INNOVATIONS IN BRAIN INJURY RESEARCH

Rehabilitomics Research: Dopamine System Pathway Genetics and Recovery after TBI

The CONNECT Trial: Remotely Connecting Traumatic Brain Injury Experts with Those Who Need Them

Decision Support and Behavioral Informatics to Improve Safety and Independent Living Following TBI

Using Biomarkers to Discover Pathways to Healing for Veterans with Traumatic Brain Injury

Chronic Effects of Neurotrauma Consortium
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Brain Injury Professional is a membership benefit of the North American Brain Injury Society and the International Brain Injury Association
When I asked Dr. Ronald Seel and Dr. Michael Jones from the Shepherd Center to serve as guest editors for an issue of *Brain Injury Professional* on research in brain injury, I knew it was no small request. The result is this truly exceptional special edition on Innovations in Brain Injury Research that samples an array of new research initiatives that can be readily translated into clinical practice. The topics in this edition include the use of precision medicine, a web-based service delivery model, and the use of behavioral informatics in risk profiling. In addition, the unique Veterans issues of biomarkers and the treatment of PTSD, as well as the summaries of 10 studies recently funded by the Department of Defense and the Department of Veterans Affairs on the chronic effects of brain injury are included.

At the time of this edition, we are headed into New Orleans for the International Brain Injury Association’s 12th World Congress on Brain Injury which will be held at the Sheraton New Orleans Hotel March 29 – April 1, 2017. As announced in the previous issue of *Brain Injury Professional*, this year NABIS officially became an affiliate of IBIA, and as such has played an active role in contributing to the educational content of the World Congress. Special NABIS sessions at the World Congress include a Pre-Congress Session entitled Evidence Based Assessment and Treatment of Concussion, and a keynote presentation by Jonathan Silver entitled Persistent Symptoms after Concussion: A Neuropsychiatric Perspective. NABIS congratulates the Congress’ scientific leadership, Drs. David Arciniegas, Nathan Zasler, Lisa Brenner, Risa Nakase-Richardson and Angelle Sander for organizing an engaging and educationally robust Congress!

The NABIS 30th Annual Conference on Legal Issues in Brain Injury also will be held in concurrently with the World Congress in New Orleans. Conference co-chairs Stewart Casper, Esq., Simon Forgette, Esq., Kenneth Kolpan, Esq., and Bruce Stern, Esq. have once again put together an outstanding panel of experts covering topics such as admissibility of DTI, case study preparation, pediatric injury, trial psychology, a view from the defense, and more. Attorneys, neuropsychologists, allied Health Professionals, expert witnesses, and others involved in brain injury litigation should attend this seminal conference. For three decades, attendees of this conference come away with the essential hands-on tools needed to successfully manage a complex brain injury case. Please refer to the NABIS website for more details at www.nabis.org.

Looking ahead, NABIS will continue to organize topic-specific and regional meetings in those years when the World Congress in not held in North America. The NABIS leadership is currently exploring educational themes and venues for several exciting events in the Fall of 2018, so look for more information in the next issue!

We hope you enjoy this special edition of *Brain Injury Professional*.
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Tree of Life Services has been helping persons with acquired brain injury optimize their functional outcomes for over 15 years under the leadership of Nathan D. Zasler, MD, internationally recognized brain injury neurorehabilitation physician. We provide transitional rehabilitation and long-term assisted living services in home-like settings in our community.

We strive to optimize client’s functional outcomes by utilizing evidence based medical and neurorehabilitation assessment and treatment strategies along with close medical oversight. Our competitive, individualized per diem rates make us a cost effective choice given our scope of services, quality of care, and beautiful living environments.
We are pleased to serve as co-editors of this edition on Innovation in Brain Injury Research. There are countless, innovative brain injury rehabilitation research efforts underway, which made selecting only a few a difficult endeavor. To be included, we targeted innovative research that directly translated to rehabilitation practice. Research also needed to address at least one of four strategic priorities advanced by the U.S. National Institutes of Health and the Agency for Community Living-National Institute on Disability Independent Living and Rehabilitation Research: (1) Incorporate precision medicine into rehabilitation, e.g., use biomarkers to stratify people into prognostic groups and tailor interventions based on predicted best response; (2) Address disparities in rehabilitation service access, utilization, effectiveness, and outcomes; (3) Advance research, development, and adoption of technology products for remote rehabilitation delivery; or (4) Integrate person-centered planning and self-directed strategies into rehabilitation.

In “Rehabilomics Research: Dopamine System Pathway Genetics and Recovery after TBI”, Myrga, Wagner, and colleagues summarize their precision medicine research program. Dopamine (DA) systems are viewed as promising companion diagnostics because DA neurotransmission is often dysfunctional following TBI, has a strong genetic impact on functioning, and predicts TBI cognitive and behavioral outcomes. Their research found that adult women with moderate-to-severe TBI who have high DA genetic risk scores (GRS) have worse cognitive outcomes compared to women with low GRS; this association was absent in men. These findings establish an evidence-basis for conducting clinical trials in which people with TBI are stratified based on sex and DA GRS to identify the best response to DA enhancing medications per stratified subgroup.

In “The CONNECT Trial: Remotely Connecting TBI Experts with Those Who Need Them”, Bergquist, Moessner and Brown describe their pragmatic randomized trial to test the effectiveness of providing remote specialty brain rehabilitation resources to underserved rural, elderly, and Native Americans in the Upper Midwest. CONNECT links adults recently hospitalized with TBI, their family members, and their local healthcare providers to TBI experts at the Mayo Clinic, primarily using CareHubs®, a customized, web-based network. CONNECT allowed people with TBI to choose their preferred educational materials, services, and care coordination to meet personal goals. The authors discuss early findings and lessons learned in remotely providing TBI rehabilitation specialty services.

In “Using Biomarkers to Discover Pathways to Healing in the Lives of Veterans with TBI and Post-Traumatic Stress,” Chen and colleagues describe an intensive guided learning experiences intervention, in which veterans are taught “brain state-regulation” skills to improve goal-directed functioning.

about the guest editors

Ronald T. Seel, PhD, FACRM, is the O. Wayne Rollins Director of Brain Injury Research at the Shepherd Center in Atlanta, GA. His primary research interests are evidence-based practice, clinical decision support, and self-directed approaches to safe, independent living for people with disabilities. Dr. Seel chairs the American Congress of Rehabilitation Medicine (ACRM) Evidence and Practice Committee. He previously chaired the ACRM Brain Injury-Interdisciplinary Special Interest Group. He received the ACRM 2010 Deborah Wilkerson Early Career Award and the ACRM 2012 Distinguished Member Award. Prior to Shepherd Center, he was Executive Director of the Southeastern Parkinson’s Disease Research Education and Clinical Center and Associate Director of Research for the Defense and Veterans Brain Injury Center at the McGuire VAMC in Richmond, VA.

Michael L. Jones, PhD, FACRM, is Vice-President of Research and Technology, at Shepherd Center, and co-director of the LiveWell RERC for Information and Communication Technology (ICT) Access, a partnership between Shepherd, Duke University, and Northeastern University. A behavior analyst by training, Mike’s research interests address the design and management of programs and services that promote full inclusion of people with disabilities. His work includes applications of universal design, ICT, and behavior management strategies to promote health, wellness, and community participation. Mike received his PhD from the University of Kansas, where he also served as associate director of the Research and Training Center on Independent Living. Prior to joining Shepherd in 1996, Mike was director of the Center for Universal Design at NC State University.
Clinical trial results indicated that veterans who received training to regulate aspects of their brain state improved their ability to maintain goal-relevant information, manage distractions, and re-direct attention to their goals. Based on neuroimaging findings, brain network modularity is an important biomarker of outcomes. The authors found that individuals with baseline well-organized, brain sub-networks (high modularity) exhibited greater treatment response in attention and executive functioning compared to those with random or distributed brain connections (low modularity).

In “Decision Support and Behavioral Informatics to Improve Safety and Independent Living following TBI”, Seel, Jimison and Pavel present an automated decision support program named the Safe@Home Roadmap. The automated program takes the family member’s and client’s observations and applies decision rule logic and regression modeling to tailor recommended goals, a safety risk profile, and a dashboard summarizing the client’s health, functioning, adjustment and resources. They also present their behavioral informatics research program, in which computational modeling converts data acquired from active and passive sensor arrays into inferences about individuals’ performance and recommends just-in-time interventions. The authors use a TBI case example to demonstrate how behavioral informatics can be used in synergy with automated decision support programs to guide self-directed goals.

In “The Chronic Effects of Neurotrauma Consortium (CENC)” Cifu and Carne provide an update on the dually-funded, $62 million Department of Defense/Department of Veterans Affairs grant to improve diagnostics, prognostics, and interventions for veterans who experienced mTBI and have persistent symptoms and co-morbidities. The authors summarize 10 CENC funded projects led by mTBI scientific experts across the country. In addition to longitudinal registry studies, projects described include evaluating the effects of abnormal otolith organ function (an inner ear balance organ), identifying the microstructural nature and functional effect of diffuse heterogeneous white matter abnormalities associated with primary blast injury, standardizing diffusion tensor imaging acquisition techniques, testing psychological and biological markers of mTBI-related neurodegeneration, and studying ocular biomarkers.

Our interview with Michael Choo, MD, Chief Medical Officer of Paradigm Outcomes, LLC, presents a case management perspective on catastrophic rehabilitation care challenges and needed innovations in TBI research. Dr. Choo emphasized the need for better prognostic data for benchmarking service needs and expected outcomes. He added that better treatment data is needed to specify the most effective timing, dose and duration of treatments.

In closing, we thank our article authors and interviewee who are passionate about conducting high quality research in order to improve the lives of people with TBI. They worked diligently to distill sophisticated, scientific approaches in a way that would be accessible to non-researcher, practicing clinicians. We are optimistic that the research in this edition will be of interest to brain injury professionals and show how science and compassion can be synthesized to help people with TBI-related disability.

REFERENCES
Traumatic brain injury (TBI) is a challenging condition to manage clinically. People with similar injury profiles can experience very different functional, cognitive, emotional, and behavioral outcomes. To date, almost every area of medicine uses biomarkers in some capacity to aid in understanding how personal biology informs clinical care. One common approach to using biomarkers is through technologies collectively called "-omics". These approaches enable simultaneous, multiple measurements of a very large number of biomolecules via genomics, proteomics, and transcriptomics assay platforms to tailor and individualize treatments for subgroups based on these results. Our body of work to date suggests that "-omics" technologies can inform rehabilitation-relevant outcomes, including outcome metrics linked to the World Health Organization’s International Classification of Functioning, Disability, and Health (ICF) domains of impairments in body structure and function, activity limitations, and participation restrictions.

