Driving reorganization following brain injury

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Role of activity in:

- Development of nervous system.
- Maintenance of brain maps.
- Lesion-induced plasticity.

Neural Darwinism

- **“Developmental selection”**
  - Development takes place largely within genetically determined constraints.
  - Individual differences result from the unique combination of influences on developing neurons.
- **”Experiential selection”**
  - Experience acts on this pattern of connections.
  - Modifications occur through selective strengthening or weakening of connections between neuronal groups.

(Edelman, 1987)

Neural Darwinism

Reentrant mapping:

- The linking of maps in time through parallel selection and correlation of the maps' neuronal groups.
- Maps independently and disjunctively receive inputs.
- Basis for perceptual categorization.

(Edelman, 1987)

Brain development

Neuronal activity determines the morphological development of the nervous system.

Growth of the dendritic tree

- The dendritic arbors of cortical neurons become increasingly elaborate after birth.
- An increase in the number of dendritic spines correlates with an increase in the number of synapses.

Elimination of synapses

- A selective reduction in the number of synapses is a means of refining neural connections (e.g. climbing fibre synapses on Purkinje cells; innervation of skeletal muscle).
- This integral phase in the development of the nervous system is dependent on activity.

Development and neural function

Ocular dominance columns

- Organization is determined by thalamic projections to the cortex.
- In the neonatal period there is overlap of terminal fields.
- With normal visual stimulation, there is a progressive segregation of terminal fields into columns dominated by one or other eye.

Development and neural function

Monocular deprivation

- Ocular dominance columns fail to segregate normally.
- Columns activated by the deprived eye are narrower than normal, while those driven by the normal eye are wider (Le Vay et al. 1980).
- Experience is a critical factor in the development of visual connections.

Development and neural function

- Peripheral sense organs are important in the development of maps in the cerebral cortex.
- The cortical representation of whiskers in the mouse is characterized by the arrangement of neurons in barrels, each barrel corresponding with a whisker.
- If several rows are destroyed at birth, the corresponding barrels are missing from the adult cortex (Van der Loos & Woolsey, 1973).

Development of the motor system

- The corticospinal tract is a major component of the motor system, being the only direct link between the brain and spinal cord.
- Its maturation takes place mainly in the postnatal period.
- Specific axon guidance molecules are important in ensuring correct development of its connections with target neurons.

Ephs and ephrins

- Eph receptors and their ligands are expressed in opposing gradients in projecting and target fields: basis for formation of topographic maps.
- Regulation of axon guidance occurs through mechanisms of contact repulsion rather than that of attraction.

Development of the motor system

- In the mouse, corticospinal terminals are located contralateral to the cells of origin and confined predominantly to the dorsal horn.
- EphA4-deficient animals have aberrant corticospinal development.
- In the mutant many corticospinal axons recross the midline, and terminate in the intermediate and ventral regions of the spinal cord (Coonan et al. 2001).

Development of the CST in the primate

- Corticospinal projections in the primate develop over the first 8 postnatal months.
- An increased number of projections descend to the spinal cord at birth, many of which retract over time.
- Over this period there is a progressive increase in the number of CST terminals in the spinal cord (Galea & Darian-Smith, 1995).

Activity-dependent development of the motor system

How does the CST reorganize in the postnatal period to achieve topographic specificity of connections?

Activity-dependent development of the motor system

- Martin et al. (1999) studied role of sensorimotor cortical activity in shaping the postnatal development of the CST projection in kittens.
- CST terminations from silenced cortex were sparse, and limited to the contralateral side.
- Those from the active side maintained their immature bilateral pattern, compared to controls.
- Activity seems to be important in shaping CST development at this critical stage.

Neuronal activity appears to regulate:

- Expression of cell adhesion molecules
- Synthesis and secretion of neurotrophins
- Expression of glutamate and GABA receptors at individual synapses

Maintenance of brain maps

Topographic maps in the central nervous system are dynamic and continually modified by experience.

Neuronal activity is important in maintaining synapses

- A change in synaptic efficacy between two neurons is a substrate for learning and memory.
- Hebbian plasticity (the conjunction of presynaptic and postsynaptic activity) underlies experience-dependent changes in the cortex.

Modification of sensory maps in adults

- Cortical sensory maps in adults become reorganized following a variety of perturbations affecting relevant afferent signals (e.g. nerve section, digit amputation, Kaas et al. 1991).
- Environmental enrichment is associated with expansion of cortical sensory representations (Coq & Xerri, 1999)

A model for focal dystonia & RSI

- The neural consequences of using repetitive movements can be profound.
- Repetitive hand squeezing tasks have been shown to result in deterioration of hand movements and de-differentiation of the normally sharply segregated finger representations in somatosensory cortex (Byl et al. 1997)

Recovery following lesions

Recovery of skilled motor performance is associated with functional cortical reorganization following focal cortical lesions.

What happens following brain injury?

- Spontaneous recovery: reparative processes occurring immediately following a lesion.
- Recovery is accompanied by significant structural brain reorganization over time.
- The assumption that no relationship exists between what the patient does (including physiotherapy) and his recovery is incorrect.

Mechanisms underlying recovery

- Multiple corticospinal projections provide a substrate for recovery (Galea & Darian-Smith, 1994, 1997).
- The adult brain is capable of significant reorganization in response to peripheral perturbations (e.g. nerve lesion; enriched environment) or to cortical lesions.
- Reorganization is complex and individually variable.

Mechanisms underlying recovery

- Adaptive changes occur in both ipsilateral and contralateral hemispheres.
- The surviving penumbra has a capacity for recovery that can be exploited with training (Nudo et al. 1996).
- The 'drivers' to recovery include goal-directed training.

Dynamical systems theory

- Emphasis on process rather than hierarchical structures.
- Neural maturation and other systems and processes are equally important in promoting motor development.
- Based on cooperating systems.
- Equivalence of internal factors associated with the individual and the external context of tasks.

Self organization occurs on several levels in the nervous system

- Microscale events : morphology of neurons and activity-dependent processes at synapses.
- Mesoscale events: neural circuits.
- Macroscale events: behaviour is specified by coherent relations between neural events.

(Kelso, 1997)

Summary

- The brain is not a static machine.
- Neural representations are labile and change with experience.
- Functional reorganization occurs following injury.
- Topographic maps are dynamically maintained through spatial shifts in the collective activity of neurons (use it or lose it!).

Implications for Physio practice

- Are there constraints in subsystems that limit motor behaviour (e.g. contractures, weakness)?
- Does the therapeutic environment afford opportunities to practise tasks in a meaningful and functional context?
- Do activities promote exploration of a variety of movement patterns?