NEW OPPORTUNITIES IN TRAUMATIC BRAIN INJURY RESEARCH

Invitational Workshop on New Opportunities in Traumatic Brain Injury Research: Advancing the National Research Agenda

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New Opportunities in Traumatic Brain Injury Research:
Advancing the National Agenda

Workshop Report

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Introduction

Traumatic brain injury (TBI) research is an area of urgent and unmet medical need that holds relevance for many of the Canadian Institutes of Health Research (CIHR) and other national stakeholders, including the Ontario Neurotrauma Foundation (ONF). It also holds promise for improving the health of Canadians and the nation’s economic well-being.

Recognizing this, the CIHR Institute of Neurosciences, Mental Health and Addiction (INHMA), in partnership with the ONF, hosted an invitational workshop on New Opportunities in Traumatic Brain Injury Research: Advancing the National Agenda on April 12 and 13, 2012, in Toronto.

More than 100 scientists, clinicians, administrators, and others with a vested interest or expertise in TBI—including representatives from national and provincial government agencies, academic institutions, hospitals, and private sector organizations in Canada and the United States—attended the event, which was structured around a series of expert presentations designed to inform and stimulate discussion.

The main objectives of the workshop were to

- introduce the TBI research community to new funding opportunities that INMHA would be launching in the near future,
- identify promising opportunities in TBI research that could benefit from new networking and partnership activities, and
- help the CIHR, ONF, and their partners focus on areas in which Canada had particular strengths and expertise that could be leveraged through national and international partnerships.

In line with the new international consortium on TBI’s objectives related to best practices in early diagnosis and treatment, the workshop focused on mild TBI (mTBI) and concussion in children and youth. The number of incidents in this demographic group is alarmingly high, and many still go unreported. This is coupled with increasing concern about a possible relationship between multiple TBIs and early onset dementia, later substance-use disorders, and mental illness.

This workshop report provides a summary of each presentation, points that arose from the plenary discussions, and detailed outcomes of the brainstorming sessions that took place.
place on the second day of the workshop. It is intended for use by CIHR-INMHA and its partners in support of TBI research in Canada.

**Opening Remarks**

Dr. Anthony Phillips, Scientific Director of CIHR-INMHA, expressed his pleasure at welcoming such a large group from the national TBI community to the first invitational TBI workshop. He explained that the partnership between INMHA and the ONF was intended to bring together key stakeholders in TBI to address what had become both a national and global crisis. TBI was characterized as a fundamental yet much-neglected area of health care and health research, and one in which collaboration was necessary to achieve progress. Dr. Phillips described CIHR as just one partner in the ongoing effort to bring the issue of TBI to the attention of politicians, clinicians, and researchers.

Mr. Kent Bassett-Spiers, Chief Executive Officer of the ONF, joined representatives of four other organizations that supported the initiative in welcoming participants and thanked INMHA for its leadership role in addressing a major national and international healthcare issue. Dr. Samuel Weiss, Director of the Hotchkiss Brain Institute (HBI), reiterated the importance of collaboration in the area of TBI research and HBI’s interest in translating new knowledge into improved outcomes for people sustaining brain injury. Dr. Anne-Cécile Désfaits, Director of Partnerships and International Relations with the Fonds de recherche du Québec–Santé (FRQS), confirmed TBI as an area of major interest to the FRQS and the research community in Quebec and one in which many other government and non-government organizations were involved.

Dr. Brian Garber spoke on behalf of the Canadian Forces Surgeon General, one of a number of players in the Department of National Defence (DND) with a stake in the issue of TBI. He noted that the topic was of key importance to DND because many men and women serving in the Forces sustained head injuries not only as a result of war but also through typical civilian mechanisms, such as sports and motor vehicle accidents. Larry Carlson, President of the Brain Injury Association of Canada (BIAC), closed by thanking all in attendance for the concern they demonstrated by attending the workshop and for their help in increasing awareness of what was often an “invisible” disability.
Part I: Setting the Stage

Presentations

Dr. Alain Ptito, of the Montréal Neurological Institute, chaired the opening series of presentations, which provided participants with a broad overview of the issue of TBI in Canada, efforts to develop a Canadian strategy on TBI research, and Canada’s involvement in the international initiative on TBI research.