As a result of this work, we developed the Rehabilomics model to represent a translational path for programs of rehabilitation research focused on linking personal biology to the biopsychosocial constructs that constitute the ICF model (see Figure 1). Rehabilomics is a conceptual framework from which to investigate diverse outcomes by examining the complex interplay between personal, biological, psychosocial, and environmental factors and to provide a foundation for personalized clinical care and management.

Our Rehabilomics work supports variation in dopamine (DA) systems as a promising biological factor that is: 1) susceptible to dysfunctional neurotransmission following TBI; 2) heavily influenced by genetics and other individual factors in terms of impact on function; and 3) predictive of later cognitive and behavioral outcomes post-TBI. The DA system, particularly the striatum, contributes to many central functions, including reward processing, executive functioning, emotional control, and gait and balance. Midbrain regions make extensive dopamine neuron projections to striatal, mesocortical, and mesolimbic regions, which, along with various cortico-subcortical feedback loops, support these central functions. Importantly, prefrontal cortex (PFC) control of subcortical and limbic structures can modulate cognition and behavior, making the PFC another

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**REHABILOMICS RESEARCH:**

Dopamine System Pathway
Genetics and Recovery after TBI

We believe that continued research into understanding DA genetic variation and its impact on TBI recovery will play an important role in better tailoring treatment interventions and better optimizing the rehabilitation management process in the clinical setting.

JOHN M. MYRGA, SHANNON B. JUENGST, PhD, PATTY M. ARENTH, MD, AMY K. WAGNER, MD
primary dopaminergic area of interest in the context of TBI.

Given the widely studied relationships between DA system function in neurological and psychiatric disorders, evaluating these systems in the context of TBI may prove to be important when: (1) characterizing TBI-relevant impairments, (2) considering optimal drug therapy choices or modalities of cognitive-behavioral therapy, and (3) determining the value of these interventions in reducing the impact of neuro-cognitive-behavioral impairments on functional activities and participation. We provide an overview of the neuro-cognitive-behavioral impairments on functional value of these interventions in reducing the impact of cognitive-behavioral therapy, and (3) determining the impact of DA genetics and cognition research and future directions for personalized treatments among individuals with TBI. 

Clinical studies
Clinical evidence has long suggested that the DA system is a reasonable target for treating cognitive-behavioral impairments. Using DA genetics as a proxy for studying DA system function has proven to be a useful tool to gauge DA system impact on cognitive and behavioral outcomes. To this extent, some researchers have worked to understand the importance of the DA system to outcomes following TBI. Under the umbrella of the Rehabilomics framework, we have taken an additional step by identifying other personal factors (i.e. sex and post-traumatic depression) that may moderate genetic influences on cognitive and behavioral recovery. To understand how Rehabilomics can be used as a tool for biomarker research, we highlight its application to DA system genetics in three major areas: cognition, emotional regulation, and behavior. Further, we highlight how this work may eventually inform personalized treatments among individuals with TBI.

Cognition
Numerous studies, including a review article in 2012, have examined how variation within DA system genes affects cognitive performance on neuropsychological tests (i.e. memory, attention, executive function, verbal fluency). Here we summarize the state of DA genetics and cognition research and future directions for advancing genetic studies among individuals with TBI.

Catechol-o-methyl Transferase (COMT) is an enzyme that primarily controls catecholamine metabolism in the PFC. Early work from Lipsky et. al. suggests the Val allele, of the well-studied Val158Met polymorphism, is associated with poorer performance on the Wisconsin Card Sorting Test (WCST) perseverative errors among those with moderate-to-severe TBI. In another study among those with predominantly mild TBI, the Val allele is associated with increased error rates. Furthermore, we highlight how this work may eventually inform personalized treatments among individuals with TBI.

Experimental studies
Seminal experimental TBI studies from our group demonstrate that striatal DA neurotransmission is impaired in the controlled cortical impact (CCI) model of experimental TBI, with impairments noted in both presynaptic release and uptake. In addition, daily treatment with a DA reuptake inhibitor (methylphenidate) is effective in reversing these abnormalities and improving cognitive performance. These studies have also demonstrated how prefrontal cortical DA system proteins are altered after experimental TBI, and how DA-enhancing agents can improve cognitive performance. Interestingly, both molecular protein expression alterations and behavioral treatment response to DA stimulants have been shown to be sex specific after experimental TBI. Females have smaller injury-induced reductions in regional DA transporter expression, more motor activation, and no cognitive benefit with treatment on spatial learning. These findings are consistent with the body of literature demonstrating a sex dichotomy with DA system function in health and disease wherein there is a higher sensitivity to the addictive effects of dopaminergic psychostimulants in females relative to males.

Ankyrin repeat and kinase domain containing 1 (ANKK1)/ Dopamine receptor D2 (DRD2). The ANKK1 gene is associated with multiple signaling pathways. One of the most frequently studied variants within this gene is the Taq1a variant. The A1 allele has been associated with poor performance on the California Verbal Learning Test (CVLT) at month after mild-moderate TBI. The A1 allele has also been associated with poorer performance on the CVLT total learning score (trials 1-5) and the Wechsler Adult Intelligence Scale (WAIS) Processing Speed Index (PSI) in a predominately mild TBI sample. The genetic variation effects on cognition noted here are consistent with this gene variant’s effects on...
cognitive performance in the general population. Interestingly, in a more severely injured population, we show the A2 allele to be associated with worse 6 and 12 month cognition, measured with a cognitive test composite scores, compared to the A1 allele. However, more studies are needed to evaluate how allelic interactions with injury severity might result in specific changes in DA system neurotransmission and cognition.

**Vesicular monoamine transporter (VMAT2)** VMAT is a vesicular membrane protein responsible for transporting monoamine neurotransmitters from the cytosol into the synaptic vesicles for subsequent storage and synaptic release. Polymorphisms in the VMAT2 gene affect this transport and are implicated with multiple types of neurological and psychiatric disease. Given its role in multiple aspects of DA release, reuptake, and activation, this gene may have an influence on how DA system variation affects outcomes. To that end, we have shown that variation at rs363226 in the VMAT2 gene is linked to our cognitive performance composite scores after severe TBI.

**A Rehabilomics Approach to DA Genetics and Cognition**

While these studies provide vital groundwork and rationale for further investigation into the relationship between DA genetics and cognition after TBI, it is important to note that our work provides concrete evidence for how DA genetics affect cognitive performance across multiple cognitive domains. Rehabilomics may eventually support studies aimed at identifying effective, personalized treatment approaches for individuals with numerous cognitive deficits that are unique to the TBI field. As we continue laying groundwork for these studies, we would like to share some of the methods we have employed from other fields to continue expanding the scope of TBI research.

One method we have employed is the use of cognitive composite scores created by averaging norm-based scores on multiple neuropsychological tests to generate a “big picture” understanding of cognitive dysfunction after TBI. Since cognitive impairment in multiple domains is common after TBI, this approach provides an aggregate summary of cognitive performance, both at the level of individual cognitive domains and overall performance, to assess the impact of DA pathway genetics. Our work and others suggests composite scores in TBI may prove to be a useful translational element for correlating biomarker levels to system level outcomes.

Since each genetic variant within a biological pathway often accounts for a small change in function, it logically follows that focusing on any one variant in isolation may not contribute greatly to overall variance in any outcome of interest. While not specific to DA systems and cognition, the acknowledgement of this phenomenon has resulted in the development of gene risk score (GRS) methodologies and best practices. GRS approaches allow researchers to examine previously identified biologically relevant polymorphisms and how they each incrementally add to observed outcomes.

**Sex-Specific GRS for Cognitive Impairment after TBI.** Rehabilomics highlights the importance of grouping, such as by sex, based on relevant biological systems. In our recent article, we built on the study by Jacobs and D’Esposito that highlighted the importance of estrogen in moderating relationships between COMT gene variants and executive functions, by stratifying our sample of adults with moderate-to-severe TBI by sex to evaluate genetic relationships with cognition and to develop a sex-specific GRS. We identified important sex differences in GRS score formulation and sensitivity to cognitive outcomes. Specifically, we showed greater influence of DA genetic variants on cognitive performance in women compared to men. Women with higher GRS scores had worse outcomes compared to women with lower GRS scores; the association between cognitive performance and DA GRS was absent in men. Using our growing repository of biomarker samples, we will next assess how concurrent estradiol levels in women may moderate pathogenesis of DA if present.

**Extending**...
of successfully studying and managing the heterogeneous population sustaining TBI. This work highlights the importance of evaluating previously studied SNPs with strong evidence of relationships to outcomes of interest in other populations, as they relate to a strong biological rationale within a TBI-specific population. This work also suggests that in addition to genetics, other personal factors like sex and depression status can markedly influence genetic associations with outcome. Finally, the body of work described here begins to outline the potential for Rehabilomics-guided research to address important questions about multi-dimensional outcome prognostication and biological susceptibility to complications across the range of populations with disabilities that rehabilitation professionals treat.

While these results prove interesting from a research perspective, it’s important that we are able to then translate them into the clinic where they can be used and directed to effective and personalized patient care. With the clinical importance of the DA system in cognitive-behavioral function and disease, we believe that continued research into understanding DA genetic variation and its impact on TBI recovery will play an important role in better tailoring treatment interventions and better optimizing the rehabilitation management process in the clinical setting. These studies may even be used to help create diagnostic decision trees to determine who is at greatest need for often limited psychosocial resources (See Figure 2 for conceptualization). Finally, we believe that this integrated approach to research and clinical care, using a Rehabilomics model, provides us with the framework for working towards truly personalized care, including medical, pharmacological, behavioral and psychosocial treatments for all individuals living with disability.

Behavior and Emotional Dysregulation
Mood and behavioral problems are common complications after TBI. Based on the theoretical premise of the Rehabilomics model and our growing body of work on depression and behavioral dysfunction after TBI, we developed a conceptual model that defines behavior as the outward manifestation of the interactions between cognitive control, emotional regulation, personal factors (e.g. personal genetics), and one’s environment. We have conducted two studies that support this conceptualization, lending particular evidence to behavioral dysfunction manifesting from, rather than in, depression. These studies, however, did not assess personal factors, such as personal biology or personal genetics.

To investigate how personal biology influences our behavioral model, we examined relationships between behavioral dysfunction, DA system genetics, and depression in a study titled COMT & ANKK1 Genetics Interact with Depression to Influence Behavior Following Severe TBI. We found that the Val158Met and Taq1a polymorphisms were not directly associated with behavioral dysfunction following injury. However, examining these genetic relationships in the context of depression showed that those who were depressed and also Val158Met Met-homozygotes and/or were Taq1a A2-Homozygotes reported significantly worse behavior at 6 and 12 months after moderate to severe TBI. This finding is consistent with previous work demonstrating that the relationship between Taq1a and behavioral dysfunction may differ in the context of emotional dysregulation such as that which occurs in clinical syndromes like PTSD or depression.

