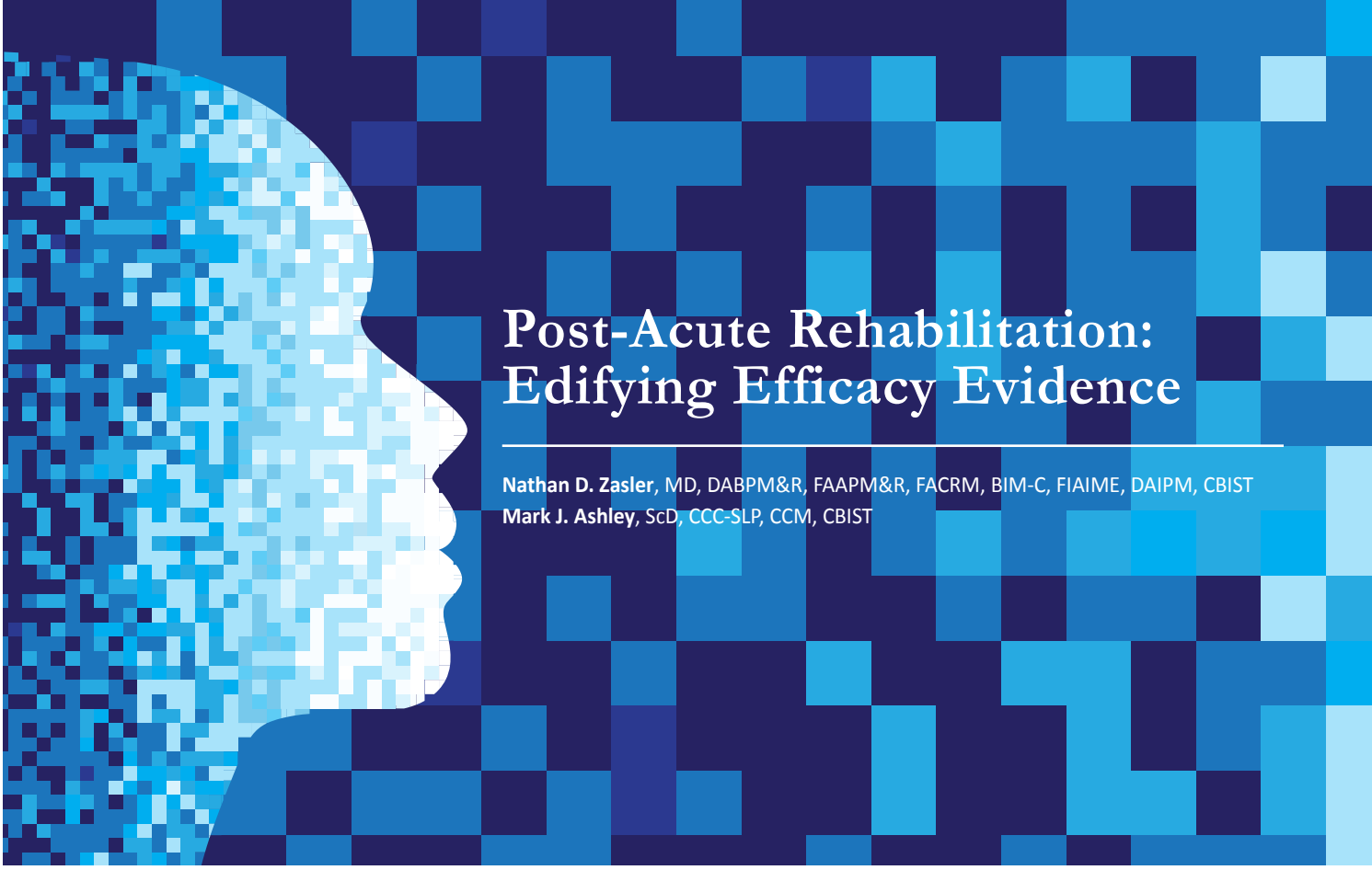

Post-Acute Rehabilitation: Edifying Efficacy Evidence

Nathan D. Zasler, MD, DABPM&R, FAAPM&R, FACRM, BIM-C, FIAIME, DAIPM, CBIST
Mark J. Ashley, ScD, CCC-SLP, CCM, CBIST