TBI: Incidence, Vulnerable Populations, and Economic Burden in Canada
- Dr. Michael Cusimano, St. Michael’s Hospital, University of Toronto

TBI accounts for the third-highest number of hospital days in Canada and half of all deaths from trauma, yet there is a disproportionately small amount of research directed toward it. While the prevalence of TBI is not well known, about two percent of people in the U.S. have some form of disability from TBI. The degree of injury varies widely, with an estimated 11 severe and 600 mild cases per 100,000 people. Two thirds of those affected are males, with the young and elderly (women in particular) also among the most vulnerable. The most common mechanism overall is falls; however, motor vehicle accidents are a major cause among young men. In the U.S., there are some 52,000 deaths and 275,000 hospitalizations per year (many of those affected don’t seek medical attention). Canadian data show similar proportions, with the same basic epidemiologic trends reported by all higher-income countries.

U.S. data show a slow upward trend in emergency visits and hospitalizations for TBI, with fall-related injuries in youth and the elderly and sports-related TBI (primarily mild) on the rise. One trend that will have a major influence on TBI in Canada is that the proportion of elderly people will double to about 26 percent of the population by 2025. A serious global trend is that road traffic injuries are expected to soon become the third most-common cause of death, because economic improvements are causing motorization rates to increase around the world.

While good data on the financial costs of TBI are lacking, falls alone cost the Canadian economy about $7 billion each year, with direct costs from TBI estimated at about $151 million. Based on U.S. estimates of the direct and indirect costs of TBI being $76 billion annually, Canada’s costs can be extrapolated to about $10 billion. Another American study shows the lifetime costs of a severe TBI survivor to be approximately $6.7 million.
The human cost is even higher, with a number of significant neurological and psychosocial problems resulting from TBI. Although people in all spheres are affected, risks related to injury, treatment, and outcome are affected by such factors as sex, age, and social groups. Studies have shown high rates of TBI in vulnerable populations such as homeless, disabled, incarcerated, and Aboriginal people, as well as those in mental health institutions. More research is needed not only on TBI treatment but also on TBI prevention, as a study out of Arizona showed 90 percent of TBIs are preventable.

Points from Plenary Discussion:

- It is important not only to study risk factors separately but also to look at how they are related. Several U.S. studies on socioeconomic status (SES) and TBI found differences related to the mechanism of injury: middle-class children were more likely to be hurt playing elite sports and poor ones by being hit by a car. So SES is also a predictor of the severity of the injury as well its treatment and outcome, because poor families have fewer resources to deal with it.
- This goes beyond injury, because some of the problems being seen in the same groups have the same underlying, modifiable risk factors. This is an opportunity to link with healthy lifestyles in general and put that into that broader context.
- With respect to the notion of prevention, several ONF-supported studies focused on the consequences of TBI have found that a lot of them pre-existed the traumatic event. So there may be other upstream predictors of a health disparity that might lead to TBI that should be considered (e.g., early life, development)—not only to minimize disparity but to tackle this particular problem.
- SES is related to a lot of variables, but it doesn’t explain everything. There are other critical aspects that affect both incidence and outcome, such as education, alcohol use, employment, etc., that need to be investigated.

Towards a TBI Research Strategy for Canada: Report from the ONF-BIAC Advisory Committee
- Dr. Grant Iverson, UBC

The ONF and BIAC assembled an advisory committee to help lay the foundation and develop some preliminary steps for a national research strategy for both acquired and traumatic brain injury. The BIAC has a network of smaller organizations in each province and is aimed at advocacy and advancing knowledge; the ONF is the largest provincial funder of TBI in Canada and has provincial, national, and international partners. The need for a national strategy was identified to foster collaboration, reduce
duplication, ensure evidence-informed practice and policy, ensure future research capacity, inform the national fundraising strategy, and promote Canada’s expertise on the international stage. The committee’s early position was to focus on TBI, translational and applied research, improving quality of life, building on existing capacities, and bridging the gap between knowledge and practice. Key steps in the process were to identify knowledge gaps and priorities, determine mechanisms to ensure that evidence informs practice, create a research network, and devise a funding and advocacy strategy to achieve the research plan.

Several of the initial steps in the committee’s plan were completed with the identification of seven priorities and an environmental scan of TBI researchers in Canada and their areas of interest and activity. The initial environmental scan revealed 161 individuals involved in this work, nearly half of them in cognition, behavioural outcomes, and rehabilitation. Ways will be explored to align this effort with the CIHR’s interest in creating a Canadian consortium to take part in the international initiative on TBI research and with other outcomes of the TBI workshop.

Points from Plenary Discussion:

- There is growing evidence that early severe TBI is a factor in Alzheimer’s disease and that some early markers of neurodegeneration are present in severe TBI. There is an opportunity to build capacity by linking TBI more broadly as a comorbidity to psychiatric illness, Alzheimer’s disease, etc. The concept of repetitive head trauma and subsequent neurodegeneration is poorly understood and further study in this area would be useful.
- With regard to neurodegeneration, there appears to be a second wave of damage that occurs within the first few years of a severe brain injury in some people.
- Prevention research has been fairly diversified across funding portfolios. The intention, in moving away from this area initially, was to focus on clinical research and translating research into practice, which is the area of greatest need.