We have now generated a conceptual framework, which we will test in future research, for DA genetic associations with behavioral dysfunction, associations that may help brain injury professionals stratify “at-risk” individuals into intensive monitoring of emotional and behavioral symptoms in order to mitigate, manage, and prevent the negative impact of these sequelae on TBI recovery (see figure 2 for conceptualization).

Conclusion:
We believe that our work, as summarized in this paper, helps to integrate the wide-ranging areas of contemporary neuroscience, biomarker, and genetic research that has been growing in the TBI field. This type of integration is essential to the aims of successfully studying and managing the heterogeneous population sustaining TBI. This work highlights the importance of evaluating previously studied SNPs with strong evidence of relationships to outcomes of interest in other populations, as they relate to a strong biological rationale within a TBI-specific population. This work also suggests that in addition to genetics, other personal factors like sex and depression status can markedly influence genetic associations with outcome. Finally, the body of work described here begins to outline the potential for Rehabilomics-guided research to address important questions about multi-dimensional outcome prognostication and biological susceptibility to complications across the range of populations with disabilities that rehabilitation professionals treat.

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Moderate to severe traumatic brain injury (TBI) is often associated with activity-limiting impairment that is long-lasting (Brown et al., 2011), high levels of disability (Selassie et al., 2008; Zaloshnja et al., 2008), and ever changing chronic medical needs (Masel and DeWitt, 2010). This makes it crucial to link individuals and their families with outpatient rehabilitation, medical services, and community resources to establish a long-term continuum of care. However, many factors make these connections difficult. First, few comprehensive brain rehabilitation practices are integrated into the acute services of trauma centers, where most severe injuries are managed and linkages to outpatient rehabilitation are customarily made. Second, shorter acute lengths of stay reduce time to establish connections. Third, funding for outpatient care is often limited or services are unavailable, particularly for individuals of low socioeconomic means, the uninsured, and underserved ethnic groups. Last, individuals living in rural settings face transportation obstacles to access urban rehabilitation centers. The upper Midwest population served by Mayo Clinic’s TBI Model System Center has a uniquely high risk for unmet service needs due to its low population density, and high proportion of elderly and Native Americans. These access barriers increase risk for poor outcomes while adding to personal and societal health-related costs.

Some health care systems, state agencies, and community-based organizations have developed procedures for linking individuals hospitalized for TBI with resources after hospital discharge. Studies using telephone follow-up and remote caregiver training to influence TBI outcomes have shown mixed results (Bell et al., 2011; Trexler et al., 2016). The practice of remotely providing medical and rehabilitation services to increase access and reduce health-related cost has rapidly expanded over the past decade, as information and communication technology has advanced and become widely available (Forducey et al., 2003; Bergquist et al., 2009; Turkstra et al., 2012). Given the paucity of evidence, there has been a universal call for rigorous studies to test remote service delivery. Individuals hospitalized for TBI, their families, and local healthcare providers have consistently identified connection to TBI rehabilitation and community resources as an unmet need (Corrigan et al., 2004; Heinemann et al., 2002). The CONNECT Trial tests a model of care that remotely connects specialty brain rehabilitation resources to underserved populations. Establishing and maintaining these connections is expected to improve participation and satisfaction with healthcare.

The CONNECT Trial

The CONNECT Trial (clinicaltrials.gov) tests the effectiveness of a novel, complex behavioral intervention provided remotely to improve outcome for individuals hospitalized for TBI. A community-based, randomized, pragmatic clinical trial design was used, to compare a usual care control group to CONNECT intervention. A pragmatic trial differs from a randomized control trial by allowing patient and provider choice that typically occurs in everyday clinical practice. The CONNECT Trial aims to remotely connect the following groups to Mayo Clinic’s brain rehabilitation specialists and to each other: 1) individuals at least 18 years old recently hospitalized (with or without an inpatient rehabilitation stay) for at least one night with a medically confirmed diagnosis of TBI; 2) their family members and significant others; and 3) their local health care providers (primary care providers, other medical specialists, therapists, counselors, social service staff, vocational counselors, case managers). The study is being conducted in Minnesota, Iowa, North Dakota, and South Dakota. Research participants are identified through state trauma registries in Minnesota and Iowa and at large regional trauma hospitals in North Dakota and South Dakota. Individuals who received inpatient care at Mayo Clinic Hospital-Saint Mary’s Campus
in Rochester, MN, are excluded.

Once consented, CONNECT Trial participants identify one family member/significant other and up to two local providers who are approached for study participation. Individuals with TBI are randomly assigned to one of two groups: the Remote Care study intervention group or the Usual Care group. Consented others and local providers are assigned to the same group as the identifying participant. Study hypotheses are: 1) Participants in the Remote Care group will show greater improvement in participation compared to those who receive usual care; 2) Participants and their family members in the Remote Care group will be more satisfied with their health care compared to those in the Usual Care group; and 3) Local providers in the Remote Care group will report greater satisfaction with caring for individuals with TBI compared to local clinicians providing usual care.

Nature of the CONNECT Intervention
An Advanced Practice Nurse and the participant with TBI discuss current level of function and TBI related needs. Clinical and interview data are evaluated by the research team. Interventions offered include guidance, education, and support services from Mayo’s Interdisciplinary Brain Rehabilitation Clinic, which include a physiatrist, neuropsychologist, rehabilitation nurses, speech language pathologist/cognitive rehabilitation specialist, physical therapist, clinical social worker, and vocational counselor. Commonly used educational resources include those developed through Mayo Clinic’s Office of Patient Education, as well as print and video available from the Model System Knowledge Translation Center (www.msktc.org). The type and frequency of education, supportive services, and remote communication technology used (i.e., phone, mail, e-mail, texting, social media, skype, web-based technology) is determined by participants’ needs and preferences. Remote Group participants receive a personalized combination of services with no in person interaction with Mayo Clinic providers. In collaboration with Mayo’s Centers for Social Media and Innovation and CareHubs® (carehubs.com), a password protected, web-based community was created and made available to all Remote Care participants. This online community allows for interaction among individuals with TBI, their families and local and Mayo Clinic providers in three ways: 1) a home page/main feed where all participants can post questions or comments, read what has been posted, and respond; 2) a peer only feed (i.e., TBI group, family group, and provider group); 3) a ‘Personal CareHubs®’ group for each participant with TBI, family member, and provider set, and their Mayo Clinic providers (see Figure 1 for CareHubs® examples). The CONNECT Trial CareHubs® site is monitored daily in order to respond promptly to new postings and introduce topics of conversation and resources on a weekly basis.

Remote Group participants are regularly notified about study activities, TBI educational offerings, and other resources. Regardless of need, ongoing access to TBI expertise and peer support occurs throughout the 18-month study period. This lasting connection to TBI healthcare providers is the most common need identified by statewide needs assessments funded by TBI Health Resources Service Administration Planning Grants.

Individuals in the Usual Care group receive the care and follow up they would normally receive from local providers. The research team does not interact with participants in the Usual Care other than collecting data.

Data Collection
Outcome measures are grouped by World Health Organization (WHO) International Classification of Functioning Disability and Health (ICF) realms and include measures of impairment (clinical measures of injury severity by medical record review), activity limitations (Activity Measure for Post-Acute Care, AM-PAC™; am-pac.com) and participation restrictions (select PROMIS® measures including Neuro-QOL; healthmeasures.net) using the Assessment CenterSM (assessmentcenter.net). Additional outcomes include satisfaction with health care experiences and a quarterly survey of the type and amount of healthcare services used. The same data is collected for participants in the Remote Care and Usual Care groups at enrollment, and 6- and 18-months post-enrollment. Outcome data are acquired either electronically, or by mail or phone.

Preliminary Findings
Towards a target of 450 participants with TBI, we have accrued more than 260 to date. The average age is 58, 50% are male, and 40% are rural dwellers. Falls are the leading cause of injury
and the majority had positive intracranial imaging. The average time-since-injury at enrollment is nearly 4 months. The majority of participants have been recruited from Minnesota and Iowa. There are no differences in demographic or injury-specific characteristics between treatment groups.

Challenges and Recommendations for Future Interventions

Many participants reported they no longer needed rehabilitation or other services when approached for study participation. TBI education and support was reported as an unmet need in the early weeks following injury. A notable challenge has been the limited response of local healthcare providers to participate. This important group was targeted to build TBI expertise and capacity in the region. The poor response rate may reflect local provider’s perceptions that study time demands outweigh benefits. The interactive, web-based CareHubs site is effective only to the extent that it is used. While recent research indicates that a large percentage of individuals with TBI have access to the internet and use it regularly (Baker-Spar, et al., in press), a sizeable portion of CONNECT participants, even those with internet access, prefer to interact with our clinical team via telephone. Phone calls demand real-time communication and coordination of schedules that can be challenging for health care providers during the work day, potentially affecting the sustainability of this care coordination model.

Advances in information technology have provided an increasing number of pathways to connect patient populations with specialized medical and rehabilitative services. Integrating this technology into the design of Electronic Health Record systems could make these interactions between consumers and providers a natural part of medical care, promoting transparency and better health outcomes.

Summary

The link between hospital-based and outpatient services is of primary importance to establishing a continuum of care as individuals with TBI and their families transition from the hospital to their communities. Rapid advances and access to information technology makes the remote delivery of TBI education, services and care coordination to underserved individuals increasingly appealing. The CONNECT Trial is designed to test a community-based intervention that targets unmet needs consistently identified by individuals with TBI and their families using specialized brain rehabilitation resources provided remotely by a variety of means, including web-based technology. If study results support our hypotheses, a hub-based system of remotely coordinated brain rehabilitation care might be feasible in other national regions. Regardless of this trial’s outcome, CONNECT has provided investigators and participants with valuable experience that will shape future models of clinical care in our communities.

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Decision Support and Behavioral Informatics to Improve Safety and Independent Living Following TBI

Impaired attention, memory, and self-awareness are common following moderate to severe TBI and affect people’s ability to self-manage activities and health, recognize risk, take preventive action, and learn safe strategies. Unintentional injuries are common and result from falls, improper use of motor vehicles and equipment, burns, poisonings, being struck by objects, and firearm-related incidents. Other risks of harm include errors when managing medical conditions, loss of money or valuables, inappropriate responses in emergency situations, and victimization. Increasing independence and decreasing harm and caregiver burden are primary outcomes important to people with TBI, their families, healthcare providers, payers, and policy makers. This article describes research to create innovative, scalable, and portable approaches to improve safety and independent living for people with moderate to severe TBI. This work is funded through the NIDILRR Rehabilitation Engineering Research Center for Information and Communications Technology Access (www.livewellrerc.org).

