/// EMERGING NEUROSCIENCE CONCEPTS in Spinal Cord Injury Rehab (March 23, 2010)

// INTRODUCTION

Definition of Neuroplasticity: the capacity for continuous alteration of the neural pathways and synapses of the living brain and nervous system in response to experience or injury. (from Merriam-Websters Medical Dictionary)

Advances in neuroscience are unlocking the mysteries of recovery after SCI. Although all of the pieces of the puzzle are not in place, physical therapists should shift their paradigm (Behrman, p. 1406). The variability in outcome with people with spinal cord injuries (SCI) depends on these factors:

- intensity and duration of training
- severity and location of injury
- age at time of injury
- time since injury
- presence of interactive medications
- personal factors (personal motivation, family support, premorbid history)
- Achievement of quadriceps femoris muscle strength greater than 3/5 within 3 months of SCI, has been strongly associated with ambulatory potential
- Preservation or recovery of pinprick sensation after acute SCI (72hrs) is highly predictive of recovery of walking function at time of dis charge from rehab)

(Behrman, p. 1409-13).

Reorganization of cortical maps has been reported to occur spontaneously after both complete and incomplete SCIs in humans. The underlying mechanisms include:

- Dis-inhibition of latent cortical connections and axonal sprouting in multiple levels of the neuro-axis
- Injury-induced structural plasticity in the dendritic spines of cortical motoneurons

(Lynskey J., 2008, p. 230)

Some of these spontaneous changes appear to be adaptive (promoting recovery and providing targets for therapy) and some appear to be maladaptive (inhibiting recovery and impairing function) *(Lynskey J., 2008, p. 230).*

// EMERGING SCI REHAB CONCEPTS

Standard rehab of patients is founded on a model of compensation. However, neuroscientists are providing new therapeutic intervention strategies based on the neurobiological control of walking and physiologically based activity-dependent plasticity. Training strategies such as "Locomotor Training," (explained in detail below), that remediate disability, in lieu of compensating for impairments, may promote recovery of function for other biological systems after SCI *(Behrman, p. 1414).*

The phenomenon of appropriately responding to sensory input supports the view of the intrinsic capacity of the neural network at the level of the spinal cord to integrate incoming information, interpret it and respond with a motor output. This finding has lent support to the concept of "task specificity" when retraining after SCI *(Behrman, p. 1407).*

These are the main concepts emerging in rehab and some of these concepts will be discussed in greater detail in this paper:

1. Recovery is based on intense practice of the specific task – locomotion.

2. Appropriate sensory input (speed, loading and unloading, trunk posture, hip extension, limb kinematics) associated with the locomotor task is required to tap the intrinsic neural networks generating stepping activity.

3. A willingness and open-minded attitude of the training environment (treadmill speed, BWS) to enhance practice of the locomotor task

4. An ability to attain postural control as a co-requisite for locomotion. We must train the task of walking with 2 legs and not with 6 legs. Balance is a co-requisite of the task of walking and a significant requirement for successful walking. Retraining balance may more effectively be trained within the specific task of walking without upper extremity support (Behrman, p. 1410).

5. Minimizing compensation (load bearing through the legs vs load bearing through the arms, hip hiking for swing) (Behrman, p. 1409)

6. The importance and relevance of CPGs (central pattern generators) and their effect

7. Locomotor training (LT) and Body Weight Support Treadmill Training (BWSTT)

8. Exercise and its effect on BDNF

9. Drug therapy

10. Electrical stimulation methods

// MINIMIZING COMPENSATION

Repetitive practice using conventional gait rehab may teach a compensatory mode of ambulation that may not take advantage of the plasticity of the neuromuscular system. For instance, when using a walker, attaining hip extension may be compromised due to the forward flexion of the trunk while weight bearing through the arms. This posture reduces lower-limb loading, thereby altering the sensory input that facilitates the swing phase. Lower-extremity bracing that provides support for the lower extremities against gravity may limit normal joint range of motion. *(Behrman, 2000, p. 697).*

Hip extension position and load are two examples of sensory input specific to the task of walking that contribute to the inherent mechanism in the neural axis of generating

stepping. These sensory signals are interpreted by a network of spinal interneurons CPGs (central pattern generators) which combine with descending supraspinal input in order to control walking. The pattern of locomotion is attributed to the CPG, which promotes the rhythmic oscillations of the extremities. It is intuitive to develop rehabilitative strategies that emphasize the provision of hip extension and load, as well as other sensory elements to the control of walking *(Behrman, p. 1408).*