Overview of the EU-NIH-Canada “International Initiative for Traumatic Brain Injury Research”
- Dr. Anthony Phillips, CIHR-INMHA

INMHA’s new five-year Strategic Plan and the CIHR Roadmap both emphasize the importance of translational research and the urgent need to forge links between basic and clinical research. A major focus of the Institutes, at present, is on leveraging strategic funding from CIHR through external and internal partnerships focused on the
eight Signature Initiatives. At the top of this list of initiatives is a Strategy for Patient-Oriented Research (SPOR) that envisages the creation of several new national networks (including one for mental health) with their own support units.

TBI is a major area of unmet medical need in the European Union (EU), with more than 1.2 million new patients each year and over 2.5 million people suffering from long-term consequences. Seventy five percent of the victims are children and young adults. The total cost of TBI injuries in the EU is €33 billion annually, yet there has been little progress in treatment over the past 20 years. The EU and the U.S. National Institutes of Health (NIH)–National Institute of Neurological Disorders and Stroke (NINDS) began meeting in late 2009 to discuss a possible cooperative effort on TBI research and hosted two workshops on the subject over the following two years.

On the basis of these discussions, the decision was made to leverage global resources by launching the International Initiative on TBI Research (InTBIR), the intent of which is to develop empirical evidence for identifying interventions to improve outcomes in TBI patients. CIHR attended the third InTBIR workshop in Brussels in October 2011, and Canada has joined the consortium—agreeing to contribute approximately $5 million in funding (now about $9 million due to added contributions from new partners). The EU has committed about €30 million to the effort over the next seven years, and the NINDS and the United States Department of National Defense are partnering to create a $10 million data management infrastructure and issue a targeted request for applications (RFA). InTBIR is expected to start in mid-2013 and is open to all funding agencies.

As part of the InTBIR partnership, Canada’s research community will have access to shared international data and data management systems, while its leading scientists will have the chance to influence the consortium’s research directions. The creation of a project directory and website will identify other opportunities for collaboration. While some commonalities will link partners from the outset—and the group will identify specific priority areas—each will proceed with its own national programs and areas of focus. In Canada, a series of funding opportunities will be launched in the near future related to best practices in the recognition, diagnosis, and treatment of mTBI. The importance of working together to identify areas of opportunity, foster partnerships, and convince decision-makers of the importance of investment in TBI research was emphasized.
Points from Plenary Discussion:

- Politicians need to understand that a reduction in the burden of TBI of as little as two or three percent would repay the cost of the research program within a year (given that, in Canada, the lifetime cost of one severe TBI is $6.7 million). This is a political problem as well as a research and public health issue.
- Thought needs to go into a campaign strategy not only to raise awareness but also to look at private-sector sources of funding, such as sports organizations.
- The focus of Canada’s RFA was chosen to align with the interests of INMHA, as the primary funder, the national strategy, and InTBIR. This is also a huge opportunity to link the consequences of brain trauma to altered psychological states, comorbidities and psychiatric conditions—all of which sit squarely in INMHA’s mandate.
- The opinion was voiced that rehabilitation seems to fall through the cracks with CIHR/INMHA, because quality of life issues don’t score as high priorities when an application is up against neuroscientists and brain biomarkers. While a lot of ONF-BIAC work is about long-term outcomes and quality of life, there is no real place for this type of research to be funded by CIHR.
- INMHA made training and capacity building one of its primary focuses during its first 10 years through five-year grants called Strategic Training Initiatives in Health Research (STIHRs). While the program had many successes, it also consumed much of the Institute’s budget. The program ends in 2013, at which point its outcomes will be analyzed to determine its future.
- Growing re-conceptualization of TBI as a disease process rather than a discrete injury could open it up to additional sources of funding. Linking the field of TBI to Alzheimer’s and related dementias, neurodegeneration, etc. is very important.
Part II: State of Play and Unmet Needs

Presentations

Dr. Fergus Craik, of the ONF, chaired the second series of presentations, which focused on the current state of TBI research and its application to practice, gaps in knowledge, and needs moving forward.