Challenges in meeting safety and independence needs—A case example
John Smith, 46 years old, sustained a severe TBI in a work-related motor vehicle crash. He had a 21 day acute care stay and 28 days of inpatient rehabilitation. He experienced disordered consciousness and post-traumatic confusion for 46 days. He was discharged home and remains closely supervised by Mary Smith, his wife of 22 years. John received outpatient therapies for 8 weeks. Now at 6 months post-injury, his worker’s comp case manager is making a home and community-based service referral to address what Mary describes as her husband’s worsening attention and memory, lack of initiation, fatigue, and safety risk. John’s goals are to get his life back, do the things he used to do on his own, and feel better. Mary is feeling burned out from providing recommended full-time supervision and wants her life back too.

Balancing the independence, safety, and supervision needs of a person with TBI can be complicated. Families and payers often rely on rehabilitation providers’ determination of supervision needs, but full-time supervision and activity restrictions are often recommended to maximize risk mitigation. Providers of home and community based services typically have little experience assessing or treating people with severe TBI, who often have multiple chronic impairments and health conditions, behavioral issues, wide variability in day-to-day performance, and limited social support and resources.

Improving decision support in the home and community
Our team used state-of-the-science methods to develop the Safety Assessment Measure (SAM). This assessment stratifies safety risk following TBI in four primary functional areas: Carrying Out Activities, Mobility, Judgment, and Self-Control (Seel et al, 2016). The SAM scales have proven to be valid and reliable in predicting unsafe events such as unintentional injuries, medical events, victimization, and harm to others (Seel et al, 2013). Carrying Out Activities and Mobility scores, awareness of impairments, sleep quality, alcohol use, and family’s level of supervision have been identified as key predictors of unsafe events.

We then developed a web-based prototype of a tool to generate a personalized safety risk assessment named the “Safe@Home Roadmap.” An automated program takes the family member’s and client’s observations reported on the SAM and applies decision rule logic and statistical modeling to generate: (1) activity goal recommendations; (2) an evidence-based risk profile; (3) a dashboard summarizing the client’s health conditions,
functional abilities, adjustment to disability, and resources; and (4) recommended safety strategies and environmental modifications. The Roadmap was developed based on focus-group feedback from people with TBI and their families. Home health professionals, life skills coaches, family members, or high functioning clients can use the Roadmap as a starting point for assessing needs, setting person-centered goals, and securing services and supports.

**John Smith's Roadmap to Safe, Independent Living**

Once the client and family member complete the web-based survey, a roadmap is automatically generated that provides personalized information in a standard format (see Figure 1). In this section, we highlight key aspects of John Smith's Roadmap report.

- John Smith's Roadmap (see Figure 2) provides recommendations on specific activities that can be done independently (page 2-green coding), “next step” goals to work on with professionals or family (page 3-yellow coding), and activities to be temporarily avoided (red coding, page not shown).

  - These specific activity recommendations are custom coded based on the family member's ratings of the client's ability, the difficulty of each activity based on Rasch analysis, and the decision rule logic.

  - The Roadmap then presents John Smith's risk profile (see Figure 3). Regression modeling indicates he has a 39% likelihood of having an unsafe event in the next 4 weeks. John's level of safety risk associated with Carrying Out Activities, Mobility, Judgment, and Self-Control (low-green, medium-yellow, or high-red) is then presented. Tree modeling algorithms define the extent that secondary factors such as awareness of impairments, alcohol use, sleep quality, and family involvement (full-time supervision) increase or reduce risk relative to each primary factor. A modified risk rating is then generated for each primary factor.

  - John Smith's risk profile highlights Carrying Out Activities (cognitive impairment), Mobility, and Judgment as primary factors that drive his safety risk. Alcohol use and poor sleep in essence cancel out Mary's positive involvement in his recovery and worsen his risk associated with Judgment and Self-Control. The risk profile implicitly suggests that abstaining from alcohol use and improving sleep would decrease his risk across functional abilities.

  - John Smith's Vital Signs dashboard from his Roadmap presents his current medical and mental health conditions, functional abilities, adjustment to disability, assistive equipment used, family re-sources, family coping, and cultural preferences (see Figure 4). A provider can review John's dash-board for critical areas that require immediate intervention (coded red), identify potential interactions between risk factors, and use motivational interviewing to reach consensus on next steps that address John's goals and resolve risks. John has five health conditions (coded...
yellow) that require medication but “resources” indicate they can’t afford medical expenses (coded red). The provider will need to check which prescriptions (if any) the Smiths are filling and problem-solve how to cover healthcare expenses. John screens positive for sleep apnea, insomnia, heavy alcohol use, and depression (coded red), which may exacerbate attention, memory, and initiation impairments. Prioritizing a referral to diagnose and treat sleep, depression, and anxiety, and resolving alcohol use issues will help John meet his goal of feeling better. It will also clarify the residual severity of cognitive impairments and inform the need for additional services. Improving social support will improve client and family adjustment.

The Safe@Home Roadmap synthesizes a considerable amount of assessment information to high-light risks and recommend next steps for intervention planning. However, decision rule logic and statistical models are dependent on family and client observations that sometimes are too inaccurate, incomplete, or contradictory to provide a valid presentation of the functional abilities, risks, and service needs of the person with TBI. Incorporating objective data to complement subjective observations would likely improve precision in assessing behaviors, making diagnoses, and selecting services and supports that best address specific needs.

Using Behavioral Informatics to Improve Assessment, Treatment Decisions and Outcomes

Researchers at Northeastern University have developed behavioral informatics systems to support safety and independence in aging adults (Jimison et al, 2007, Pavel et al, 2013, Ofli et al, 2015, Hagler et al, 2014, Jimison et al, 2004) Behavioral informatics (BI) is a scientific and engineering area that encompasses behavior monitoring, assessment, computational modeling, inference, and intervention (Pavel et al, 2015). BI uses data from active and passive sensor arrays to monitor physical and physiological aspects of behaviors, convert raw data into behavioral inferences, and generate behavioral interventions. BI can be used as a companion diagnostic along with observational assessment to improve: (a) performance measurement; (b) differential diagnosis; (c) identification of activity level and participation; (d) severity and risk stratification; (e) decision support to improve the precision of matching evidence-based treatments, services, and supports to the client’s needs; and (f) assessment of intervention effects.

The foundation of BI rests upon the reliable and valid acquisition of raw data from sensors and accurate recognition (or inference) of behavior and activities from these raw data. Recent advances in sensor and communication technology coupled with computational modeling have led to an unprecedented ability to quantify real world behavior. Many wearable or active sensors such as accelerometers, heart rate monitoring devices, and other electrode based sensors are readily available in the commercial market and collect physiological data that are transformed based on inferential algorithms into performance measures (see figure 5.)

The use of minimally obtrusive or unobtrusive heterogeneous (passive) sensors such as passive infrared (PIR) motion-based sensors, piezoelectric bed sensors, radio-frequency identification (RFID) tags, global positioning system (GPS) tracking units, environmental sensors, and contact switches provide broad data acquisition capabilities around the home to infer and monitor walking performance, activity level, sleep quality, medication compliance, activities of daily living, use of assistive equipment, and environmental context (see illustration in figure 6).

Just as limiting inaccurate and incomplete data is critical to the optimal use of self- and family-reported observations, data quality assurance is also critical to producing reliable and valid behavioral inferences from sensors. Wearable sensors have the advantage of directly measuring physiological effects associated with activity. Yet, relying on people to put on, operate, and maintain these devices can only be sustained in the short-term, and in cases of people with cognitive and physical impairments, wearables may not be implementable at all. Unobtrusive (passive) sensors embedded in the environment are more easily sustained in the long-term but
provide only surrogate markers of activity and behavior. Missing and censored data, apparent outliers, environmental distortions, and lack of context are challenges when trying to infer activity from sensors, and are particularly problematic when using passive sensor data. Multiscale computational modeling, which uses data from multiple sensor sources, is frequently employed to minimize data quality challenges and improve inferences.

**Synthesizing Clinical Decision Support and Behavioral Informatics in TBI Practice**

So how can we use BI to improve John Smith’s safety and independent living? We begin with the premise that home technology in healthcare is a complimentary tool that can extend the reach of clinical practice, increase precision in behavioral and diagnostic assessment, and improve the selection and delivery of best evidence interventions (see Figure 7).

In Step 1, we identify key clinical questions in which technology might be useful to obtain more precise measurements of John’s alcohol use, sleep, activity, medication use, social life, and their interactions in order to resolve diagnostic dilemmas and better specify needs. In Step 2, we use passive sensors and an activity tracker to acquire physical data and computational modeling to make inferences about the activities relevant to our key questions. In Step 3, we review the BI findings about John’s: (a) alcohol use and its impact on his mood and self-control; (b) sleep hygiene, quality, and quantity; (c) depression level; (d) activity level; (e) medication use; and, (f) social contacts. In Step 4, we tailor interventions based on BI results to abstain from alcohol use, treat depression, increase meaningful activity, take needed medications, and increase social contact. Continued monitoring of symptoms and activities using self-report and sensor-driven data also provides time sensitive feed-back, tracks and rewards progress on goals, and updates or identifies new clinical questions.

Our research and development collaboration is still in the early stages. Several efforts are under-way to improve our knowledge and generate usable products:

- The web-based Roadmap is currently being used as a core component in a NIDILRR-funded clinical trial, in which life skills coaches deliver between 6 to 14 home visits to individuals with TBI and their families with a focus on setting shared goals, providing education and training, and improving safety and participation. Evidence on program effectiveness and helpful aspects of life skills coaching will inform the further development of the Northeastern virtual coach system.

- The proof of concept, web-based, automated clinical decision support programming used to generate the Roadmap presented in this article has produced reliable and valid information. The survey administration and Microsoft table formatting of the Roadmap are not commercially viable. Shepherd Center is collaborating with ChartAssist LLC—a software development company specializing in multidisciplinary, electronic medical record, data collection and predictive analytics—to develop a commercially viable web-based, mobile, decision support app that will facilitate assessment, service selection and delivery, and outcome tracking for people who have sustained moderate to severe TBI. The app platform will accommodate future development and implementation of behavioral informatics into TBI care.

- As part of the LiveWell RERC project, our interviews with people who have sustained severe TBI reveal diverse interests, needs and abilities in using sensors and communication technologies to increase safety, performance and independence. These perspectives inform the development of decision support and behavioral informatics technology products.

- Northeastern’s approach to helping people with TBI manage their lives involves the use of a Health Coaching Platform. Sensor and participant self-report data are collected and processed via model-based assessment, predictive inference, and assessment algorithms that translate the data into useful information for a remote coach and the person with TBI. The proof-of-concept Health Coaching Platform has worked well in research settings. It too is evolving and being “renovated” for home use in order to increase usability and commercial viability.