Introduction

The role and benefits of post-acute rehabilitation (PAR) are often underappreciated by payors and clinicians, particularly, how appropriate services provide at the right time and intensity can contribute to improved neurological outcome. There is a lack of understanding regarding the benefits of continued neuro-rehabilitation in the PAR setting which perpetuates reduced funding support for PAR which results in decreased access to medically necessary services. It is the opinion of the authors that clinical care should be driven by good science and the cost/benefit of the intervention rather than by payor-mandated cost controls. We hope this review helps to educate all parties involved with traumatic brain injury (TBI) care to gain insights into post-acute care issues and efficacy.

Challenges in PAR outcomes research

Challenges exist in assessing PAR outcomes and include the following: 1) heterogeneity of the patient population; 2) a lack of standardized paradigms for assessment and treatment for most conditions for which PAR is provided; and 3) substantive differences in treatment settings (i.e. location, staff specialization level, intensity of treatment, length of stay and nature of treatment) (Glenn, et al, 2005). Recent research on multidisciplinary PAR efficacy after more significant TBI noted some of the limitations of the current literature; however, it should be noted that the study focused on cognitive rehabilitation and social functioning and no other areas of outcome (Brasure, et al, 2012). Further research should be encouraged that emphasizes the use of standardized measurement of patient characteristics as well as outcomes (Malec & Basford, 1996).

Moving forward, research must also better examine how the timing, duration, and treatment intensity of specific therapies and/or combination therapies, whether traditional, pharmacologic, neuro-modulatory or other possibilities, might impact recovery and outcome durability.

Basic science literature supporting PAR

The brain has a lifelong capacity for plasticity which is driven by a variety of different factors. In fact, plasticity is the brain's normal state. Environmental enrichment (EE) has been reliably shown to drive plasticity at molecular and morphological levels (Alwis, 2014; Wang, 2016). As such, EE serves as a potential basis of adaptive changes in neuronal function, and, ultimately, behavior in all animals, brain injured or not. EE typically involves providing multisensory stimulation at levels much greater than those that occur under circumstances such as those provided in home care and outpatient periodic therapies.

Two paradigms exist for providing EE. Specific EE focuses on one specific area of function such as cognitive or motor function. Generic EE, however, occurs when the entire environment is non-selectively enriched. Animal studies demonstrate improvement in intellectual functioning, behavioral modulation, and certain motor behaviors. Adverse effects may occur that have yet to be fully delineated (for example, overstimulation in the environment may produce increased agitation). Adverse effects may also constitute maladaptive plasticity. PAR provides for a controlled application of EE together with structured behavioral paradigms that combine to promote adaptive and discourage maladaptive plasticity. Significant data supports changes in neuronal function involving subcortical structures such as the hippocampus.

However, further research assessing optimal parameters for same remain lacking (Wogensen et al, 2015).

Lack of EE, whether from limitations in participation, ability, or funding support may play a part in the functional decline observed in a significant percentage of persons with moderate to severe TBI. Frasca and colleagues (2013) published a scoping review of literature on EE in animals and humans as well as post discharge experiences related to barriers to recovery.

Their findings provide support for attempting prophylaxis against long-term decline following TBI through continued and optimal EE. There is much to be learned about specific mechanisms of EE in neurorehabilitation; however, there is certainly evidence that ongoing and individualized environmental stimulation/enrichment is likely a key element in facilitating further neurorecovery and maintaining achieved gains (Ashley, 2012).

