Restorative Neurology and Motor Control

First Meeting of the International Society for Restorative Neurology

Melbourne, Victoria, Australia

May 15, 2012

Restorative Neurology: Consideration of the New Anatomy and Physiology of the Injured Nervous System

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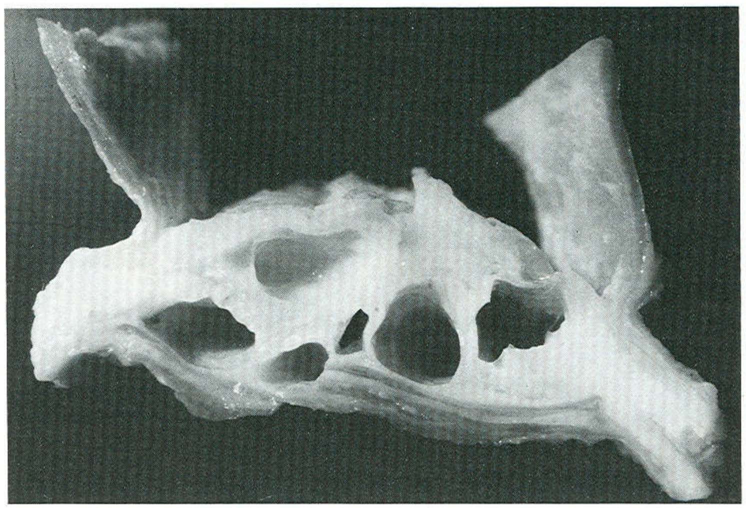
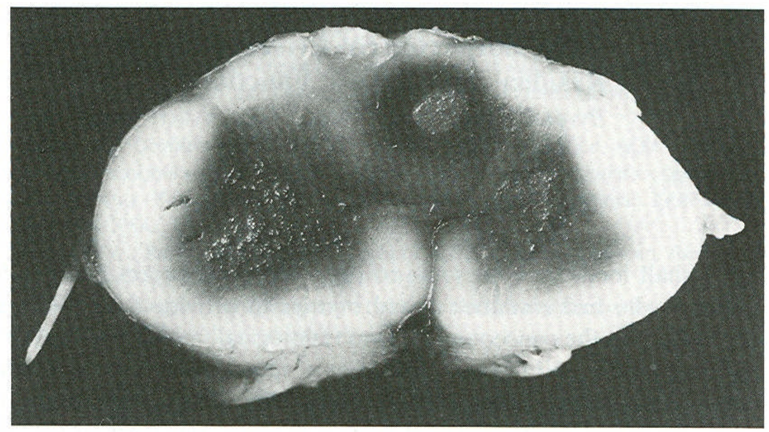
Restorative Neurology
What is the problem?