- We have many remaining challenges in applying BI approaches to people with TBI and specific functional domains. Considerable work remains in developing measurement processes to transform raw data from unobtrusive, continuous sensors and people with TBI into actionable information. In the near future, we will be testing explicit computational models of individuals with moderate to severe TBI.
Summary
Automated clinical decision support programming has the potential to assist a myriad of healthcare stakeholders in sorting through the complexity of multiple chronic health conditions, functional abilities and impairments, and environmental risks and protective factors experienced by people with severe TBI in order to identify critical factors and prioritize interventions. BI has the potential to provide people with TBI, their support network, and healthcare professionals with reliable and valid information on clients’ activity levels, participation, mood, sleep quality, alcohol use, and medication adherence. Applying BI systems in synergy with automated clinical decision support programming may improve: (1) empirically-based stratification of safety risk; (2) early identification of primary and secondary factors that drive risk across situations; (3) increased precision in measuring symptoms, functional ability, and environmental factors that expedites differential diagnosis; (4) the selection and delivery of individualized treatment plans including medications, supervision and supports, functional training, and behavior and environmental modifications; and (5) evaluating longitudinal change in performance, including evaluating individual treatments and service program effectiveness. The potential of these approaches to increase the precision, efficiency, and individualization of TBI long-term services and supports holds great value for a financially strapped healthcare system that seeks to deliver high value services.

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A combat medic in the wars in Iraq and Afghanistan encountered daily challenges years later as a Student-Veteran: “… I can't remember anything unless I go over it a thousand times, I can't keep focused on anything, and I just can't seem to figure out a way to make myself better! I will be in lecture, and every time someone opens a door, stands up, coughs behind me too loud, or whatever, I go completely off the professor to look at what it is. Then I look back at the professor and I realize I've totally lost track of what they are saying, and as I scramble to catch up, I get so nervous about it, that I am again not paying attention to what he is saying!”

This is the lived experience of many Veterans who struggle with traumatic brain injury (TBI) and post-traumatic stress (PTS) symptoms. Difficulty holding information in mind, remaining focused in the presence of distractions, recalling information, and adaptively regulating emotions can have far-reaching and devastating effects on goal-directed functioning, undermining success in school, work, and other aspects of personal life. Help from brain injury professionals is vital to preventing these experiences from devolving into a downward trajectory of setbacks and disappointments. There is a great need for intervention research and development focused on the issues most commonly affecting current generation Veterans (Cooper et al., 2015).

One area of critical importance for intervention development is helping individuals regulate their cognitive and emotional states, focused on and guided by their personal goals. The story above highlights the need for interventions that address chronic difficulties, unify complexities of neuro-cognitive-emotional functioning in an individualized goal framework, and empower the individual to improve their well-being and achieve their life goals (i.e. taking a strength-based approach). This Veteran's story also draws attention to the need to minimize gaps in care, helping Veterans 'where they are.' In this article, we review a line of work focused on helping individuals better regulate cognitive-emotional states to pursue their goals, discuss our process of using neural biomarkers to test and build a foundation in intervention theory, and describe implications for service delivery.

Over the past decade, we have collaborated with Veterans and others to develop tools and approaches for improving goal-directed functioning. We have worked to bring together...
clinical rehabilitation best practices, cognitive neuroscience, technology, education, and individualized goals to forge innovative pathways to improve brain functions essential to pursuing and attaining goals in the face of challenges. We have adopted a rehabilitation neuroscience approach to developing interventions for real-world application, which involves testing our interventions systematically to examine their practical applications as well as theoretical underpinnings. This work allows for ongoing, iterative improvements and has led to a series of interventions that emphasize intensive guided experiential learning to improve functioning in the lives of brain injured individuals.

**Targeting Regulation of Internal (Brain) States Utilizing a Goal Framework**

Our goal is to help individuals improve abilities fundamental for learning, adapting, problem-solving, and, more generally, achieving goals in challenging situations (Chen & Loya, 2014; Chen & Novakovic-Agopian, 2012). We argue that impairments with goal-directed functioning are often related to underlying problems regulating internal (brain) states during goal pursuit. At the behavioral level, continuous and dynamic regulation is needed throughout the entire goal pursuit endeavor, from the initiation of goal-directed activities to overcoming potential challenges to goal achievement. At the neural level, modulation of brain states affects signal and noise properties of information processing systems upon which goal-directed functioning is based. Some brain states, reflected in parameters of functional brain networks, may be associated with enhanced learning, memory, and self-control, and this has direct implications for rehabilitation (Arnemann et al., 2015). This foundation has informed our approach to training state-regulation skills (SRS). Improving the goal-directed regulation of brain states is hypothesized to help individuals better achieve their goals by strengthening their abilities to direct and sustain attention toward goal-relevant information, selectively maintain this information over time, manage non-relevant distractions, and re-direct attention.

We argue that for SRS to be effectively learned, training should include at least four key elements (Chen, Loya, & Binder, in press). First, training should facilitate each trainee’s conceptual understanding of trained skills, including the underlying rationale and intended benefits of skill use. Second, training should include opportunities where skill use can be extensively practiced across a wide range of goal contexts and challenges. This may help with skill development and promote automaticity in skill use, increasing the likelihood that a state regulation response will be triggered in-the-moment during any challenge context. Third, training should increase trainees’ awareness of situations where their goal-direction is vulnerable to disruption, and foster their intentions to apply skills in instances when they are most likely to be derailed. Finally, these elements need to be tied together in a goal framework, explicitly supporting the strategic application of SRS to bolster goal attainment efforts. Together, these elements may maximize application of SRS in situations when and where they are needed most.

With these principles in mind, we first designed a group-based experimental intervention protocol for training goal-oriented attentional self-regulation (GOALS; Novakovic-Agopian et al., 2011). The primary focus of training is learning to strategically apply SRS across multiple settings and contexts. Training involves supported practice of a Stop-Regulate strategy, cued using the mantra Stop-Relax-Refocus, during in-session exercises and in relation to personal life goals and individual and group projects. To help guide strategic skill application in a goal framework, participants are instructed in stepwise goal management strategies (Levine et al., 2007). In an initial pilot, 16 brain injured individuals receiving training demonstrated greater improvements on neurocognitive measures of complex attention and executive functions, a real-world functional task, and self-reported abilities relative to a brief educational control intervention. The vast majority of these participants (94%) also reported continued strategy use 2-3 years following training (Loya et al., 2017). Larger controlled studies for Veterans with TBI and TBI-PTS are ongoing; preliminary findings of these studies parallel improvements found in our pilot investigation.

**Harnessing Technology to Enhance Neurocognitive Skills Training**

We next sought to intensify training of SRS by providing a greater range of contexts, with a calibrated progression of challenges for experiential learning. Providing additional active learning opportunities during training may enhance skill learning and facilitate skill transfer to everyday goal pursuit, particularly if reinforced by coaching supported by direct observations and quantification of skill application. This approach is intended to directly address the limited amount of ‘hands on’ coaching possible in traditional rehabilitation settings.

We therefore developed training systems that support intensified guided learning of SRS via stepwise experiences. This approach integrates skill instruction, interactive coaching, and intensive skill practice across multiple contexts and settings, bridging from digital game-based scenarios to personal life. We developed a series of digital game scenarios drawn from ‘real-life’ situations to increase the intensity of experiential learning opportunities, ensure that targeted brain functions are challenged in a wide range of complex contexts, increase the relevance of skill practice, and provide concrete experiences to guide discussions of skill transfer to personal life. (See Figure 1.) To maximize learning, an underlying neuroscience-
What Neural Mechanisms Support Improvements in Functioning?

In order to investigate neural mechanisms that support functional improvements, we have worked with two lines of functional magnetic resonance imaging (fMRI) biomarkers that capture processes of interest (Arnemann et al., 2015; Chen et al., 2011; Chen et al., 2012; Nomura et al., 2010). These two lines reflect complementary aspects of the working brain in terms of functionally integrated networks. (See Figure 2.)

Individuals were scanned before and after GOALS training vs. a brief comparison education activity, and we examined individuals were scanned before and after GOALS training that support functional improvements; however, the training system implementation also has practical implications for addressing gaps in rehabilitation care.

**Figure 2**: Multi-voxel patterns from functional imaging of posterior brain networks (left) were decoded by a neural network pattern classifier to index processing of goal-relevant (represented by red) vs. non-relevant (blue) visual information (center), with the finding that training resulted in an increased balance of processing of goal-relevant information (right).

**Neural markers of ‘readiness to learn?’**: Parameters of functional brain network organization as predictors of learning in response to training. Cognitive actions always occur in the context of a pre-existing brain state, and the ability to regulate one’s state likely influences goal-directed cognitive action. Brain state can be described by parameters of functional brain networks such as modularity, a summary of the extent to which a large-scale brain network can be characterized by sub-networks (i.e. modules) vs. being organized with more random or distributed connections. We posit that parameters of brain network state may ‘tune’ how the brain handles tasks, influencing the responsiveness, efficiency and, potentially, the plasticity of brain networks in response to experiences. This may help explain variability that occurs with post-injury rehabilitation. As an initial test, we examined the extent to which individual pre-training brain network modularity might explain variability in response to GOALS training (Arnemann et al., 2015). We found that pre-training modularity predicted the degree of improvement in attention and executive functioning following training, such that higher baseline modularity exhibited greater treatment response. (See Figure 3.) These results support the hypothesis that the regulation of brain network states may influence learning, adding impetus to pursuing training of brain state regulation skills, while also suggesting further investigations of potentially predictive biomarkers.

**Figure 3**: Functional brain networks from each individual prior to training (example, left) were entered into calculations of modularity (center), and this index was found to be predictive of changes in attention/executive functioning following training (right).

**Implications for Service Delivery – Reaching Veterans ‘Where They Are’**

While many Veterans (and others) who might benefit from brain injury rehabilitation lack access to care, few research efforts have focused on designing training systems for use in remote settings – in particular, to facilitate intensive skill practice and individualized guidance on skill application. We adapted our technology-assisted training system for tele-video implementation. In a pilot study of eight brain injured individuals, participants were highly engaged with training, accumulated significant skill practice in game scenarios,
reported benefit in both game and personal life, and showed improvements on measures of complex attention and executive functions.

Reaching Veterans in school is another challenge. Over 1 million Veterans are attending school on the GI Bill, and stigma is one among many barriers to care. Innovative approaches to service delivery are needed to reach these individuals ‘where they are,’ in alignment with their life goals. We have been conducting a pilot investigation of training integrated into the college setting to engage students with TBI-PTS. Feedback and preliminary data have indicated that it is feasible and helpful to offer SRS training in the college setting.