Importantly, the aforementioned discussion does not address how additional interventional variables can either augment or complement the effects of EE. Issues such as the timing, context and content of PAR including the psychosocial environment, quality and intensity of therapy services, medical expertise, diet, and other factors may all contribute to improved quality of life as well as functional and neurological recovery. As one example of the aforementioned, recent animal research has shown that the effects of even low dose EE can be augmented with certain medications (de la Tremblaye, et al, 2017).

Regardless of the type of post-acute program, intensity seems to be well correlated with level of functional gain if there is active rehabilitation occurring as opposed to post-acute programs that just provide supported living services. Postacute community based treatment, even when of lower intensity, can improve survivor ability to function more independently and result in less supportive care needs, the latter thereby decreasing caregiver burden.

Studies examining the effects of EE on sensory cortices have generally demonstrated alterations in neuronal responsivity and suggest that cortical plastic changes seen with EE operate independently of other previously described mechanisms of neuroplasticity (Alwis, 2014).

Multiple mechanisms are involved in induction of EE-related changes in molecular function and, as a result, also in brain morphology and neuronal function. Data strongly suggests that EE may serve to facilitate neuroplasticity and modify aberrant neuronal activity in a way that promotes function as opposed to dysfunction following traumatic brain injury. It has been theorized that EE may have therapeutic benefit due to balancing cortical excitation and inhibition; thereby, improving behavior, whether cognitive or sensorimotor (Alwis, 2014). Pleiotropic interventions, including not only EE but also such interventions as exercise and task specific training (probably in combination with other treatments), can clearly enhance motor recovery after acquired brain injury (Livingston-Thomas, et al, 2016; Mala et al, 2017) and may also improve cognitive recovery.

What evidence exists to show that PAR results in long-term functional gains?

Studies have found functional benefits of PAR as well as decrements in life-long cost projections resulting in overall economic savings (Seale, et al, 2002; Braunling-McMorrow, et al, 2010; Duchnick, et al, 2015; Griesbach, et al, 2015). Greisbach et al found an average of $2 million life-time cost reduction associated with PAR.
Geurtsen and colleagues conducted a systematic review of the efficacy of comprehensive rehabilitation programs for adults in the chronic phase of severe acquired brain injury. While there were some methodological limitations in their analysis, substantial improvement in daily life functioning and community integration including work reentry with persistence of gains at follow-up resulted from such programming (Geurtsen, et al, 2010).
Furthermore, research has shown that post-acute rehabilitation is not only associated with functional gains but that those gains cannot be explained by undirected recovery alone (Hayden et al, 2013).

Regardless of the type of post-acute program, intensity seems to be well correlated with level of functional gain if there is active rehabilitation occurring as opposed to post-acute programs that just provide supported living services (Eicher, 2012). Post-acute community based treatment, even when of lower intensity, can improve survivor ability to function more independently and result in less supportive care needs, the latter thereby decreasing caregiver burden (Eames et al, 1996; Wood et al, 1999; Worthington et al, 2006; Middag-van Spanje et al, 2017).

Gains achieved during PAR are generally maintained at long-term follow-up; although, this is not a universal finding and there are likely many factors that influence maintenance of gains (Ashley et al, 1997; Sanders et al, 2001; Geurtsen et al, 2010 and 2012). The implications, however, are that there is a need for long-term regular surveillance by specialized professionals familiar with TBI chronic care as well as long-term services that engage and stimulate patients after moderate to severe TBI to help prevent decline.

Does the intensity of PAR rehabilitation therapies matter?

Multiple lines of research have shown the benefit of more intensive therapy as a key factor in activity-based therapies across skilled and non-skilled interventions (Breceda et al, 2013).

In a study published in 2001, the general principal that more rehabilitation is better than less was addressed by Sheil and colleagues in a two center, prospective, controlled study with random allocation as to groups. Increasing intensity of rehabilitation therapy without change in content was associated with enhanced functional recovery and shorter hospital stays when an integrated service was delivered that provided ongoing community support. Interestingly, there was no evidence of any ceiling effect of therapeutic intensity beyond which no further response was observed (Shiel, 2001). A prospective, multicenter, non-randomized assessment of inpatient treatment intensity found therapy intensity was predictive of motor functioning at discharge but did not predict cognitive gain.

