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The lingering effects of a busted myth—false time limits in stroke rehabilitation

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running head: active plasticity remains accessible always

Abstract:

It was once falsely believed that neurological and functional recovery after stroke occurred only in the first six months after lesion. The perception of this "6 month myth" continues to negatively impact the attitudes of patients towards their rehabilitation and on the clinicians and therapists making optimal training plans. Here we briefly outline some evidence that debunked the "6-month myth", where the concept of this temporal limit may have originated, and the lingering misunderstanding that individuals with stroke reach a plateau of recovery after six months even with rehabilitation training. We present evidence that significant functional improvement can occur years after stroke when rehabilitation training is applied. We frame the concepts of active and passive neurological recovery and that active neurological recovery continues far beyond any temporal limit. Because the effects of this busted "6 month myth" persist, we aim to remind active physicians, therapists, exercise professionals and people with stroke to continuously seek opportunities for active rehabilitation training. Meanwhile, trained and certified exercise professionals can play critical roles in facilitating rehabilitative training for community-dwelling stroke survivors.

Key words: stroke recovery, rehabilitation training, neuroplasticity,

For many decades there was a popular belief that neurological and functional recovery after stroke occurs only in the first six months after the lesion. During that time, though, research in neuroscience, exercise science, and rehabilitation revealed a very different picture that was incorporated into the work and practice of the research community, and many clinician-scientists. Despite that, many active clinicians trained some time ago, those in the general public and those in primarily teaching roles, continue to experience dissonance. For example, UpToDate (Wolters Kluwer Health Publishing), the common research-based resource for practicing clinicians, in 2015 continues to a study suggesting “Patients with severe disability who recovered did so within four months, and those with the most severe disability within five months from onset” and concluded that patients who are less severely affected would stop recovering after an even shorter time period (Dashe 2014). Similar statements can be easily found in text books frequently used by clinicians (Wiebers et al. 2014) or in literature reviews about stroke rehabilitation (Kwakkel and Kollen 2013), and is still repeatedly observed anecdotally in clinical training and research (e.g. personal observations from one author YS in clinical research, one author JB as a medical student and one author EPZ teaching in a major Canadian medical program).

There is in fact scant supporting evidence supporting temporal limitations about recovery and many clinical practice guidelines and reviews do include the corrected, modern view. In Canadian Best Practice Recommendations for Stroke Care (2013), the inclusion criteria for stroke rehabilitation include both acute and greater than one year post-stroke patients. Lohse et al (2014) explored dose-response relationship after stroke

by assessing the results from 37 studies and conclude that the benefit of large increases in therapy is similar across a range of post-stroke times regardless of whether a client is several month or several years after stroke.

The “6-month myth” has already been debunked by biomedical science. However, the false perception about the time limitation in stroke recovery continues to linger and the new research findings, housed mostly in the primary scientific literature, have not been translated effectively. Many practicing clinicians, general public end users, and media who inform the masses remain unaware about how the six month time limit arose or how it has already been “debunked” in the scientific literature (NIH. 2014, Stroke recovery. 2014). This has significant negative impact on rehabilitation training plans and may cause patients themselves not to anticipate motor recovery and result in a feeling of helplessness and a corresponding failure to seek rehabilitation (Page 2004a).

To help sweep away all vestiges of the “6-month myth”, here we re-iterate that the myth has been debunked by research by briefly examining work that may have been the source, citing evidence that clearly contradicts such a limit, and framing the concepts of active and passive neurological recovery.

Please note that our article is not meant as an exhaustive literature review nor is such a review necessary to again highlight that the “6-month myth” is well and truly “busted”. Our intent is to reveal that this myth was not founded on experimental evidence but rather on earlier studies that accidentally misunderstood the power of activity-dependent neural plasticity and had limited measures in place to assess it, or confused with the time window found in molecular or cellular level studies based on reduced animal models. Despite the fact (well-known in biomedical research circles) that

experimental observations have destroyed the basis for the myth, it continues to have lingering effects. Firmly eradicating these lingering effects requires explicit highlighting, especially for those clinicians many years removed from initial training, the general public who receive conflicting messages, and the media who unwittingly transmit them.

