

Treating Persons With Traumatic Brain Injury: History and Updates

Janet P. Niemeier, Lori M. Grafton, Tara Chilakamarri

The scientific traumatic brain injury (TBI) literature chronicles 50 years of epidemiologic data, neurobehavioral and cognitive symptoms, diagnostic tools for measuring outcomes, and treatments for persons with TBI. In this article, we review the state of our knowledge about TBI causes and symptom complexities, evidence-based treatments, and ongoing treatment needs.

Each year, 235,000 Americans are hospitalized for non-fatal traumatic brain injuries (TBIs), 1.1 million people are treated in emergency departments, and 50,000 people die [1]. TBI survivors share a list of common goals: attaining preinjury levels of productivity, enjoying a social and support network, and experiencing improved quality of life [2]. Their journey has received much attention in the scientific TBI literature over the past 50 years. The first 30 of those years were largely devoted to studying the epidemiology of TBI; the complexity of neurobehavioral and cognitive symptoms and their impact on family and community; and the variability in pace, degree, and rate of recovery [3-7]. In addition, tools for accurately diagnosing TBI, for measuring variables that contribute to the heterogeneity of the population, and for assessing treatment outcomes were (and still are) a prominent focus of research [8, 9].

This foundational work was essential for understanding the heterogeneity and complexity of TBI. Since the late 1980s, however, trials of treatment interventions have increasingly been a focus of investigation [10-12]. Federal agencies such as the National Institute on Disability and Rehabilitation Research [13] and the National Institutes of Health [14], through the Eunice Kennedy Shriver National Institute of Child Health and Human Development, began to support investigations into efficacious treatments for persons with TBI. Private businesses, the National Football League [15], and the US government are also continuing to support TBI research priorities and external funding initiatives through programs such as the Brain Initiative [16].

There is still a significant need to conduct research focused on improving the effectiveness of treatments for persons with TBI. However, evidence from the last 15 years has helped clinicians have some confidence in their ability to meet the challenges involved in working with persons with TBI [10-12, 17, 18]. In the area of prevention, research

amassed since 1998 has led to a greater understanding of the diverse aspects of TBI [12]. We have identified children and older adults as at-risk groups for falls resulting in head trauma [12]. Due to increased vehicular crash-related TBIs, we have implemented preventive measures regarding drunk driving, seat belt use, and helmet use [12]. To date, multiple social-behavioral, targeted therapeutic rehabilitation, and medication intervention trials have been conducted with both civilian and military TBI populations [10-12, 17-21].

Major systematic and selective reviews of trials now exist [10-12, 17-21]. Reviewers present trials classified according to the quality of evidence as recommended by the American Academy of Neurology [22]; they also provide recommendations for clinical application or use of methodologies based on these levels of evidence [10, 11]. In a general sense, the literature tells us that early and comprehensive inpatient rehabilitation improves both function at discharge from acute care and subsequent community integration [23]. We know that caregiver support and skills training of caregivers have a direct and positive effect on the person with TBI [24]. The literature also shows that injury-related information, work or other productive activity, and a social network result in the best perceived quality of life after TBI [2].

The following is a selective list of some of the most promising evidence-based treatments for TBI, by specific post-TBI symptom domain.

Depression and Anxiety Following TBI

Perhaps as a result of the deficits in problem solving and coping resources that are common after TBI, up to 53.1% of people with TBI develop clinical depression [25]. There are also accompanying post-TBI problems with anxiety, sleep disturbance, agitation, anger outbursts, and impulsivity [25, 26]. Potential helpers or caregivers, whose support is critical for people with TBI, are stressed and sometimes pull away in the face of these injury-related challenges [6]. Specific medications (such as sertraline [27]), physical

Electronically published April 1, 2015.

Address correspondence to Dr. Janet P. Niemeier, Carolinas Medical Center, 1100 Blythe Blvd, Charlotte, NC 28203 (Janet.niemeier@carolinashealthcare.org).