Summary and Conclusions

The effects of TBI on cognitive functioning are complex and have challenged clinicians throughout history, as well as deterred neuroscientists from pursuing studies in this “messy” area of inquiry. The complexity is compounded by combinations of physical and experiential injury. Building a strong scientific foundation is valuable for guiding the development of new therapies. Further, approaches that bridge the basic neuroscience of neural-cognitive functioning with the practical realities of clinical rehabilitation are valuable for intervention development, potentially opening the way for therapies that target biological systems and synergistically augment the specific effects of training. Keeping in mind ongoing learning across the lifespan as a goal of post-injury ‘brain health and wellness’ will expand the horizons for improving the lived experiences of individuals who have suffered brain injury.

REFERENCES


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Anthony J.-W. Chen, MD is on faculty with the Veterans Affairs Northern California Health Care System and University of California, San Francisco (UCSF). Dr. Chen has dedicated the past decade to serving Veterans and others with brain injury through clinical care, innovations in care programs, and neuroscience-driven treatment advancements. He developed a ‘continuum of care’ to support Veterans in their journey from injury to wellness, integrating clinical and research efforts in the *Program in Rehabilitation Neuroscience*, the *Center for Integrated Brain Health and Wellness*, and the *Successful Transitions and Re-integration Program*. Dr. Chen completed Bachelor’s and Master’s degrees in Neuroscience from Harvard and his MD from Harvard-Massachusetts Institute for Technology. He interned at Harvard Beth Israel-Deaconess, received Neurology training at UCSF, and had a fellowship in cognitive neuroscience, patient-oriented research, and cognitive/rehabilitation neuroscience at UCSF/UC Berkeley.

Fred Loya, PhD is a clinical and research neuropsychologist at VANCHCS. In his clinical work, he provides assessment, cognitive rehabilitation, and psychological counseling services to Veterans with TBI and related comorbidities as part of the interdisciplinary Community Intensive Translational Re-Integration Program. His research focuses on intervention design and development to address impairments in self-regulation associated with TBI, particularly the integration of digital game technologies into training and the adaptation of training for Veterans with different needs, including students with TBI, and for tele-rehabilitation. Dr. Loya completed his Bachelor’s degree in psychology from Yale, his PhD in clinical science from UC Berkeley, his internship training at VANCHCS, and his post-doctoral research and clinical training at VANCHCS and VA San Francisco.

Tatjana Novakovic-Agopian, PhD is a clinical and research neuropsychologist at VA San Francisco. Her clinical work involves providing neuropsychological evaluations and cognitive rehabilitation services to Veterans with TBI in an outpatient setting. Dr. Novakovic-Agopian also provides consultations services across the SFVA catchment area up to the border of Northern California. In her research, Dr. Novakovic-Agopian spearheaded the development of the goal-oriented attentional self-regulation (GOALS) training as well as innovative tools for assessing complex, goal-directed functioning in ecologically-valid settings. Her current work is focused on assessing GOALS training for Veterans with comorbid TBI and post-traumatic stress disorder. Dr. Novakovic-Agopian received her doctorate from California School of Professional Psychology and specialty training at Johns Hopkins University and UCSF.

Nick Rodriguez, B.A. has a background in cognitive science from UC Davis. He has been a research associate with *Program in Rehabilitation Neuroscience* since 2012 and is involved with multiple aspects of ongoing research, including design and administration of experimental tasks measuring working memory, executive functioning and other cognitive abilities; directly training Veterans in longitudinal interventions; and grant administration. He is currently enrolled in a Master’s program in clinical social work through University of Southern California.

Mark D’Esposito, MD, is a Staff Neurologist and Director of the Neurorehabilitation Unit in the Center for Rehabilitation and Extended Care with the VA Northern California, Professor of Neuroscience and Psychology and Director of the Henry H. Wheeler, Jr. Brain Imaging Center at the Neuroscience Institute at the University of California, Berkeley, and Adjunct Professor of Neurology at UCSF. He received his MD at SUNY Syracuse and completed neurology residency and fellowship at Boston University before joining the University of Pennsylvania in 1993. At UC Berkeley, his lab investigates the role of prefrontal cortex in working memory and cognitive control utilizing approaches such as functional MRI, transcranial magnetic stimulation, pharmacological interventions and behavioral studies of healthy individuals and those with neurological disorders.
The **Chronic Effects of Neurotrauma Consortium** (CENC; www.cenc.rti.org) is a response to the federal National Research Action Project (NRAP)\(^1\) initiated by President Obama in August 2013. CENC is a dually-funded, $62.175M Department of Defense (DoD) and Department of Veterans Affairs (VHA) project intended to investigate the short and long term consequences associated with mild traumatic brain injury (mTBI = concussion), to develop scientifically valid, confirmatory diagnostics, and to test innovative interventions for both mTBI and the multiple co-morbidities that frequently accompany it.

After three highly competitive, peer-reviewed selection rounds that considered over 300 proposals, CENC leadership selected and funded 10 independent research studies, while simultaneously establishing five research support cores: biostatistics, neuroimaging, biorepository, study and data management and neuropathology. Presently, CENC is comprised of 30 academic universities, 15 Veterans Affairs medical centers (VAMC), 2 non-profit research institutions, and 7 military medical centers. Additionally, a scientific advisory board, a consumer advisory board, a data safety committee, a research coordination committee, and a scientific publication committee serve as advisory and support mechanisms. In October 2016, CENC passed the 3-year mark in the current five-year funding cycle and is planning on additional funding of key elements of the program. The overall CENC is administered by Virginia Commonwealth University, led by principal investigator David Cifu, MD, and is governed by a government steering committee (GSC) comprised of DoD, VHA and other relevant government representatives. The GSC has the final authority in CENC's overall operation.

**RESEARCH INVESTIGATIONS**

CENC is currently supporting 7 clinical investigations, 1 epidemiologic database project, 1 basic science study and an MRI standardization and calibration project.

A **Longitudinal, Observational Study** that utilizes a wide array of measures, including neuropsychological instruments, laboratory and biophysical samples, electrophysiological measures and neuroimaging to evaluate a cohort (projected n = 880) of U.S. Operation Enduring Freedom (OIF - Afghanistan), Operation Iraqi Freedom (OIF) and Operation New Dawn (OND – Entire Gulf region after 9/1/2010) combatants who have had at least one mTBI and a control group of participants (projected n = 220) who have experienced combat, but have not had a mTBI. Each participant is assessed annually (in person or via telephone), with the goal of following the cohort for as long as funding is continued. Presently, there are 8 study sites and that have consented over 700 participants. One of the emerging benefits of this study has been the development of standardized and validated interview technique that identifies potential concussive events and any mTBI that may have resulted, which may help remediate a long-standing weakness in unwitnessed mTBI research methods. In addition, this study is utilizing the NIH Toolbox and will be able to validate these measures with older, established neuropsychological instruments.

An **Epidemiology Study** that aims to integrate and analyze existing VA and DoD healthcare data to study the chronic effects of mild traumatic brain injury (mTBI) on neurodegenerative disease and other comorbidities, and the methods to treat and rehabilitate adverse effects of mTBI, in Veterans and Service Members over time. Presently, this study includes 9 VA and DoD datasets with more than 2 million unique subjects, and has been successful in accessing, coordinating and harmonizing numerous
other databases to combine the analytical power available.

A Tau Modification Study that examines one of the few known biological changes seen in mTBI, massive intraneuronal accumulation of the Tau-protein in very specific and recognizable patterns in the human brain. The consequences of repeated mTBI (r-mTBI) over a prolonged period have not been well studied, and the factors and mechanisms that contribute to the long-term consequences of r-mTBI are still poorly understood. The goal of this study is to develop an animal model of r-mTBI model that will allow the tracking of these progressive intraneuronal tau alterations that can be correlated with behavioral dysfunction, fluorescent in situ hybridization, and gene expression signatures. The model could be used to assess the effects of interventions. The observations made in the animal model will be tested for agreement in soldiers who have died after sustaining r-mTBI. Exploitation of such a model will have great translational significance by providing seminal data needed to develop new and better treatments for our military personnel with mTBI. More than 220 experimental animals have been tested to date.

An Otolith Dysfunction Study that examines the importance of abnormal otolith organ (an inner ear balance organ that senses gravity and contribute to maintaining upright posture or balance) function in the evaluation of concussed individuals suffering from dizziness and imbalance. Although newer otolith organ tests are available, horizontal canal tests are still most commonly used, in part because it is unclear if abnormal otolith organ function has a direct negative affect on balance and participation in activities of everyday living. There is recent evidence to suggest that otolith organ dysfunction can occur in participants with mild traumatic brain injury (TBI) or blast exposure, which is important because symptoms of dizziness and imbalance resulting from mTBI can last six months or longer; far longer than recovery from other types of inner ear balance disturbances would be expected. If the dizziness and imbalance symptoms that occur following head injury or blast exposure are related to injury to the otolith organs rather the horizontal semicircular canal, then new treatment approaches may be necessary to focus on otolith organ pathway recovery rather than horizontal canal recovery. In addition, these research findings may direct the development of new clinical protocols to better assess individuals with dizziness and balance problems. More than 95 subjects have been consented.

A Novel White Matter Study that recognizes that since traditional structural neuroimaging techniques are largely insensitive to the subtle damage resulting from mTBI and even newer magnetic resonance imaging (MRI) acquisition methods, such as Diffusion Tensor Imaging (DTI) have shown more promise in identifying changes in white matter integrity following mTBI, even this advanced technology produces equivocal results, and lacks the sensitivity or specificity to identify the underlying cause of any white matter changes. To address these limitations, this study incorporates a new approach for specifically assessing myelin abnormalities through multicomponent-driven equilibrium single-pulse observation of T1 and T2 (McDESPOT), which calculates myelin volume. For this study subjects with a history of combat-associated mTBI, PTSD, or both are included. More than 35 subjects have been consented.

The ADAPT Study is investigating acute and long-term advanced MR imaging and clinical outcome measures of concussive TBI in military personnel injured during deployment. As part of previous collaborative efforts, the investigators completed early prospective, longitudinal studies enrolling active-duty US military at 0-7 days, 0-30 days, and 0-90 days post-injury both with and without mTBI. Early MR imaging and clinical information was collected and then at 6-12 months, MR imaging was repeated and a battery of neurological, neuropsychological and psychiatric evaluations were repeated. In total, 591 subjects were enrolled through these initial efforts; 54% TBI and 46% control. This study re-examines a subset of these subjects at 3-5 years post-injury, comparing their current clinical and imaging presentation to acute and 1 year data. The study has been completed (n = 94) and data analysis is underway.