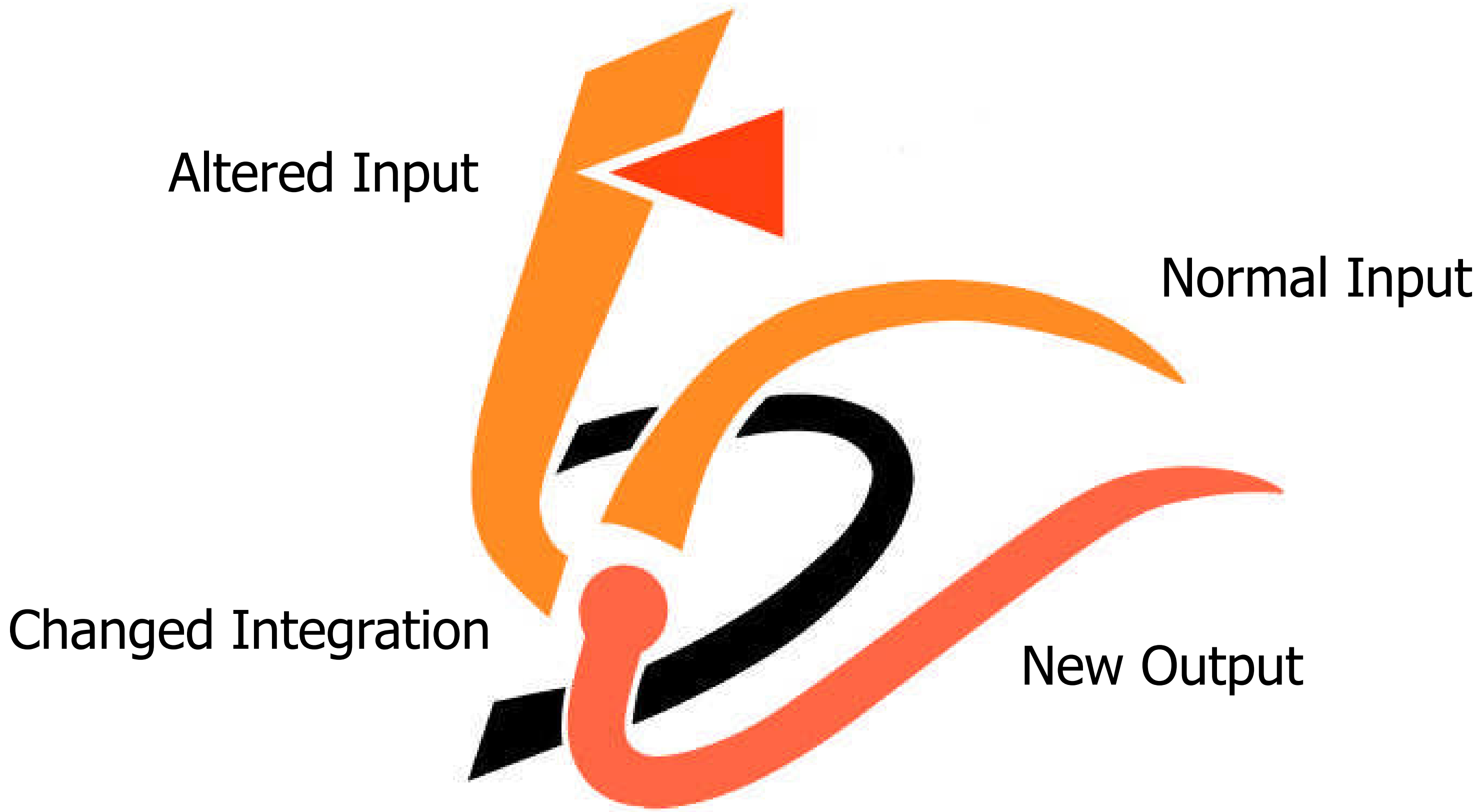


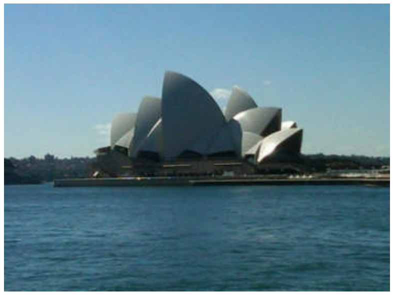
This spinal cord
can walk. How?



This one cannot.
Why not?

The New Anatomy and Physiology





The New Anatomy and Physiology: The Nervous System and Its Development

Number of neurons = 10^{11}
Number of synapses = 10^5 per neuron
Not "on/off" switches, rather "dimmer" switches with gradations

Developmental Strategies for "wiring together"

- Spatial molecular cues
- Temporal molecular cues
- Establishment of excess neurons and synapses
- Subsequent apoptosis and synapse elimination
- Activity based shaping of synaptic strengths
- Shutting down of "wiring" with perineural nets

How much can developmental processes play a role after injury?

The New Anatomy and Physiology: Development and Neural Plasticity

Despite long distance wiring established early, function develops and changes over time – walking, talking, playing piano

Neural plasticity, in fact, does not end – learning and memory

These functions are probably the result of rather local neural circuit anatomical plasticity

- sprouting
- synaptogenesis

and physiological plasticity

- long term potentiation or depression
- pre- and post-synaptic modulation
- synapse activation or deactivation
- changed temporal coding between neuronal populations

The New Anatomy and Physiology: The Physiology of Neural Circuits

Neural circuits are capable of functioning in multiple different physiological states despite a single anatomical state

Neural circuits interact with other neural circuits in different combinations of activity to add to the repertoire of functional states

Control strategies are employed – feed forward, feed back, closed loop, open loop, etc.

Some redundancy is built in so it is possible to execute a single behavior by different neurophysiological means

The New Anatomy and Physiology: Altered Neural Circuits in Neurological Injury

Injury can cause disruption within circuits, across circuits, in one but not another of connected circuits and between unaffected circuits – diaschesis

Injured neural circuits probably have a limited ability to perform input/output functions

Uninjured neural circuits must integrate old normal inputs and new altered inputs to generate new outputs

These circuits may be changed in their processing capacities by these new conditions so re-establishing lost connections later may not result in a return to pre-injury functioning

The New Anatomy and Physiology: Altered Function in Neurological Injury

Neurological injury generates sensorimotor “loss of function”

- weakness
- loss of coordination
- loss of endurance
- loss of sensation

and “gain of function”

- spasticity (hypereflexia, spasms, dysynergias, hypertonia)
- neuropathic pain

The two combined cause functional deficits but treating one (spasticity) might worsen another (weakness)

The New Anatomy and Physiology: Assessment of Residual Function after Injury

Anatomical assessment is partially possible in animal models but limited to low resolution in humans with current imaging (MRI, DTI)

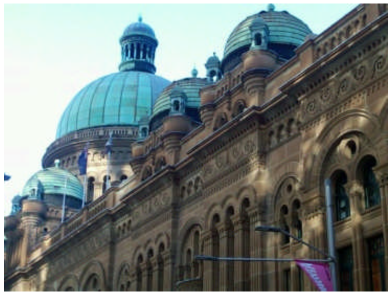
Physiological assessment can be done to some extent with imaging (fMRI) but electrophysiological methods are the gold standard

Electrophysiology can assess the possibility of conduction through the injured nervous system but this does not tell us what signals actually come through connections that remain after injury

Electrophysiology can assess input/output processing of signals in some situations, testing reflex modulation for instance, and can characterize output patterns during attempts at behaviors in both animals and humans

The New Anatomy and Physiology: Assessment of Residual Function after Injury

Clinical assessments can be revealing but often clinical scales group large numbers of diverse individuals into few, broad categories and following those groups, as is done in current clinical trials, usually fails to adequately detect individual changes or add clarity to the mechanisms at play to cause those changes



The New Anatomy and Physiology: Restoring Function in Neurological Injury

Anatomical restoration has been shown to be possible in animal models but it is limited at best and not currently translatable to clinical application

Issues include

- generating axon growth
- overcoming environmental barriers
- target finding
- re-re-organizing local neural circuit function

Physiological restoration is, therefore, the current focus of Restorative Neurology and uses a variety of methods to generate functional change through the physiological mechanisms of neural plasticity described earlier

The New Anatomy and Physiology: Clinical Practices in Restorative Neurology

"The best thing they can give you after neurological injury is a good physiotherapist"

Early "truths" from current practice

- early activity is important
- sustained and repeated activity is important
- task specificity can be important

Next steps

- understand what physiology is being changed and how
- determine the relationship between substrate and effect
  - better clinical assessment and tailored treatment
- add interventions to further drive neural plasticity to gain recovery in the new anatomy and physiology