a limbic system brain injury. He was definitely correct but the injuries extended much further. The mid-left temporal lobe encircled in yellow is the area of conduit to retrieve and deliver memory data to the anterior temporal lobe. These injured brain areas largely explain the cause of the patient's major cognition and memory dysfunction.

The black area within the left temporal lobe indicates a severe loss of function in standard deviations from normal. The changes are so severe, they could be compared to a major cerebrovascular injury (stroke). However the damage is at a diffuse, microvascular, and neuron injury level so it cannot be seen on a normal CT or MRI.



Motor Cortex Injury

I have circled the brain's primary motor cortex, Brodmann 4, located in the posterior area of the frontal lobe **in orange** in the above SPECT brain map utilizing Segami NeuroGam software. Although final peripheral motor ability is activated through the anterior horn cells of the spinal cord, the motor signal originates in the motor cortex noted in the above defective brain cortex. Dr I. Mena, then of Harbor, University of California (UCLA) demonstrated that, following physical activity, the motor function worsens in M.E. post-encephalitic brain injury patients for several days. Similar findings may be seen in many non-enteroviral and toxic chemical brain injuries.



Location of Dysautonomia Brain Injury

Myalgic Encephalomyelitis (M.E.): Dysautonomia, one of the M.E. patient's most disabling symptoms, was first recognized by Civil War physicians, Drs. Da Costa and S. Weir Mitchell circa 1865. It has been known by several names over the years. However, in 2015, Drs. Sonia Neubauer and Byron Hyde[iii] noted that patients with dysautonomia had a SPECT brain lesion at the amygdala and also at the vermis of the cerebellum. These consistent CNS area injuries are clearly identified in orange in the above Segami Brain map. This suggests that dysautonomia * can be a post-infectious brain injury and that dysautonomia * is not due to disuse but to a specific brain area injury identified with Segami NeuroGam SPECT software.

This easily-read, "three dimensional" Segami brain mapping imagery* readily demonstrates areas of the brain which can identify dysfunction of (a) memory, (b) motor and (c) autonomic control (homeostatic or cardiovascular pressure and blood shunting regulation). These are just three of several * chronic brain injuries we can observe with modern brain SPECT mapping. Although these illustrations of significant brain injury were related to post-infectious brain injury, this tool can be utilized with equal efficiency in diagnosing chemical and traumatic brain injury not seen on CT or MRI*.

[i] i The three explanatory SPECT brain images are from * Understanding Myalgic Encephalomyelitis, Nightingalepress.ca 2020

ii Betrayal by the Brain, Dr. Jay Goldstein, 1996

iii Sonia Neubauer 1, Byron Hyde2, Jacqueline Cornejo1, WFNMB18 Postural Orthostatic Tachycardia Syndrome associated with Myalgic Encephalomyelitis and Chronic Fatigue Syndrome, Brain perfusion findings. 1 Nuclear Medicine, Clinica Las Condes, Santiago, Chile, 1 The Nightingale Research Foundation, Ottawa, Canada 2017

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