A Structural And Functional Neurobiology Study that is investigating the microstructural nature and functional effect of diffuse heterogeneous white matter abnormalities present in post-deployment Veterans and Service Members exposed only to primary blast, without exposure to other mechanisms likely to injure the brain. This study aims to characterize white matter abnormalities present, examine how history of primary blast exposure and mild TBI are related to the presence of white matter abnormalities, and characterize the clinical sequelae of white matter abnormalities, including effects on brain function, cognitive processes, and symptom presentation. More than 100 subjects have been consented.

A DTI Phantom Diffusion Study that capitalizes on the fact that Diffusion Tensor Imaging (DTI) holds particular promise for evaluation of individuals who have experienced TBI, because damage to white matter pathways is considered to be an important component in the causation of the many types of neurocognitive impairment that can result. If diffusion imaging is to be developed as a means to evaluate individuals with suspected TBI, a uniform type of image acquisition is needed across the different types of imaging systems available within hospital and research networks. This study uses diffusion imaging phantoms to evaluate differences between and within scanners, with the goal of providing acquisition techniques that will allow data to be compared across different participant groups and combined into large data collections.

A Clinical and Neuroimaging Study that seeks to improve the characterization of long-term, ongoing damage associated with mTBI among active duty service members and Veterans, thereby, reducing clinical costs and improving long-term health outcomes. This study tests several psychological and biological measures for utility as markers of mTBI-related neurodegeneration, and characterizes the utility and limitations of self-report measures in the context of mTBI and comorbid psychopathology. The results of this research may offer implications for the assessment and documentation of mTBI during deployment, education of soldiers and military medical providers, long-term monitoring of individuals who sustain mTBI, and enable more efficient provision of long-term care. More than 55 subjects have been consented.

A Visual Sensory Study that capitalizes on the fact that although visual symptoms are a common sequelae of TBI, very little is known about the chronic visual consequences of mild TBI, its progression, and its correlation with other central nervous system deficits. Additionally, it is unknown if neuronal loss in the retina and brain after mTBI continue to progress over time. Closing this knowledge gap is important for understanding and treating TBI-related visual symptoms and for establishing whether ocular biomarkers can be used to predict risk of CNS dysfunction and its progression over
time. The purpose of this study is to identify the spectrum of visual sensory disturbances after mTBI by utilizing detailed tests of visual function and ocular motility, and newer structural analyses of optical coherence tomography (OCT) in combination with functional MRI imaging of visual pathways and volume analysis of corresponding grey and white matter locations. More than 65 subjects have been consented.

**SUMMARY**

In only three years after inception, the CENC has initiated and put into place a fully matured research leadership and infrastructure system, and its researchers have initiated 10 peer-reviewed research investigations that have consented more than 1,100 Veteran and Service Member subjects, published 27 peer-reviewed scientific publications, delivered 39 scientific presentations and displayed 54 poster presentations. CENC’s nationwide team of scientific experts in combat-associated concussion have begun the long and complex journey towards an evidence-influenced understanding of the longitudinal nature of self-report symptoms, clinical findings, neurophysiologic findings, neuroimaging, and biomarkers after injury.

**ACKNOWLEDGEMENT**

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**REFERENCES**


**ABOUT THE AUTHORS**

David Cifu, MD is Chairman and the Herman J. Flax, MD Endowed Professor (tenured) of the Department of PM&R at the Virginia Commonwealth University (VCU) School of Medicine in Richmond, Virginia. He is also Chief of PM&R Services of the VCU Health System and Founding Director of the VCU-Center for Rehabilitation Sciences and Engineering (CERSE). He is the Senior TBI Specialist for the U.S. Department of Veterans Affairs. He has been funded on 42 research grants for over $135 million, including Principal Investigator of the VA/DoD $62.2 million Chronic Effects of Neurotrauma Consortium (CENC). He has published more than 215 scientific articles and 65 abstracts, and co-authored or edited 30 books and book chapters. He is Past President of the American Academy of PM&R (2007-8).

William Carne, PhD is an Associate Professor in VCU’s Department of PM&R with over 35 years of clinical experience in private, public and academic settings. He has supervised over three dozen psychology interns, residents and fellows in a variety of outpatient and in-patient settings. Dr. Carne is the co-author of a graduate level text on writing psychological reports as well as a book chapter on Parkinson’s disease. He has published over 30 peer reviewed scientific articles. In addition to his private practice, he consults at the Richmond Veterans Affairs Medical Center. Additionally, he is a co-principle investigator in the jointly funded ($62.3M) VA/DoD Chronic Effects of Neurotrauma Consortium (CENC) designed to investigate the long term effects of mild traumatic brain injury.
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NORTH AMERICAN BRAIN INJURY SOCIETY
NABIS looks forward to announcing the location of several important brain injury events for 2018 in the next issue of BIP and on our website, www.nabis.org.

INTERNATIONAL BRAIN INJURY ASSOCIATION
IBIA congratulates scientific committee members Drs. Lisa Brenner, David Arciniegas, Risa Nakase-Richardson, Angelle Sander, and Nathan Zasler, for organizing an educationally rich and scientifically stimulating World Congress on Brain Injury at the Sheraton Hotel in New Orleans, Louisiana, March 29-April 1, 2017. With over 200 oral presentations, panels, and workshops, plus over 600 poster presentations the 2017 Congress was one of the largest in IBIA history. It is not too early to start planning for the 13th World Congress on Brain Injury! The 2019 World Congress will be held in the culturally vibrant city of Toronto, Canada, at the Sheraton Centre Hotel from March 13-16 2019. For more information, visit www.internationalbrain.org.

UNITED STATES BRAIN INJURY ALLIANCE
March is Brain Injury Awareness Month! USBIA has developed a range of posters, website banners and other collaterals that are free to download from our website. The leadership of USBIA welcomes all those with an interest in brain injury to join the Alliance as an Advocate Member. This includes persons with brain injury, family members, and professionals. Be a part of a nationwide community of advocates seeking to prevent brain injury and improve lives. Best of all, there is no cost to joining USBIA as an Advocate Member! By joining USBIA as an Advocate Member, you will be uniting with others around the country in a common mission to prevent brain injury and improve lives. For more information or to join USBIA as an Advocate Member, visit our newly redeveloped website, www.usbia.org.
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INTERVIEW WITH MICHAEL CHOO, MD,
CHIEF MEDICAL OFFICER OF PARADIGM OUTCOMES, LLC

Michael Choo, MD, FACEP, FAAEM, is Paradigm Outcome’s Chief Medical Officer. Dr. Choo is responsible for enhancing Clinical Operations and Care Management; and leading Outcomes Research & Development and Innovations in Care Management Outcomes. He also develops and manages the Paradigm network of high quality providers, medical directors, consulting physicians, and centers of excellence. Dr. Choo holds a BA and MD from Boston University’s accelerated six-year honors program in medicine, as well as an MBA from University of Tennessee Haslam College of Business. He is residency trained and board certified in the specialty of emergency medicine/trauma. Dr. Choo has served on the boards of EPIC Insurance Company as well as American Academy of Emergency Medicine. Formerly, he was President and CEO of Clinton Memorial Hospital, CMH Regional Health Systems in Southern Ohio.

Would you tell us a little bit about Paradigm Outcomes and its role in serving people who have sustained traumatic brain injuries?

Paradigm Outcomes is a unique company in our care management industry where for the past 25 years, we have been guaranteeing clinical outcomes at a fixed price for injured workers with catastrophic injuries. These injuries include traumatic brain injuries, spinal cord injuries, severe burns, multiple traumas, and amputations. We take financial risks to make sure we deliver on what we promise. Hence, we are responsible for paying all of the injured worker’s medical costs until we achieve the promised clinical outcome. So it’s a significant promise. Our focus is all about returning injured people back to their highest level of function, as much as possible. With spinal cord and brain injuries, complete recovery is very uncommon, and most often become chronic conditions with significant impairments. But, it is very important to distinguish between impairment versus disability. So, we work hard to ensure that people adapt to their chronic impairments and become as functionally productive as they can – minimizing one’s disability.

The unique feature of our company is that we take responsibility for managing care from the time of injury to the point where injured workers achieve the promised clinical outcome as well as their maximum functional state. We care manage using Paradigm’s systematic care management model and remain accountable to both our injured workers and our clients from beginning to end of our agreed terms. By taking the long view of injured workers that is “patient function-centric”, we have been very successful in helping our injured workers get their lives back after experiencing terrible catastrophic injuries.

The US healthcare system is in a dynamic period in terms of rising federal debt and health care costs, and a mandate to improve the value of services. What policy issues and implications are important for brain injury professionals to consider related to long-term service and support delivery?

My multi-faceted healthcare background as a clinician, academician, and hospital executive as a hospital CEO, helped me to infer that the crux of the US healthcare problem is all about the misalignment of incentives that exist in our system. I think that the level and growth rate of US health care costs in our country is extremely high and is not sustainable. So, the main thrust of initiatives is to cut and control costs. Now the big question for me is, “As you cut cost, what is the implication to the health care system? And what’s the end point?” It’s only helpful to talk about cutting costs if you have a clear endpoint relating to value. I think that our industry needs clarity about outcome and value definitions and their relation to cost. So as a clinician, physician executive, and administrator, my biggest concern is, “What is the outcome that they’re basing the value on?” This question has great implications in the brain injury world. If the brain injury world’s outcome is, “Let’s just get TBI patients home, rather than being in an institution,” that’s only one outcome. But if you say, “Let’s get patients with brain injury home but help them be productive so that they have better quality of life and become less of a financial burden to society,” that’s another outcome. There is a big difference between getting people home and getting people home with a certain level of functional ability, community integration, productivity and quality of life. So, it is my opinion that our health policies must bring together the Brain Injury experts and get assistance toward defining the clinical outcomes being desired and appropriately figuring out what services will be necessary to achieve them at what reasonable costs. This then helps everyone get back to providing clarity to the idea of health care value equation.

What innovative clinical rehabilitation service provision have you seen that you think has potential for broader implementation?

I believe Paradigm Outcomes’ innovative approach to clinical rehabilitation by guaranteeing a clinical outcome for an injured worker at a specific set cost has great potential. By fixing the medical costs at the onset of the case based upon the individual patient’s specific characteristics and attributes and the guaranteed outcome, clinical providers’ ability to innovate care is heightened towards improving care delivery and quality outcomes achievement. In addition, by paying providers for a specific outcome achievement, the care givers will be also given the flexibility to spend the money the way they feel is necessary to achieve the clinical outcome efficiently and effectively. For patients with TBI, the provider might say “This is the clinical outcome we’re going to deliver.” Then you give the provider the payments and the opportunity to use the funds in any way they’d like to use it to get to the outcome promised. So, as an example, if one patient with a brain injury needs more psychosocial services to reach their functional outcome versus another, the provider can have the flexibility to use the dollars as deemed necessary to achieve the best outcome; and not be locked...
into limited categories of services that can get reimbursed. This allows for customization of care to specific individuals.