N C Med J. 2015;76(2):105-110. ©2015 by the North Carolina Institute of Medicine and The Duke Endowment. All rights reserved. 0029-2559/2015/76210

exercise [28], and cognitive behavioral therapy [29-31] are high on the list of evidence-based practices for improving mood and coping after TBI. In addition, there is evidence that online and telephone delivery of counseling and psychotherapy are effective [32, 33]. Cognitive behavioral therapy, which includes a range of methods geared toward changing disruptive and maladaptive thinking habits, is consistently shown to help reduce anxiety, improve restorative sleep, and improve self-management and behavioral self-regulation [11, 12, 29-31]. Gold standard methods used by the military to treat co-occurring TBI and post-traumatic stress disorder are prolonged exposure and cognitive reprocessing [19, 21]. Prolonged exposure provides therapist-supported, repeated situational and imagined exposure to aspects of the trauma incident [34]. Cognitive processing therapy is a manualized cognitive behavioral therapy that includes education about emotional and thought responses to trauma, cognitive restructuring, and writing of trauma narratives [35]. These 2 methods are currently being tested in a large, multisite comparative effectiveness trial [21].

Cognitive Deficits

Multiple evidence-based cognitive rehabilitation intervention protocols are now available to clinicians for improving the declines in memory, attention, and executive function that are typical after TBI [10-12]. Examples of cognitive rehabilitation methods for improving memory include training and supported practice of a range of compensatory strategies that can be helpful when used together to address specific problems [11]. Both low-tech (paper) and high-tech methods (computers, cell phones) have been shown to be effective for improving memory [36]. Pagers, personal data assistants, computers, smart phones, and accompanying applications are all highly effective memory prostheses for the person with TBI, and these devices can be individually tailored to his or her needs [37]. While the steps to use these devices must be carefully trained and practiced, a memory log with a calendar, schedule, and important telephone numbers or e-mail addresses can be an effective, low-tech, low-cost intervention [36].

Attention

There are a variety of interventions for improving visual and general attention [36]. Improving attention is important given its role in memory on a day-to-day basis [36, 38, 39]. Evidence-based methods for increasing attention include the Lighthouse Strategy, which is a 3-session mental imagery and cognitive rehabilitation strategy for improving hemispatial inattention and neglect [38]. Neglect of left or right visual fields is a notoriously poor prognostic sign after brain injury [38]. Higher-functioning individuals with mild TBI can significantly improve their concentration for work and independent living skills through trained use of meta-cognitive self-instruction strategies [40].

Problem Solving

Several methods, some provided in a standardized manualized format, have been shown to improve problem solving [24, 41, 42]. Protocol components include training, practice, and rehearsal of situational analysis; generation of multiple options; emotional control; decision-making strategies; and evaluation of outcomes [24, 41, 42]. Many clinicians have successfully employed group therapy models during implementation [24, 41, 42]. Caregiver training in problem solving, which can be implemented in person or online, has also shown promise for improving caregiver confidence and competence and for reducing caregiver anxiety [24, 32].

Pharmacological Approaches to Behavioral and Medical Complications of TBI

While evidence has disproved the utility of intravenous steroids or long-term seizure prophylaxis after TBI, hypothermia treatments are being investigated for potential morbidity benefits [12, 26, 43]. In addition, various medications can be effective for addressing certain aspects of TBI. Dopamine, serotonin, and acetylcholine augmentation (with agents such as amantadine, methylphenidate, sertraline, and donepezil) have improved post-TBI hypoarousal and inattention [43]. Amantadine has been shown to accelerate the pace of functional recovery during active treatment in patients with post-traumatic disorders of consciousness [44]. Data on methylphenidate shows improvement in attention and memory impairments; similarly, cholinesterase inhibitors have shown improvement in memory impairments, but with worsening of behavioral issues [45].

Post-TBI complications—including deep venous thrombosis, heterotopic ossification, spasticity, dysautonomia, hydrocephalus, depression, and post-traumatic stress disorder—are readily identified [12, 26, 43]. Pituitary dysfunction, specifically of the anterior pituitary, exists in 25-40% of moderate and severe TBI survivors due to incompletely understood mechanisms [46]. In severe injuries, signs and symptoms of sympathetic storming can include hypertension, tachycardia, tachypnea, pupillary dilatation, diaphoresis, hyperthermia, posturing, and dystonia [47]. Data supports the use of intrathecal baclofen for spasticity and beta-blockers for central storming [26]. In addition to using evidence-based cognitive behavioral therapy approaches [31], agitation and delirium are successfully managed with new generation antipsychotics such as quetiapine fumarate and antiseizure medications like valproate and carbamazepine [43]. Trazodone for sleep onset and modafinil for reducing daytime sleepiness are effective for addressing sleep-wake cycle issues [43]. However, there is no specific medication that addresses all post-TBI challenges [12].

