Clinical Applications of Functional Neurology

Randy W Beck
BSc(Hons) DC PhD DACNB FAAFN FACFN
Senior Lecturer
Clinical Diagnosis and Neurology
Murdoch University, WA

Associate Professor
Clinical Neurology
Carrick Institute, USA

Director
Institute of Functional Neuroscience
Perth, WA
The Neurobiology of Exercise

The proteins produced in the neuron are a result of stimulation of receptors on the cell surface from environmental stimuli.

Thus, the types and amounts of protein present in the neuron at any given moment are determined by:

- the amount of oxygen and nutrients available
- the amount and type of stimulation it has most recently received.
The central integrative state of a neuron (CIS) is the total integrated input received by the neuron at any given moment and the probability that the neuron will produce an action potential based on the state of polarization and the firing requirements of the neuron to produce an action potential at one or more of its axons.

The concept of the central integrative state can be used to estimate the status of a variety of variables concerning the neuron or neuron system such as:

- the probability that any given stimulus to a neuron or neuron system will result in the activation of the neuron, or neuron system;
- the state of pro-oncogene activation and protein production in the system;
- the rate and duration that the system will respond to an appropriate stimulus.

Functional Activities that Determine CIS

The CIS of a neuron or neuron system is attenuated by three basic fundamental activities present and necessary in all neurons.

1) **Adequate gaseous exchange**, namely oxygen and carbon dioxide exchange. This includes blood flow and anoxic and ischemic conditions that may arise from inadequate blood supply;

Functional Activities that Determine CIS

2) Adequate nutritional supply including glucose, and a variety of necessary cofactors and essential compounds;

3) Adequate and appropriate stimulation in the form of neurological communication, including both inhibition and activation of neurons via synaptic activation.

Synaptic activation of a neuron results in the stimulation and production of immediate early genes and second messengers within the neuron that stimulate DNA transcription of appropriate genes and the eventual production of necessary cellular components such as proteins and neurotransmitters.

Immediate Early Genes (IEG)

- Special transmission proteins called immediate early genes (IEG) are activated by a variety of second messenger systems in the neuron in response to membrane stimulus.

- Type 1 IEG responses are specific for the genes in the nucleus of the neuron and type 2 IEG responses are specific for mitochondrial DNA.

When you decrease appropriate stimulation to a neuron the following events may take place.

↓ CIEGr (cellular Immediate Early Gene responses).

↓ Protein production.

↓ Cellular respiration (via mitochondrial electron transport chain).

↓ ATP synthesis.

↑ Resting membrane potential (RMP).

↑ Free radical formation.

Further inhibition of cellular respiration (electron transport chain) in the mitochondria.

Transneuronal degeneration (TND) & Downstream Diaschisis
Transneural Degeneration (TND)

In situations where the neuron has not had adequate supplies of oxygen, nutrients or stimulus, the manufacturing of protein is down-regulated. This process of degeneration of function is referred to as trans-neural degeneration.
Diaschisis refers to the process of degeneration of a downstream neuronal system in response to a decrease in stimulus from an upstream neuronal system.

This reemphasizes the point that neuronal systems do not exist in isolation but are involved in highly complicated and interactive networks. Interference or disruption in one part of the network can impact other parts of the network.
Neural plasticity results when changes in the physiological function of the neuraxis occur in response to changes in the internal or external milieu.

The development of synapses in the nervous system is very dependant on the activation stimulus that those synapses receive.

The synapses that receive adequate stimulation will become strengthen and the synapses that do not receive adequate stimulation will weaken and may eventually be eliminated.
Cerebral Hemispheric Asymmetry (Hemisphericity)

- The concept of hemispheric asymmetry or lateralization involves the assumption that the two hemispheres of the brain control different asymmetric aspects of a diverse array of functions and that the hemispheres can function at two different levels of activation.

The level at which each hemisphere functions is dependant on the central integrative state of each hemisphere, which is determined to a large extent, by the afferent stimulation it receives from the periphery as well as nutrient and oxygen supply.
Efferent Functional Systems of the Neuraxis

Effects of PMRF Asymmetric Activity

- Increase in blood pressure, ipsilateral to side of decreased PMRF stimulation, which results in differences in blood pressure between right and left sides of the body.

- Increased Vein to Artery ratio in the ipsilateral retina of decreased PMRF stimulation

- Increased sweating globally or ipsilaterally to the side of decreased PMRF stimulation

- Decreased skin temperature ipsilaterally to the side of decreased PMRF stimulation

- Arrhythmia if decreased left PMRF stimulation occurs or tachycardia if decreased right PMRF stimulation occurs
Effects of PMRF Asymmetric Activity

- Large pupil (also due to decreased mesencephalic integration) to the side of decreased PMRF stimulation
- Ipsilateral pain syndromes to the side of decreased PMRF stimulation
- Global decrease in muscle tone ipsilaterally to the side of decreased PMRF stimulation
- Flexor angulation of the upper limb ipsilaterally to the side of decreased PMRF stimulation
- Extensor angulation of the lower limb ipsilaterally to the side of decreased PMRF stimulation
Spinal Signs

Subluxation

Spinal stiffness – increased extensor tone

Spondylosis

Intrinsic spinal weakness – decreased postural tone

Increased postural sway in sagittal or coronal planes (autonomic or motor concomitants)

Pelvic floor weakness
Extra-ocular signs

- Corneal reflection abnormalities
- Weakness on gaze
- Nystagmus
- OPK dysfunction or asymmetries
- Poor visual tracking (pursuits)
- Poor fixation
- Poor control of scanning eye movements (saccades)
How can we Measure Asymmetric Brain Function?