Age predicted the intensity of both psychologic and total therapy services (Cifu et al, 2003). A synthesis of best evidence compiled in a Cochrane review of randomized controlled trials was compared with the literature examining long-term neurological conditions concluded:

1. strong evidence exists that more intensive programming was associated with more rapid functional gain; and
2. moderate evidence that continued outpatient therapy could assist in sustaining gains made in earlier PAR (Turner-Stokes, 2008).

Other researchers have shown that cognitive and functional recovery after acquired brain injury can be optimized by more intensive rehabilitation therapy to help the brain repair itself and facilitate neuroplasticity (Wang et al, 2016).

What is the proper duration of PAR?

PAR addresses one of the single most variable diseases in medicine. Brain injury varies with the nature, mechanism, and location of the injury and is further complicated by age, gender, genome, comorbid conditions at the time of injury, socioeconomic status, education, and intelligence, at least.

While disease management for other organs proceeds along clear clinical pathways, the endpoint for PAR is far more patient-specific, variable, and dependent upon interactions of combinations of the above factors. To that end, Dobkins suggested that termination of neurological rehabilitation should depend upon the period of time during which the individual fails to make further improvement (Dobkins, 2005); however, one must differentiate between neurological improvement per se and a patient's ability to make functional gains even without ongoing neurological change. Additionally, ongoing rehabilitative intervention may serve to prophylax against later decline and must therefore be considered in the context of such decisions to terminate therapy. Several studies have reported PAR treatment intervention periods exceeding several months (Wood et al, 1999; Worthington et al, 2006; Ashley et al, 1993; Klonoff et al, 2001; Cope et al, 1991). These studies provide support for the notion that late rehabilitation can be effective in improving functional capabilities even though longer treatment durations may be necessary to accomplish those gains. A more recent study reported comparisons between mean durations of PAR for individuals with TBI or CVA, and highlighted differences in variability among the two groups for PAR that was uninterrupted by insurance coverage and within months of injury rather than years. Both group treatment duration means were over 200 days with far more variability in the TBI group than the CVA group (Griesbach et al. 2015). This treatment duration finds support in earlier reports of larger study populations (Ashley et al, 1993; Cope et al, 1991; Turner-Stokes, 2007).

Why advocate for PAR? Implications for prophylaxis of neural and cognitive decline post-TBI.

Cost containment measures by third party insurance companies and other payors limit and/or direct care without necessarily being attuned to current scientific evidence substantiating the benefits of early and ongoing treatment. The aforementioned practice results in treatment often being terminated prematurely to decrease cost exposure, or, alternatively, not being provided or paid for at all. A prime example of this is the observed substantial reduction in acute inpatient rehabilitation length of stay over the last 20 years (Kreutzer et al, 2001). Many patients with moderate to severe TBI end up being discharged to non-specialized nursing homes where they receive little or no ongoing rehabilitation. This change in care provision only further amplifies the need for advocating for post-acute continuation of specialty services as the literature has clearly shown that those individuals with moderate to severe brain injury who receive more intensive rehabilitation services earlier than later show greater levels of functional improvement. Additionally, as is implied above, earlier treatment results in better functional outcomes than delayed treatment assuming treatment is even provided (Turner-Stokes, et al, 2015).

Importantly, a proportion of patients (approximately 25-40% depending on the study referenced) show a tendency towards decline in function over life span after more significant TBI. The aforementioned fact has implications relative to treatment that may serve to protect against such deterioration (Kolakowsky-Hayner, et al, 2012; McMillan, 2012; Wilson, et al, 2017)). Advancing age alone does not account for the observed decline nor does impaired cognitive functioning (Griesbach et al, 2017; Wilson, et al, 2017). There is accelerated cognitive decline following more severe traumatic brain injury, particularly in areas of attention and working memory that have been apportioned to diminished cognitive reserve, which may potentially increase the risk of dementia (Wood, 2017).