Ongoing Needs and Future Promise

While the aforementioned range of evidence-based therapies is encouraging, there is still much work to do. Given the

heterogeneity of this patient population, researchers need to identify which treatments work best for which patients. Use of telephone- and Internet-based therapies is bringing needed evidence-based therapies to more consumers with TBI. However, there is ongoing need for reducing other barriers to treatment, such as cost, and for improving access for even more consumers, especially for rural populations and veterans.

The study of diagnostic biomarkers of TBI, while still in its infancy, has potential for improving the accuracy of TBI diagnosis and more timely provision of treatment services to affected individuals [48-50]. Several proteins synthesized in astroglial cells or neurons—such as the BB isozyme

of creatine kinase, glial fibrillary acidic protein, myelin basic protein, neuron-specific enolase, and S100B—are being investigated as diagnostic and prognostic biomarkers for patients with moderate to severe TBI [48-50]. In addition, positive findings of studies of hormonal neuroprotection, which is thought to have been demonstrated in animal research, have been inconsistent in human research [51]. Current studies on measures of injury severity suggest that the duration of post-traumatic amnesia may be the most meaningful predictor of a patient's functional level at discharge [52].

All these newer areas of research are improving our understanding of the effects of sex and other variables on

outcomes. We are continuing to study post-TBI psychosocial and vocational outcomes and the variables that predict more positive trajectories of recovery, including pre-injury substance use disorders, caregiver burden and stress, and factors that affect quality of life. Despite the significant work ahead, TBI clinicians and researchers are highly motivated and aspire to establish clinical pathways that will lead toward greater improvements in post-injury functional and neurobehavioral outcomes for individuals with TBI. **NCMJ**

Janet P. Niemeier, PhD, ABPP (RP) professor and director of research, Department of Physical Medicine and Rehabilitation, Carolinas Medical Center, Charlotte, North Carolina; adjunct professor, University of North

Carolina at Chapel Hill, Chapel Hill, North Carolina.

Lori M. Grafton, MD brain injury program director, Department of Physical Medicine and Rehabilitation, Carolinas Medical Center; codirector, Carolinas Concussion Network, Charlotte, North Carolina.

Tara Chilakamarri, MD brain injury fellow, Department of Physical Medicine and Rehabilitation, Carolinas Medical Center, Charlotte, North Carolina.

Acknowledgments

Potential conflicts of interest. All authors have no relevant conflicts of interest.

References

1. Andelic N, Sigurdardottir S, Schanke AK, Sandvik L, Sveen U, Roe C. Disability, physical health and mental health 1 year after traumatic brain injury. *Disabil Rehabil*. 2010;32(13):1122-1131.