How did the “6-month myth” arise?

Highly cited articles from the 1960s to early 1980s measured functional changes in the first few months after stroke and mention very short recovery windows of recovery. The origin of the “6-month myth” could be based on results suggesting functional recovery was obtained early after stroke and then stopped. Bard et al. (1965) found that 116 stroke participants with a hemiplegic upper extremity reached a maximum recovery during the sixth and seventh months. In 39 stroke participants, Newman (1972) found recovery began as early as the first week or as late as the seventh, yet little neurological improvement after the fourteenth week. Wade et al. (1987) measured early rapid recovery of speech, walking and arm use within the first three months after stroke.

Data from reduced animal preparations indicate there is a “critical time window” of recovery, such that axonal sprouting in the rat is fully mature by the end of one month with rehabilitation training failing to alter morphology of cortical dendrites (Carmichael 2006, Biernaskie 2004, Murphy 2009) and a time frame to promote stroke recovery by limited by manipulating GABA (γ -aminobutyric acid) signaling pathway (Hutchinson 2011).

The information above suggested a time-limited recovery of function after stroke and may have been the basis for older conclusions that “widespread investment in rehabilitation service beyond six months following a stroke is likely to be wasteful” (Andrews 1981). However, a time window based on reduced animal models cannot necessarily be directly applied to humans without knowledge about recovery mechanisms and training effects (Murphy and Corbett 2009). Revisiting some of the human studies mentioned above and found elsewhere, few involved rehabilitation training to access “active plasticity”-- neurological plasticity occurring as a result of targeted training and rehabilitation.

In the studies of Newman (1972) and Wade et al. (1987), there were no interventions applied and thus no “active plasticity” was assessed. Further, Bard and Hirsherg’s study (1965) only involved passive range-of-motion exercises. Thus, only “passive” recovery—the innate recovery of neurological function occurring independently from therapeutic guidance—was measured.

We suggest that a major reason earlier studies demonstrated little improvement after six months is that measurement was only made of the natural history of recovery contained in passive neuroplasticity. Even when earlier studies tried to measure plasticity, measurement scales might not have been sensitive enough to detect small but continual improvements over longer time spans. Bard and Hirsherg (1965) graded motion on a categorical scale of four and walking ability with three categories. Without using more detailed and continuous measurement techniques, improvements in joint range-of-motion, muscle activities and walking speed may not be detected. In fact, Wade et al. (1987)

suggested that measurement scales could be insensitive in the upper range leading to a "ceiling effect" that would not allow measurement of improvement after six months.

When viewed in light of the research methods of many early articles about stroke recovery, the origins of the "six-month myth" seem quite natural, if not grounded in evidence.

Some examples that continue to bust the "6-month myth"

Page et al.(2004a, 2004b) argued that the "plateau" of functional improvement during rehabilitation indicated limited adaptation to therapeutic exercise after stroke. These adaptive states can be overcome by modifying training techniques such as intensity, duration, and environment. With the continuing development of novel rehabilitation strategies and techniques, many studies in chronic stroke years after lesion show significant functional improvements after rehabilitation training.

Constraint-induced movement therapy (CIMT; forced use of more affected limb by restraining the less affected) has been used widely in post-stroke arm training. Despite participants receiving the clinical message that motor recovery was doubtful this late after stroke (> 6 months after lesion), Page et al. (2004a, 2004b) showed improvements in their Fugl-Meyer Assessment and Action Research Arm Test scores.