// CPGs AND THEIR EFFECT

Several evidences suggest that a wide range of sensory motor recovery can be achieved in adult mammals after a total or subtotal SCI. This capability is dependent upon various forms of neuroplasticity occurring within spinal CPGs spared descending pathways and sensory afferents, and could be collectively named as “spinal learning.” Evidence indicates that functional recovery after SCI is use-dependent. Exercise training is a potent tool to improve the sensory-motor recovery after SCI in animal models as well as in clinical subjects *(Gulino et al, 2007, p. 148).*

If the spinal cord has a critical role in locomotion and can relearn to execute stepping with training, and if supraspinal centers in the brain can also reorganize, then these approaches can potentially have a dramatic impact on the recovery of walking after neurologic injury *(Behrman, 2000, p. 699).*

// LOCOMOTOR TRAINING AND BWSTT

"Locomotor training" (LT) has arisen to describe a physiologically based approach to retraining walking after neurologic injury that capitalizes on the intrinsic mechanisms of the spinal cord to generate stepping in response to specific afferent input associated with the talk of walking.

LT is based on two assumptions:

1. The spinal cord has the ability to respond to appropriate afferent information to generate stepping.

2. Activity-dependent plasticity occurs in the neural circuitry responsible for locomotion at both spinal and supraspinal levels.

Guidelines for LT include:

- Maximizing loading of the lower limbs instead of the upper extremities during training. Facilitate more upright standing and adjusting the height of assistive devices overground to promote greater load bearing by the lower limbs relative to the arms.
- Ensure that the leg hits the ground before a forearm crutch emphasizes load bearing through the legs.
- Increasing speed increased lower-limb EMG activity and improved stepping kinematics on a treadmill.
- Facilitate swing phase of the step cycle by ensuring sufficient hip extension and unloading of the limb at the end of stance because this is a spinally mediated response.
- Weight bearing on the arms inhibits rhythmic stepping with the lower extremities but a reciprocating arm swing, in a natural, coordinated form, facilitated stepping.

(Behrman, 2000, p. 697).

Using BWSTT where as much as 50% of body weight is supported, patients with complete thoracic spinal cord injuries, are able to develop rhythmical flexor and extensor electromyographic activity in their paralyzed leg muscles, but they cannot step independently. Greater sensory input, such as increased loading of the joints can evoke hip flexion *(Dobkin, 1993, p. 58).*

Upper extremity wt-bearing results in decreased EMG muscle activity in lower limbs and asymmetry in the limb kinematics. Thus a compensatory strategy emerged when individuals used an assistive device for weight-bearing support. In contrast, overhead BWSTT resulted in a more symmetrical pattern of EMG activity and gait. Thus, using BWSTT without a handrail would be more beneficial than with upper extremity support. The erect posture and diminished load bearing on the arms become critical components of the training. The BWSTT provides a permissive environment to elicit walking capacity *(Behrman, p. 1410).*

// EXERCISE AND BDNF

The metabolic cascade by which neuronal activity could modify synaptic strength, involves BDNF (brain-derived neurotrophic factor) *(Gulino et al, 2007, p. 148).*

Intense repetitive training (mass practice) after a cervical spinal injury and robotic locomotor training after a thoracic spinal injury appear to promote cortical plasticity as cortical map reorganization. Cortical motoneurons "learn" to control additional muscles and produce novel movements when stimulated due to increases in BDNF *(Lynskey J., 2008, p. 232)*

In animals, post-injury exercise has been suggested to improve recovery from both brain and spinal cord injury by increasing neurotrophic factors such as BDNF in CNS and peripheral nervous system. In the adult CNS of uninjured animals BDNF promotes synaptic plasticity and neurogenesis. BDNF has impact on the survival of motoneurons, outgrowth and synaptic remodeling of injured axons. *(Rojas, 2008, p. 1064).*

Short moderate intensity exercise but not immediately following long lasting high intensity exercise increases serum BDNF concentrations. *(Rojas, 2008, p. 1068).*