2. Corrigan JD, Whiteneck G, Mellick D. Perceived needs following traumatic brain injury. *J Head Trauma Rehabil.* 2004;19(3):205-216.
3. Levin HS, Grossman RG, Rose JE, Teasdale G. Long-term neuropsychological outcome of closed head injury. *J Neurosurg.* 1979;50(4):412-422.
4. Levin HS, Grossman RG. Behavioral sequelae of closed head injury. A quantitative study. *Arch Neurol.* 1978;35(11):720-727.
5. Lewin W, Marshall TF, Roberts AH. Long-term outcome after severe head injury. *Br Med J.* 1979;2(6204):1533-1538.
6. Rogers PM, Kreutzer JS. Family crises following head injury: a network intervention strategy. *J Neurosurg Nurs.* 1984;16(6):343-346.
7. Haboubi NH, Long J, Koshy M, Ward AB. Short-term sequelae of minor head injury (6 years experience of minor head injury clinic). *Disabil Rehabil.* 2001;23(14):635-638.
8. Levin HS, O'Donnell VM, Grossman RG. The Galveston Orientation and Amnesia Test. A practical scale to assess cognition after head injury. *J Nerv Ment Dis.* 1979;167(11):675-684.
9. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet.* 1974;2(7872):81-84.
10. Cicerone KD, Dahlberg C, Malec JF, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. *Arch Phys Med Rehabil.* 2005;86(8):1681-1692.
11. Cicerone KD, Langenbahn DM, Braden C, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. *Arch Phys Med Rehabil.* 2011;92(4):519-530.
12. Gordon WA, Zafonte R, Cicerone K, et al. Traumatic brain injury rehabilitation: state of the science. *Am J Phys Med Rehabil.* 2006;85(4):343-382.
13. US Department of Education. Welcome to NIDRR. US Dept of Education website. <http://www2.ed.gov/about/offices/list/oseers/nidrr/index.html>. Accessed January 17, 2015.
14. Eunice Kennedy Shriver National Institute of Child Health and Human Development. Traumatic Brain Injury (TBI) and Stroke Rehabilitation (TSR) Program. National Institutes of Health website. <http://www.nichd.nih.gov/about/org/ncmrr/tsr/Pages/index.aspx>. Updated November 5, 2014. Accessed January 17, 2015.
15. NineSigma. GE NFL Head Health Challenge. NineSigma website. <http://www.ninesigma.com/ge-nfl-head-health-challenge>. Accessed January 17, 2015.
16. National Institutes of Health (NIH). The Brain Initiative. NIH website. <http://www.braininitiative.nih.gov/index.htm>. Accessed January 17, 2015.
17. Cicerone KD, Dahlberg C, Kalmar K, et al. Evidence-based cognitive rehabilitation: recommendations for clinical practice. *Arch Phys Med Rehabil.* 2000;81(12):1596-1615.
18. Cicerone KD, Mott T, Azulay J, et al. A randomized controlled trial of holistic neuropsychological rehabilitation after traumatic brain injury. *Arch Phys Med Rehabil.* 2008;89(12):2239-2249.
19. Salazar AM, Warden DL, Schwab K, et al. Cognitive rehabilitation for traumatic brain injury: a randomized trial. Defense and Veterans Head Injury Program (DVHIP) Study Group. *JAMA.* 2000;283(23):3075-3081.
20. Finley EP, Garcia HA, Ketchum NS, et al. Utilization of evidence-based psychotherapies in Veterans Affairs posttraumatic stress disorder outpatient clinics [published online ahead of print November 24, 2014]. *Psychol Serv.* <https://iims.uthsca.edu/sites/iims/files/VAMH/EBP%20Utilization%20Finleycorrected.pdf>. Accessed March 9, 2015.
21. Schnurr PP, Chard KM, Ruzek JI, et al. Design of VA Cooperative Study #591: CERV-PTSD, Comparative Effectiveness Research in Veterans with PTSD [published online ahead of print November 29, 2014]. *Contemp Clin Trials.* doi: 10.1016/j.cct.2014.11.017. [http://www.contemporarylclinicaltrials.com/article/S1551-7144\(14\)00183-9/fulltext](http://www.contemporarylclinicaltrials.com/article/S1551-7144(14)00183-9/fulltext). Accessed March 9, 2015.
22. Ashman EJ, Gronseth GS. Level of evidence reviews: three years of progress. *Neurology.* 2012;79(1):13-14.
23. Heinemann AW, Hamilton B, Linacre JM, Wright BD, Granger C. Functional status and therapeutic intensity during inpatient rehabilitation. *Am J Phys Med Rehabil.* 1995;74(4):315-326.
24. Berry JW, Elliott TR, Grant JS, Edwards G, Fine PR. Does problem-solving training for family caregivers benefit their care recipients with severe disabilities? A latent growth model of the Project CLUES randomized clinical trial. *Rehabil Psychol.* 2012;57(2):98-112.
25. Bombardier CH, Fann JR, Temkin NR, Esselman PC, Barber J, Dikmen SS. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. *JAMA.* 2010;303(19):1938-1945.
26. Zasler ND, Katz DI, Zafonte RD, eds. *Brain Injury Medicine: Principles and Practice.* New York, NY: Demos Medical Publishing; 2013.