Aside from the evidence from basic science as well as clinical studies supporting the benefit to such treatment, the benefit, and cost savings over time for patients and/or society at large has been well demonstrated (Ashley et al, 1990; van Heugten, et al, 2011; Greisbach et al, 2015).

Future directions and conclusions

We hope that this article will stimulate interest in prospective and controlled research that further delineates factors that drive better outcomes from PAR, determine ways to modulate or negate neurological and functional decline through proactive assessments and treatments, and demonstrate the cost efficacy of different levels of PAR services. Most importantly, we must advocate for our patients and their families and know the literature that supports the services that we are claiming are medically necessary. Furthermore, we must educate payors regarding the scientific evidence that supports what we do, and what they should consider as standard and evidence based treatments.

References

Alwis DS, Rajan R. Environmental enrichment and the sensory brain: The role of enrichment in remediating brain injury. *Frontiers in Systems Neuroscience*. 8:1-20, 2014.

Ashley MJ. Repairing the injured brain: Why proper rehabilitation is essential to recovering function. *Cerebrum*. Epub 2012 Jul 30.

Ashley MJ, Krych DK, Lehr RP. Cost-benefit analysis for post-acute rehabilitation of the traumatically brain injured patient. *Journal of Insurance Medicine*. 22: 156-161, 1990.

Ashley MJ, Persel C, Krych DK. Changes in reimbursement climate: Relationship among outcome, cost, and payor type in the post-acute rehabilitation environment. *Journal of Head Trauma Rehabilitation*. 8(4), 30-47, 1993.

Ashley MJ, Persel CS, Clark, MC, Krych, DK. Long-term follow-up of post-acute traumatic brain injury rehabilitation: A statistical analysis to test for stability and predictability of outcome. *Brain Injury*. 11(9), 677-690.

Brasure M, Lamberty GJ, Sayer NA, et al. Multidisciplinary post-acute rehabilitation for moderate to severe traumatic brain injury in adults. *Agency for Health Care Research and Quality*. 72: 1–33, 2012.

Braunling-McMorrow D, Dollinger SJ, Gould M, et al. outcomes of postacute rehabilitation for persons with brain injury. *Brain Inj*. 24(7-8):928-938, 2010.

Breceda EY, Dromerick AW. Motor rehabilitation and stroke in traumatic brain injury: Stimulating and intense. *Curr Opin Neurol*. 26(6): 595–601, 2013.

Cifu DX, Kreutzer JS, Kolakowsky-Hayner SA, et al. The relationship between therapy intensity and rehabilitative outcomes after traumatic brain injury: A multicenter analysis. *Arch Phys Med Rehabil*. 84(10):1441-1448, 2003.

Cope N, Cole, J, Hall K, et al. Brain Injury: Analysis of outcome in a post-acute rehabilitation system: Part1: General Analysis. *Brain Injury*. 5:111-125, 1991.

Cullen N, Meyer MJ, Aubut JA, et al. Efficacy and models of care following acquired brain injury. Evidence based review of moderate to severe acquired brain injury. *ERABI*. Accessed 12/1/17. http://www.abiebr.com/

De la Tremblaye PB, Wellcome JL, de Witt BW, et al. rehabilitative success after brain trauma by augmenting a subtherapeutic dose of environmental enrichment with galantamine. *Neurorehabilitation and Neural Repair*. 31(10–11):977–985, 2017.

Duchnick JJ, Ropacki S, Yutsiss M, et al. Polytrauma transitional rehabilitation programs: comprehensive rehabilitation for community integration after brain injury. *Psychological Services*. 12 (3): 313-321, 2015.

Eames P, Cotterill, G, Kneale, TA Storrar AL, Yeomans P. Outcomes of intensive rehabilitation after severe brain injury: AS long-term follow-up study. *Brain Injury*. 10(9): 631-650, 1996.