Management Best Practices: Guidelines for mTBI and Persistent Symptoms

- Dr. Shawn Marshall, University of Ottawa

Mild TBIs and concussions are common in Canada—often caused by sports, such as hockey, as well as by other mechanisms, such as motor vehicle accidents and falls. Although the two terms do not mean the same thing, post-concussion syndrome and mTBI can have overlapping symptoms, such as fatigue, sleep disorders, headaches, and dizziness. Eighty to 95 percent of TBIs are classified as “mild”, which describes the injury severity and not the outcome or prognosis. Ten to 15 percent of mTBI patients continue to experience symptoms more than three months post-injury. Delayed treatment and the mechanism of injury also play a role in outcomes (e.g., motor vehicle accidents are often polytrauma). Symptoms have been found to be worse and more prolonged the older the victim (e.g., age 18+ have more longer-term effects).

In addition to controversy over the lack of standardized criteria for mTBI, there are no specific diagnostic tests available, and many complex variables are involved, including pre-injury factors. Somatic, cognitive, psychological, and behavioural symptoms and complications are often seen post-mTBI; however, many symptoms are subtle, non-specific, or overlap with other diagnoses. Mild TBI is not managed in a holistic way or owned by a specific health-care specialty, and an absence of guidelines for care has meant variations in the way it has been managed across regions and specialties.

Recognizing the need for guidance, an international expert consensus group was formed to develop a plan for identifying and treating patients at high risk of persistent symptoms and to devise formal guidelines for care. Based on the results of its literature review and scan of existing guidelines from both within and outside the field of mTBI, the group made 77 recommendations that were published on the ONF website and in Canadian Family Physician. The Mild TBI and Persistent Symptoms Guidelines, which
also include a list of resources, are currently being evaluated and will be revised based on results. Endorsement is being sought from professional associations and groups.

Points from Plenary Discussion:

- There is a broad spectrum of severity in mTBI; putting everything into the same category adds to the challenge of understanding risk factors for recovery.
- Risk factors do predict outcome, and those red and yellow flags (e.g., social factors) have to be applied. The reason TBI is broken down into mild, moderate, and severe is because of the healthcare system, which uses those categories to determine which cases require urgent medical management.
- Special attention needs to be given to sport-related concussions, because most athletes minimize or underreport their injuries and resume playing when they are still injured and symptomatic, so they are vulnerable to even more damage.
- What we owe to sport concussion is recognition that not everybody gets better. Sport concussion guidelines often end at “return to play”, but we are also looking beyond that at how to manage patients who don’t return to play.
- These guidelines are meant to help people manage mTBIs from all types of etiologies vs. not manage them at all, which is often the case.

Child and Youth TBI: Incidence, Treatment Best Practices, Clinical Perspectives
- Dr. Jamie Hutchison, The Hospital for Sick Children

TBI in children and adolescents is different from TBI in adults for a number of reasons. The mechanisms of primary and secondary injury are different in a brain that is still being developed, as is the physiology (e.g., cerebral blood flow is much higher during the first three years of life). Since outcomes are developmentally specific, measures are required that have been created and validated in a paediatric population.

TBI is the leading cause of death and acquired disability between the ages of 1 and 24, with the main causes being falls, motor vehicle collisions, and sports. While TBI is the second-most common reason for injury-related hospital admissions, a larger percentage of TBIs are seen in emergency departments, outpatient clinics, or not at all. The myth that most children recover from mTBI has been disproven by several recent studies—one showing that 21 percent had symptoms that persisted more than three months, and another that symptoms can last even longer, especially after repeated incidents. Predictors include loss of consciousness, Glasgow Coma Scale below 15, other injuries,
acute symptoms of concussion, and intracranial abnormalities on magnetic resonance imaging (MRI).

Treatment guidelines were developed based on systematic reviews of the peer reviewed literature, consensus, and expert opinion for use during a randomized controlled trial (RCT) of hypothermia therapy in children with severe TBI. These were implemented at The Hospital for Sick Children in 2007. They include a hierarchy of therapies to control intracranial pressure (ICP), rapid treatment of hypotension and promote the involvement of multi-disciplinary teams and a holistic approach to patient care. The guidelines have been proven to improve knowledge and satisfaction with care among health care practitioners.

The Hospital for Sick Children has recently announced an endowed chair in TBI research and a number of studies are being conducted that show potential for improving patient outcomes. For example, animal studies show a reduction in brain-cell death after TBIs when recombinant neuronal apoptosis inhibitory protein is injected after the injury. There is urgent need for research in many other areas—including prevention and epidemiology, neuromonitoring, biomarkers, mechanisms, RCTs, prognostic studies, genetics (e.g., attention deficit) and risk—and for studies that are specific to paediatrics.

Points from Plenary Discussion:

- According to data from a birth cohort out of New Zealand, about one third of the population in the country had suffered a TBI that required medical attention by age 25. There is also some Ontario data showing that, in one year, three to four out of 100 children had a head injury reported to school officials.