27. Ashman TA, Cantor JB, Gordon WA, et al. A randomized controlled trial of sertraline for the treatment of depression in persons with traumatic brain injury. *Arch Phys Med Rehabil.* 2009;90(5):733-740.
28. Wise EK, Hoffman JM, Powell JM, Bombardier CH, Bell KR. Benefits of exercise maintenance after traumatic brain injury. *Arch Phys Med Rehabil.* 2012;93(8):1319-1323.
29. Ouellet MC, Morin CM. Cognitive behavioral therapy for insomnia associated with traumatic brain injury: a single-case study. *Arch Phys Med Rehabil.* 2004;85(8):1298-1302.
30. Bédard M, Felteau M, Marshall S, et al. Mindfulness-based cognitive therapy: benefits in reducing depression following a traumatic brain injury. *Adv Mind Body Med.* 2012;26(1):14-20.
31. Hart T, Vaccaro MJ, Hays C, Maiuro RD. Anger self-management training for people with traumatic brain injury: a preliminary investigation. *J Head Trauma Rehabil.* 2012;27(2):113-122.
32. Wade SL, Walz NC, Carey J, et al. Effect on behavior problems of teen online problem-solving for adolescent traumatic brain injury. *Pediatrics.* 2011;128(4):e947-e953.
33. Bell KR, Temkin NR, Esselman PC, et al. The effect of a scheduled telephone intervention on outcome after moderate to severe traumatic brain injury: a randomized trial. *Arch Phys Med Rehabil.* 2005;86(5):851-856.
34. Paul LA, Gros DF, Strachan M, Worsham G, Foa EB, Acierno R. Prolonged exposure for guilt and shame in a veteran of Operation Iraqi Freedom. *Am J Psychother.* 2014;68(3):277-286.
35. Suris A, Link-Malcolm J, Chard K, Ahn C, North C. A randomized clinical trial of cognitive processing therapy for veterans with PTSD related to military sexual trauma. *J Trauma Stress.* 2013;26(1):28-37.
36. Mateer CA, Sohlberg MM. Cognitive rehabilitation revisited. *Brain Impair.* 2003;4(1):17-24.
37. Wilson BA, Emslie H, Quirk K, Evans J, Watson P. A randomized control trial to evaluate a paging system for people with traumatic brain injury. *Brain Inj.* 2005;19(11):891-894.
38. Niemeier JP. The Lighthouse Strategy: use of a visual imagery technique to treat visual inattention in stroke patients. *Brain Inj.* 1998;12(5):399-406.
39. Couillet J, Soury S, Leborne G, et al. Rehabilitation of divided attention after severe traumatic brain injury: a randomised trial. *Neuropsychol Rehabil.* 2010;20(3):321-339.
40. Mateer CA. Executive function disorders: rehabilitation challenges and strategies. *Semin Clin Neuropsychiatry.* 1999;4(1):50-59.
41. Rath JF, Simon D, Langenbahn DM, Sherr RL, Diller L. Group treatment of problem-solving deficits in outpatients with traumatic brain injury: a randomized outcome study. *Neuropsychol Rehabil.* 2003;13(4):461-488.
42. Cantor J, Ashman T, Dams-O'Connor K, et al. Evaluation of the short-term executive plus intervention for executive dysfunction after traumatic brain injury: a randomized controlled trial with minimization. *Arch Phys Med Rehabil.* 2014;95(1):1-9.e3.
43. Meythaler JM, Zafonte RD, Lombard L, Reddy CC. Neuropharmacology: a rehabilitation perspective. In: Zasler ND, Katz DI, Zafonte RD, eds. *Brain Injury Medicine: Principles and Practice.* New York, NY: Demos Medical Publishing; 2013:1023-1036.
44. Giacino JT, Whyte J, Bagiella E, et al. Placebo-controlled trial of amantadine for severe traumatic brain injury. *N Engl J Med.* 2012;366(9):819-826.
45. Cernich AN, Kurtz SM, Mordecai KL, Ryan PB. Cognitive rehabilitation in traumatic brain injury. *Curr Treat Options Neurol.* 2010;12(5):412-423.
46. Dusick JR, Wang C, Cohan P, Swerdloff R, Kelly DF. Pathophysiology of hypopituitarism in the setting of brain injury. *Pituitary.* 2012;15(1):2-9.
47. Lemke DM. Sympathetic storming after severe traumatic brain injury. *Crit Care Nurse.* 2007;27(1):30-37.
48. Maas AI, Menon DK. Traumatic brain injury: rethinking ideas and approaches. *Lancet Neurol.* 2012;11(1):12-13.
49. Hergenroeder GW, Redell JB, Moore AN, Dash PK. Biomarkers for

- the diagnosis, prognosis, and evaluation of treatment efficacy for traumatic brain injury. *Mol Diagn Ther.* 2008;12(6):345-358.
50. Jeter CB, Hergenroeder GW, Hyltin MJ, Redell JB, Moore AN, Dash PK. Biomarkers for the diagnosis and prognosis of mild traumatic brain injury/concussion. *J Neurotrauma.* 2013;30(8):657-670.
51. Niemeier JP, Perrin PB, Holcomb MG, et al. Gender differences in awareness and outcomes during acute traumatic brain injury recovery. *J Womens Health.* 2014;23(7):573-580.
52. Perrin PB, Niemeier JP, Mougeot JL, et al. Measures of injury severity and prediction of acute traumatic brain injury outcomes [published online ahead of print February 28, 2014]. *J Head Trauma Rehabil.*