**What innovative rehabilitation research is needed to provide solutions to anticipated healthcare reform over the next five years?**

I think that we need to be collectively looking to do research on what clinical outcomes are possible for what specific types and categories of TBI. No consensus database exists today that can tell me what is the most likely “average” and “best” functional outcomes possible for given types of TBI patients. Unlike with spinal cord injuries, we do have today such consensus information; where if you get an ASIA-A injury at T7, then we know on average, what the functional limitations and impairments will be. I am hoping to facilitate the gathering of such similar data for TBI patients. I am hoping to get our TBI experts to collaborate in working towards understanding what outcomes can be achieved on average based on specific types of TBI. TBI is one of the most difficult, most uncertain conditions. From a prognostic perspective, there are a lot of unknowns at the current time with TBI patients and what outcomes are possible, probable, and expected. Ideally, I want to know what the probabilities are of achieving a certain functional level with what type of TBI injury. Once we know that, then we can take the next steps to benchmark the care management needs and expectations.

**What can rehabilitation research do better or do more of over the next five years?**

I would like to see more research data as to the most effective dosage and timing for certain rehabilitation therapeutics specific to achieving outcomes. As an example, providers are very confident about the benefits of activity-based training since such training has shown to be beneficial in many ways. But it would be helpful to know from clinical research perspective if there are better or best “dosage and timing” of these activity based training for specific outcomes. It would be helpful to know if engaging in activity-based training every day for certain hours is better than if you do it episodically for longer hours as an example. There’s no consensus data on this, and I think we need more data to provide a rationale on rehabilitation dosage and timing that’s most effective to achieve certain outcomes.

**ABOUT THE INTERVIEWER**

Tolu Oyesanya, PhD, RN, is a Post-Doctoral Fellow in Shepherd Center’s TBI Research program. Dr. Oyesanya was awarded a National Institutes of Health F31 grant to develop empirically-based models of the inpatient rehabilitation experiences of patients with TBI and their families. Her current research focuses on hospital to home transition support with an emphasis on improving self-management, independence, and participation.

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On the last day of February, President Donald Trump gave his first address to a Joint Session of Congress outlining his priorities, including the repeal and replacement of the Affordable Care Act (ACA), cutting government regulations, and increased funding for infrastructure. Soon after the 115th Congress convened, both the U.S. House of Representatives and the Senate began clearing the path for repealing the ACA through the budget reconciliation process – the same process used to enact the ACA. Budget reconciliation is a process to fast track certain tax, spending and debt limit legislation. Under this process, the Senate is prohibited from filibustering and only a simple majority is needed to pass the bill.

Under this backdrop, the House Republican Leadership unveiled its bill, known as the American Health Care Act (AHCA), in March without opportunity for public input or scrutiny. Two House Committees – Energy and Commerce and the Ways and Means – passed the bill without testimony or opportunity for making any changes to the legislation or without even knowing the costs associated with the proposal. The legislation repealed taxes associated with the ACA; cut Medicaid by $880 million over the next decade; capped Medicaid spending through Per Capita Caps; eliminated Medicaid Expansion; and shifted the Medicaid program to the responsibility of the states. This proposal restructures Medicaid from an entitlement program to one that will be subject to an appropriation to the states.

Following the actions of the Committees, the Congressional Budget Office (CBO) released the fiscal implications. The CBO estimated that enacting the AHCA would reduce federal deficits by $337 billion over ten years and increase the number of people who would be uninsured by 24 million in 2026 relative to current law. The cost savings would largely be the result of reducing Medicaid spending and federal funding to assist individuals to obtain health insurance. Provisions include:

- Repealing the increased federal match for the Community First Choice (CFC) option, which allows individuals with disabilities to receive needed supports to remain at home, with states receiving extra Medicaid federal matching funds to cover the services.
- Eliminating a requirement that Medicaid cover the Essential Health Benefits (EHBs), which includes mental health and substance use disorder services, prescription drugs, rehabilitative and habilitative services and devices, preventive and wellness services and chronic disease management, and pediatric services.
- Replacing the ACA’s tax credits that help people pay for health care coverage with much more limited tax credits, maxing out at $4,000 per year for individuals over the age of 60.
- Repealing and replacing the Individual Mandate with a Continuous Coverage requirement. This would penalize anyone who experiences a short-term financial hardship and can no longer afford healthcare coverage, such as a job loss with unaffordable COBRA payments or a move to part time employment due to healthcare needs.
- Repeals the cost-sharing protections that the ACA put in place to help people below 250 percent federal poverty level to afford their healthcare.
- Creates a Patient and State Stability Fund, allocating $15 billion for the next two years and $10 billion per year from 2020 to 2026, to be shared between the fifty states and the District of Columbia — amounting to $80 billion over the next 9 years -- to help states with such challenges as high risk pools, providing various forms of reinsurance, prevention, and assisting with cost sharing.
- Eliminates the Prevention and Public Health Fund in 2018, reducing the budget of the Centers for Disease Control and Prevention (CDC) by 12 percent of its annual budget.
- Allows health insurance companies to charge older adults up to 5 times the premiums paid by younger individuals.

President Trump also signed an executive order directing heads of federal agencies to develop a plan for reorganization and eliminating unnecessary or duplicative or non-performing programs in order to reduce funding by $54 billion in non-defense discretionary spending. Non-defense discretionary programs refer to those which receive an annual appropriations, such as prevention, research, disability, brain injury and health care programs. The President planned to issue a “skinny budget” for fiscal year 2018 in mid-March outlining recommended program cuts with a more detailed budget to be released later.

The Congressional Brain Injury Task Force hosted its annual Brain Injury Awareness Day on March 22, 2017. The U.S. Administration for Community Living held a meeting the day before for purposes of discussing the future of the TBI State Grant Program and for developing a federal plan for coordinating resources as called for in the TBI Reauthorization Act of 2014. As many issues appear to be up in the air, advocates are increasing their efforts to ensure that programs and services supporting individuals with brain injury and their families are not harmed. This is a critical time for all who support federal programs involved in research, prevention, and service delivery.

ABOUT THE AUTHOR

Susan L. Vaughn, S.L. Vaughn & Assoc., is the Director of Public Policy for the National Association of State Head Injury Administrators and consults with the Brain Injury Association of America on state policy issues. She retired from the State of Missouri in 2002, after working nearly 30 years in the field of disabilities and public policy. She served as the first director of the Missouri Head Injury Advisory Council, a position she held for 17 years. She founded NASHIA in 1990, and served as its first president.
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Scarlett Law Group is a premier California personal injury law firm that in two decades has become one of the state’s go-to practices for large-scale personal injury and wrongful death cases, particularly those involving traumatic brain injuries.

With his experienced team of attorneys and support staff, founder Randall Scarlett has built a highly selective plaintiffs’ firm that is dedicated to improving the quality of life of its injured clients. “I live to assist people who have sustained traumatic brain injury or other catastrophic harms,” Scarlett says. “There is simply no greater calling than being able to work in a field where you can help people obtain the treatment they so desperately need.”

To that end, Scarlett and his firm strive to achieve maximum recovery for their clients, while also providing them with the best medical experts available. “As a firm, we ensure that our clients receive both the litigation support they need and the cutting-edge medical treatments that can help them regain independence,” Scarlett notes.

Scarlett’s record-setting verdicts for clients with traumatic brain injuries include $10.6 million for a 31-year-old man, $49 million for a 23-year-old man, $26 million for a 7-year-old, and $22.8 million for a 52-year-old woman. In addition, his firm regularly obtains eight-figure verdicts for clients who have endured spinal cord injuries, automobile accidents, big rig trucking accidents, birth injuries, and wrongful death.

Most recently, Scarlett secured an $18.6 million consolidated case jury verdict in February 2014 on behalf of the family of a woman who died as a result of the negligence of a trucking company and the dangerous condition of a roadway in Monterey, Calif. The jury awarded $9.4 million to Scarlett’s clients, which ranks as one of the highest wrongful death verdicts rendered in recent years in the Monterey County Superior Court.

Having successfully tried and resolved cases for decades, we’re prepared and willing to take cases to trial when offers of settlement are inadequate, and I think that’s ultimately what sets us apart from many other personal injury law firms,” observes Scarlett, who is a Diplomate of the American Board of Professional Liability Attorneys.

In 2015, Mr. Scarlett obtained an $13 million jury verdict for the family of a one year old baby who suffered permanent injuries when a North Carolina Hospital failed to diagnose and properly treat bacterial meningitis that left the child with severe neurological damage. Then, just a month later, Scarlett secured an $11 million settlement for a 28-year-old Iraq War veteran who was struck by a vehicle in a crosswalk, rendering her brain damaged.

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With his experienced team of attorneys and support staff, founder Randall Scarlett has built a highly selective plaintiffs’ firm that is dedicated to improving the quality of life of its injured clients. “I live to assist people who have sustained traumatic brain injury or other catastrophic harms,” Scarlett says. “There is simply no greater calling than being able to work in a field where you can help people obtain the treatment they so desperately need.”

To that end, Scarlett and his firm strive to achieve maximum recovery for their clients, while also providing them with the best medical experts available. “As a firm, we ensure that our clients receive both the litigation support they need and the cutting-edge medical treatments that can help them regain independence,” Scarlett notes.

Scarlett’s record-setting verdicts for clients with traumatic brain injuries include $10.6 million for a 31-year-old man, $49 million for a 23-year-old man, $26 million for a 7-year-old, and $22.8 million for a 52-year-old woman. In addition, his firm regularly obtains eight-figure verdicts for clients who have endured spinal cord injuries, automobile accidents, big rig trucking accidents, birth injuries, and wrongful death.

Most recently, Scarlett secured an $18.6 million consolidated case jury verdict in February 2014 on behalf of the family of a woman who died as a result of the negligence of a trucking company and the dangerous condition of a roadway in Monterey, Calif. The jury awarded $9.4 million to Scarlett’s clients, which ranks as one of the highest wrongful death verdicts rendered in recent years in the Monterey County Superior Court.

Having successfully tried and resolved cases for decades, we’re prepared and willing to take cases to trial when offers of settlement are inadequate, and I think that’s ultimately what sets us apart from many other personal injury law firms,” observes Scarlett, who is a Diplomate of the American Board of Professional Liability Attorneys.

In 2015, Mr. Scarlett obtained a $13 million jury verdict for the family of a one year old baby who suffered permanent injuries when a North Carolina Hospital failed to diagnose and properly treat bacterial meningitis that left the child with severe neurological damage. Then, just a month later, Scarlett secured an $11 million settlement for a 28-year-old Iraq War veteran who was struck by a vehicle in a crosswalk, rendering her brain damaged.