- Functional MRI (fMRI),
- Electroencephalography (EEG),
- Magnetoencephalography (MEG)
- Multi-electrode array (MEA)
- Positron Emission Topography (PET scan)
- Psychometric testing
- Peripheral physiological parameters?
How can we measure brain function?

- qEEG is a valid and reliable method of measuring electrophysiological activity in the cortex of the brain.
EEG signals are digitized for computer analysis.
LORETA Images can be produced from qEEG data
3D LORETA images can then be produced showing precise anatomical location.
How Does it Work in Practice

Left hemisphere infarct - Total ICA occlusion

- Delta Absolute Power
- Theta Absolute Power
- Alpha Absolute Power
- Beta Absolute Power
- High Beta Absolute Power

- Delta Relative Power
- Theta Relative Power
- Alpha Relative Power
- Beta Relative Power
- High Beta Relative Power

- Amplitude Asymmetry

Z-Score: ≥ 1.65, ≥ 2.68, ≥ 3.09
LORETA and EEG can Identify Tumours with 100% Accuracy
Cognitive Performance

- Peak cognitive function is near the top of the inverted ‘U’,
- Reduced coherence (hypocoherence) or hypoactivation is related to reduced functional connectivity (i.e., disconnection syndrome)
- Increased coherence or hyperactivation (hypercoherence) is related to reduced functional differentiation.

Yerkes–Dodson Law
EEG Indicators of Cognitive Performance

- In TBI patients or stroke patients' hypocoherence is quite common and consistent with MRIs and other imaging measures showing cell or connection loss.

- Hyper-coherence is an indication of inefficiency and compensatory systems where there is increased redundancy.

- Both hyper and hypo coherence or power are consistent with reduced speed and efficiency of information processing.

22 year male with concussion and head trauma
Changes in Afferent stimulation may produce long term changes in cortical function

AN.03.07.08

Base line vs. 7months Tx.

AN.09.02.09

Clinical Cases
Diagnosis of ADHD is Based on a Symptom Cluster Bias

Divided into three clusters of based on the predominate occurrence of each of the following symptoms:
- hyperactive
- impulsive
- inattentive

As each patient presents with a specific degree of impairment in these three categories, a patient can be cast into the following subtypes:
- the predominantly inattentive type,
- the predominantly hyperactive-impulsive type
- the combined type, (the most frequent one).

- Affects about 10% of school children worldwide average
Functional Loops Involved in ADHD
qEEG and ADHD

- An increased theta power in the frontal and central regions is the most replicated finding in ADHD literature, suggestive of under arousal and decreased cortical activity.

6 year old girl with ADHD and Depression

van Dongen-Boomsma et al., 2010)
qEEG and ADHD

An increased theta/beta ratio, also reflective of decreased cortical arousal, has also been frequently found in children with ADHD.

8 year old boy with ADHD and Emotional outbursts
EEG before and after

Montage: LinkEars

Z Scored FFT Summary Information

Delta
Absolute Power
Relative Power
Amplitude Asymmetry
Coherece
Phase Lag

Z-Score = 1.96
Z-Score = 2.58
Z-Score = 3.00

3

Montage: LinkEars

Z Scored FFT Summary Information

Delta
Absolute Power
Relative Power
Amplitude Asymmetry
Coherece
Phase Lag

Z-Score = 1.96
Z-Score = 2.58
Z-Score = 3.00

3
Post Traumatic Seizures

- Post traumatic seizures can occur following head trauma, stroke or a variety of other lesions.
- Post traumatic seizures are also known as scar epilepsy and are often medically non-responsive.
Low Resolution Electromagnetic Tomography and Seizure Activity

Patient 1
Before

Patient 1
After

Direct Current Guided by EEG to Restore hand movement
Head Injury and Concussion

- People who regularly take part in contact sports or recreational activities are at a significantly increased risk of suffering a concussion.
- Sports and recreational activities frequently register in the top five causes of traumatic brain injury (TBI) or concussion.

The incidence rate for concussion regular appears between 3.8-8.9 per 1000 athlete-exposures.

Concussions accounted for 25% of all days lost from rugby participation due to injury.

Additional Concerns

Even more compelling is the concern over the development of protracted sequelae of

1) Traumatic encephalopathy

2) Death due to second impact syndrome.
The most problematic aspects of diagnosis and management of concussion include:

1) Difficulty in reliably identifying pathological or functional changes in brain following trauma

2) Contemporary imaging techniques regularly fail to reveal any abnormalities in cases of concussion

3) Diagnostic criteria rely almost exclusively on clinical impression

LORETA Images Before Care
LORETA Images after 12 weeks of care
Results
Perception of Balance

How would you rate your perception of balance?

Balance rating (100=perfect balance)

Time (30 day periods)
Results

Intensity of Headache Pain

How would you rate the level of your headache pain?

Time (30 day periods)

Intensity of Pain

0 1 2 3 4
Results

Headache Frequency

How would you rate the frequency of your headaches?

How would you rate the frequency of your headaches?

Frequency (Low to High)

Time in 30 day periods

Frequency (Low to High)

Time in 30 day periods

Series 1
How would you rate your general feeling of well being and happiness?
Results
Systemic Blood Pressure

Systemic Blood Pressure

<table>
<thead>
<tr>
<th>Time (30 Day periods)</th>
<th>Systolic (blue)</th>
<th>Diastolic (red)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>160</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>140</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>120</td>
<td>80</td>
</tr>
<tr>
<td>4</td>
<td>100</td>
<td>80</td>
</tr>
</tbody>
</table>
Comparison before and after 12 weeks of treatment

Before

After
Hyper-activation in frontal cortex including frontal eye fields and facial upper motor neurons
Facial Upper motor neurons

Frontal eye field
QEEG 6 weeks later

Areas of hyper-activation in frontal cortical areas have resolved
Follow-up Video 6 weeks