Eicher V, Murphy MP, Murphy TF, Malec JF. Progress assessed with the Mayo–Portland Adaptability Inventory in 604 participants in 4 types of post-inpatient rehabilitation brain injury programs. *Arch Phys Med Rehabil*. 93(1):100-107, 2012.

Frasca D, Tomaszczyk J, McFadyen BJ, Green RE. Traumatic brain injury and post-acute decline: What role does EE play? A scoping review. *Frontiers in Human Neuroscience*. 7:31, 2013.

Geurtsen GJ, van Heughten CM, Martina JD, Geurts ACH. Comprehensive rehabilitation programmes in the chronic phase after severe brain injury: A systematic review. *J of Rehab Med*. 42: 97-110, 2010.

Geurtsen GJ, van Heughten CM, Martina JD, et al. 3-year follow-up results of a residential community reintegration program for patients with chronic acquired brain injury. *Arch Phys Med Rehabil*. 93:908-911,2012

Glenn MB, Rotman M, Goldstein R, Selleck EA. Characteristics of residential community integration programs for adults with brain injury. *J Head Trauma Rehabil*. 20(5): 393–401, 2005.

Griesbach, G.S., Kreber, L.A., Harrington, D and Ashley, M. Post-acute traumatic brain injury rehabilitation: Effects on outcome measures and life care costs. *J of Neurotrauma*. 32:704-711, 2015.

Griesbach GJ, Masel BE, Helvie RE, Ashley MJ. The impact of traumatic brain injury on later life: Effects of normal aging and neurodegenerative diseases. *J of Neurotrauma*. 2017 Oct 27. doi: 10.1089/neu.2017.5103. [Epub ahead of print].

Hayden ME, Plenger P, Bison K, et al. Treatment effect versus pretreatment recovery in persons with traumatic brain injury: A study regarding the effectiveness of post-acute rehabilitation. *PM&R*. 5:319–327, 2013.

Klonoff PS, Lamb DG, Henderson SW. Outcomes from milieu-based neurorehabilitation at up to 11 years post-discharge. *Brain Injury*. 15(5):413-428, 2001.

Kolakowski-Hayner SA, Hammond FM, Wright J, et al. Aging and traumatic brain injury: Age, decline in function and level of assistance over the first 10 years post-injury. *Brain Injury*. 26 (11): 1328–1337, 2012

Kreutzer JS, Kolakowsky-Hayner SA, Ripley D, et al. Charges and lengths of stay for acute and inpatient rehabilitation treatment of traumatic brain injury. *Brain Injury*. 15(9):763-774, 2001.

Livingston–Thomas J, Nelson P, Karthikeyan S, et al. Exercise as enablers of task specific neuroplasticity and stroke recovery. *Neurotherapeutics*. 13:395–402, 2016.

Mala H, Rasmussen CP. The effect of combined therapies on recovery after acquired brain injury: Systematic review of preclinical studies combining enriched environment, exercise, or task specific training with other therapies. *Restorative Neurology and Neuroscience*. 35: 25–64, 2017.

Malec JF, Basford JS. Post-acute brain injury rehabilitation. *Arch Phys Med Rehab*. 77: 198-207, 1996.

McMillan TM, Teasdale GM, Stewart E. Disability in young people and adults after head injury: 12-14 year follow-up of a prospective cohort. *J Neurol Neurosurg Psychiatry*. 2012;83:1086–91. doi: 10.1136/jnnp-2012-302746.

Middag-van Spange M, Smeets S, van Haastregt J, van Heugten C. Outcomes of a community based treatment programme for people with acquired brain injury in the chronic phase: A pilot study *Neuropsychol Rehabil*. 2017, March 28, Epub ahead of print.

Sander AM, Roebuck TM, Struchen MA, et al. Long-term maintenance of gains obtained in post-acute rehabilitation of persons with traumatic brain injury. *J Head Trauma Rehabil*. 16(4): 356–373, 2001.