Thus, specific exercise demands might be beneficial to enhance neuroprotection and neuroplasticity, but further studies are needed to find out how much and what intensity of exercise are most beneficial for neuroplasticity *(Rojas, 2008, p. 1068).*

BDNF concentrations in SCI athletes were about sixfold higher than in AB athletes. Ten minutes of moderate exercise resulted in a further increase of circulating levels of BDNF in SCI athletes. Because BDNF plays a prominent role in neuronal plasticity, these findings indicated that exercise potentially plays an important role in modulating plasticity after SCI *(Rojas, 2008, p. 1066).*

Exercise could increase the spinal expression of neurotrophins. Conversely, the reduction of muscular activity of the total or partial removal of supraspinal afferents to the lumbar spinal cord, could induce down-regulation of BDNF and synapsin I *(Gulino et al, 2007, p. 149).*

As BDNF is known to protect motor neurons from degeneration and to promote axonal sprouting in the spinal cord after injury, neuromuscular activity up-regulates BDNF in regions lying over the spinal lesion, thereby mediating spinal cord plasticity *(Rojas, 2008, p. 1066).*

// SSRIs (Serotonin Reuptake Inhibitors)

Chronic treatment with antidepressants (SSRIs) has been reported to augment hippocampal levels of BDNF. The increased activation of serotonergic pathways in response to exercise modulates antidepressant-induced neuroplasticity. Therefore the potential of exercise to enhance serotonergic activity may be used as strategy to improve functional plasticity after SCI *(Rojas, 2008, p. 1068).*

Neurotransmitters, including acetylcholine, norepinephrine, dopamine and serotonin, have also been shown to enhance motor recovery *(Dobkin, 1993, p. 58).*

// ELECTRICAL STIMULATION METHODS

1. FES (functional electrical stimulation) to elicit the flexion withdrawal reflex to assist with swing phase of gait

2. FNS (functional neuromuscular stimulation) to decrease fatigability of muscles, increase bone density and reverse atrophy

3. ESCS (epidural spinal cord stimulation) to reduce spasticity and promote stepping movements and locomotion; also alters electrophysiological properties of spinal motor pattern generating circuitry, altering amino acid neurotransmitter levels in the spinal cord (glycine and taurine) and altering blood flow (both centrally and peripherally) as well as also trigger increases in BDNF *(Lynskey J., 2008, p. 233)*

// CASE STUDIES

Patient with T5 ASIA A complete SCI 1 yr post-injury received 85 step training sessions on the treadmill and achieved the ability to generate independent steps on the treadmill with BWS, and patient improved her ability to bear weight. This challenges the validity of predicting locomotor outcomes after an SCI solely based on voluntary motor control. Patient with T5 ASIA C 1 month post-injury became a T5 ASIA D after treadmill and overground training whereby, patient initially was nonambulatory but by the end of treatment, was able to step independently on the treadmill and achieved the ability to walk overground independently with a cane *(Behrman, 2000, p. 696).*

The basis for LT is applied to people with intact lumbosacral sensorimotor neural circuits, as in people with UMN SCI lesions. (Behrman, p. 1413). Case reports have described little effect in people with lower motor neuron injuries. There are no reports of someone with ASIA A or B injuries being able to translate improved walking behaviour to an overground environment, LT is effective in achieving overground gait speed in people with acute SCI ASIA C and D *(Behrman, p. 1413).*

// CONCLUSION

The inherent adaptability offers the possibility that specific training plans and drugs that increase local synaptic activity might augment remodeling and, in turn, improve sensorimotor and higher cognitive functioning *(Dobkin, 1993, p. 56).*

A combination of neurobiologic measures might increase connections and perhaps allow axons to regenerate. The research is especially applicable to SCI because less than 10% of residual supraspinal input seems needed to recover the ability to walk *(Dobkin, 1993, p. 59).*

Using these principles as the foundation for locomotor rehab hypothesizes that the nervous system adapts to specific activity and that recovery requires relearning the task of walking by providing the spinal cord with the appropriate sensory information *(Behrman, 2000, p. 697).*

PTs should shift their paradigm of rehab from compensation to recovery. New BWS and treadmill systems may provide an alternative and permissive environment for training and allow clinicians to differentiate mechanisms of control *(Behrman, p. 1415).*

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