For those whose more affected side is too weak to be trained, "cross-education" is a recent clinical concept that has been applied in strength training after stroke (Farthing and Zehr 2014). Six weeks of at home and in laboratory dorsiflexion resistance training in the less affected leg significantly improved voluntary strength and muscle activation of

both trained and untrained legs in chronic stroke. Dragert and Zehr (2013) concluded that “potential to access these (neurological) adaptations remains present many years after the infarct (e.g., ~84 months post-stroke), which demonstrates residual plasticity and efficacy of continued motor retraining beyond typical acute rehabilitation timelines.”

In locomotor rehabilitation, body weight supported treadmill training (BWSTT) reduces the effective load needed to be carried in weakened stroke participants. Studies have showed that BWSTT helps normalize gait, improve balance (Trueblood 2001) and increase self-selected overground walking velocity (Sullivan 2002) in chronic stroke participants. Wu et al.(2014) showed that both robotic assistance and robotic resistance training can increase the walking speeds in post-stroke participants years after the initial stroke event. Recently, Klarner et al (2015; submitted) showed that 5 weeks of arm and leg cycling training on a device readily found in any community recreation centre could improve interlimb neural coupling, clinical outcomes, and walking speed even decades after the stroke event.

The pervasive and lingering effect of a busted medical myth

The earlier research on stroke recovery without any rehabilitative interventions demonstrated that passive plasticity is greatest in the first few months after injury. This was confused with timelines and the concept of a critical time window for recovery found in reduced animal preparations using molecular and cellular methodologies. The potential for recovery even when paired with active rehabilitation was treated with skepticism and

gave rise to the belief that even with rehabilitation, post-stroke recovery would be minimal after six months (Figure 1.). However, we now know “the time window for stroke recovery, as with that of normal learning, never really closes” (Murphy and Corbett 2009).

The studies in the previous section represent a small sample of research showing that exercise and rehabilitation training can benefit chronic stroke participants. With the development of new rehabilitation techniques and measurement methods, studies continue to demonstrate neurological and functional improvements in those who are many years post-stroke. Continued developments of simple training devices and methods that can be accessed readily in the community are critical and are encouraged. Although this “6-month myth” was busted already we must keep promoting information and observations on the reality of neural plasticity to end the pervasive nature of the lingering aftereffects that influence individuals with stroke from participating in and receiving targeted rehabilitation training (Table 1.).

Notably, moving the recognition of this busted myth into the public domain presents an important opportunity going forward. More and more people with stroke living in the community will feel empowered to continue exercise rehabilitation training in their communities and recreation centres. This will provide an opportunity for appropriately trained allied health personnel such as CSEP Certified Exercise Physiologists and American College of Sports Medicine Exercise Specialists to assist with community based exercise training in chronic stroke (Zehr 2011). The myth was busted long ago. It is important to firmly sweep aside its lingering after-effects wherever and whenever they are encountered.

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305 Attachments:

Key Points:

- Despite the fact that the earlier belief that post-stroke recovery occurred only in the first six months after stroke onset had been debunked by evidence, it continues to have a lingering effect. Rehabilitation training methods ranging from strength to locomotor interventions show significant improvements in chronic stroke years after injury.
 - Although functional improvement is greater in the first few months post-stroke making use of heightened passive and activity-dependent plasticity, recovery continues with proper training strategies and evaluation methods.
 - Those who have had a stroke, their physicians, caregivers and therapists should be encouraged to constantly pursue opportunities for active rehabilitation regardless of the time after lesion.
 - There are significant implications for additional roles of certified exercise professionals such as CSEP Certified Exercise Physiologists (CSEP CEP) and ACSM Exercise Specialists in delivering enhanced community based rehabilitation training after stroke.
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Table 1. Key Points of this article

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332 Figure 1. Schematic of recovery timelines making use of passive and active neural
333 plasticity. The recovery timeline of passive plasticity reflects the innate and natural
334 recovery of the nervous system which may reach a plateau after about six months. With
335 proper rehabilitation training to access active plasticity, functional improvement is faster
336 and continues after 6 months.
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