Seale GS, Caroselli JS, High WM, et al. Use of community integration questionnaire to characterize changes in functioning for individuals with traumatic brain injury participated in a postacute rehabilitation programme. *Brain Inj*. 16(11):955-967, 2002.

Shiel, A, Burn JPS, Henry D, et al. The effects of increased rehabilitation therapy after brain injury: Results of a prospective controlled trial. *Clinical Rehabilitation*. 15:501–514, 2001.

Sours C, George EO, Zhuo J, et al. Hyper-connectivity of the thalamus during early stages following mild traumatic brain injury. *Brain Imaging Behavior*. 9(3):550-563, 2015.

Turner-Stokes, L. Cost-efficiency of longer-stay rehabilitation programmes: Can they provide value for money? *Brain Injury*. 21(10): 1015-1021, 2007.

Turner-Stokes, L. Evidence for the effectiveness of multidisciplinary rehabilitation following acquired brain injury: A synthesis of two approaches. *Journal of Rehabilitation Medicine*. 40: 691-701, 2008.

Turner-Stokes L, Pick A, Nair A, et al. Multidisciplinary rehabilitation for acquired brain injury in adults of working age. *Cochrane Database Syst Rev*. Dec 22;(12):CD004170, 2015.

Van Heugten CM, Geurtsen GJ, Derksen RE. Intervention and societal costs of residential community reintegration for patients with acquired brain injury: A cost-analysis of the brain integration programme. *J Rehabil Med*. 43:647-652, 2011.

Wang L, Conner JM, Nagahara AH, Tuszynski MH. Rehabilitation drives enhancement of neuronal structure and functionally relevant neuronal subsets. *PNAS*. 113(10):2750-2755, 2016.

Wilson L, Stewart W, Dams-O'Connor K, et al. The chronic and evolving neurological consequences of traumatic brain injury. *The Lancet Neurology*. 16(10):813-825, 2017.

Wogensen E, Mala H, Mogensen J. The effects of exercise on cognitive recovery after acquired brain injury in animal models: A systematic review. *Neural Plas*. E-pub Oct. 5, 2015.

Wood RL, McCrea JD, Wood LM et al. Clinical and cost-effectiveness of post-acute neurobehavioral rehabilitation. *Brain Injury*. 13(2):69-88, 1999.

Wood RL. Accelerated cognitive aging following severe traumatic brain injury: A review. *Brain Inj*. 31(10):1270-1278, 2017.

Worthington AD, Matthews S, Melia Y, et al. Cost-benefits associated with social outcome from neurobehavioral rehabilitation. *Brain Injury*. 20(9):947-957, 2006.

Author Bios

Nathan Zasler, MD, is founder, CEO & CMO of Concussion Care Centre of Virginia, Ltd. and Tree of Life Services, Inc.. He is board certified in PM&R, fellowship trained in brain injury and subspecialty certified in Brain Injury Medicine. Dr. Zasler has several academic appointments and lectures nationlly and internationally on topics related to brain injury. Dr. Zasler has published extensively on TBI related neuromedical issues. He is co-chief editor of "Brain Injury" and "NeuroRehabilitation" and serves on numerous journal editorial boards. Dr. Zasler is active in local, national and international organizations dealing with acquired brain injury and neurodisability.

Mark Ashley, ScD, CCC-SLP, CCM, CBIST, is President/CEO of Centre for Neuro Skills® (CNS), which has operated postacute brain injury rehabilitation programs since 1980. Dr. Ashley serves on the Board of Directors of the Brain Injury Association of America, and is an Emeritus Chair. He serves on the Board of Directors of the California Brain Injury Association. Dr. Ashley is an Adjunct Professor at the Rehabilitation Institute of the College of Education at Southern Illinois University. Dr. Ashley founded the Centre for Neuro Skills Clinical Research and Education Foundation, a non-profit research organization.