**Post-TBI: Clinical, Cognitive/Imaging Research**

- Dr. Alain Ptito, MNI

McGill, the MNI and the McGill University Health Centre are involved in studying TBI in varsity football and hockey athletes to help provide guidance for “return to play” decisions. This is important, because there is increased risk of further concussion in those who have had a prior incident—in part, because reaction times are slower. Also, multiple concussions have a cumulative effect and can result in prolonging post-concussive symptoms (PCS); if two concussions occur within a short time period, the second, even if mild, can have devastating consequences, including death (a phenomenon known as “second impact syndrome”).
The use of functional magnetic resonance imaging (fMRI) to examine the brains of both concussed and non-concussed athletes performing working memory tasks showed that activation of the prefrontal region (dorsolateral prefrontal cortex) decreased as PCS severity increased. While both those with mild and moderate PCS had abnormal fMRIs, neuropsychological tests results were impaired in the moderate group only, with a general slowing of reaction times and information processing. Subjects with PCS also exhibited additional areas of activation not found in the control group, suggesting use of compensatory mechanisms to carry out the tasks.

There are also differences in depression between the general and head-trauma populations, with much higher prevalence in the latter (30-40%) than the former (4-5%)—and a higher lifetime risk. Depression also increases with the number of concussions experienced. In a study of identical twins (in each pair, one depressed and one not), fMRIs showed that the patterns of activation in certain areas of the brain correlated with the Beck Depression Inventory score: when the score was high, activation decreased in the dorsolateral prefrontal cortex, while deactivation decreased in the anterior cingulate and medial orbitofrontal cortices. These findings are consistent with existing limbic-frontal models of depression and suggest a neuropathological basis to the symptoms of depression after a concussion.

A recovery study also confirmed a connection between the presence of symptoms and areas of activation (as symptoms resolved, activation patterns increased and returned to baseline); in a comparison study, the areas activated in children and adults were identical. There is also evidence of a correlation between what is seen in fMRIs and event-related potentials, with hypoactivation occurring in all concussed groups and reduced amplitudes in one or more waves (N200, N350 and P300).

Points from Plenary Discussion:

- Emerging evidence that repetitive transcranial stimulation of the dorsolateral prefrontal cortex can increase activation of this region and possibly accelerate recuperation deserves more consideration.
- The fact that athletes with abnormal results on fMRIs can have normal results on neuropsychological testing emphasizes the need for more sensitive tools.
- An important goal of this work was to demonstrate an organic basis to symptoms, as they are difficult to assess objectively in motor vehicle accidents because of litigation in some cases and in sports because of “faking well” on the part of the athlete.
There is a whole new field looking at the mechanics of injury, factors like acceleration and deceleration, and why certain hits produce more lingering effects than others.

It would be interesting to get a psychological readout to assay regions of the brain that are particularly vulnerable.

Work is underway to develop a neuropsychological test battery that has been validated with fMRI for use in the clinic or lab.

**From Phenomenology to Mechanism: Integrating Clinical and Pre-Clinical Concussion Research**

**MRI Techniques for the Investigation of TBI**
- Dr. Alex Rauscher, UBC

There are several new methods of MRI being used for the study of TBI. Current thinking is that Susceptibility Weighted Imaging (SWI) is superior to Gradient Echo Scan, as it makes hemorrhagic lesions much easier to see. Future directions will be to use multi-echo SWI at 3 Tesla to detect smaller lesions than conventional methods. Diffusion Tensor Imaging (DTI) enables users to identify the diffusion properties of water in the tissue and how fast molecules are moving, as these values change with injury. Studies using DTI have already identified changes in fractional anisotropy in different kinds of TBI. Whole Brain Myelin Imaging is another new technology that makes it possible to calculate maps of myelin in the brain (a previously time-consuming process), while using MR Spectroscopy to sample and scan metabolic markers also yields useful information.

**Points from Plenary Discussion:**

- All of these modalities are promising; however, while efforts are being made to work out protocols, there is a lot of information in an anatomical scan (e.g., brain volume) that can be quantified. It relates to outcome and behavior in ways that are quite sensitive and can be acquired relatively consistently across centers.
- The only MRI method that works on an individual basis is SWI (either there are hemorrhages visible on a person’s scan or there are not), whereas other methods (DTI, spectroscopy, fMRI, etc.) have only produced results when averaged over larger numbers of subjects.
Chronic traumatic encephalopathy (CTE) is a long-term consequence of mild repetitive TBI. Approximately 69 percent of subjects with CTE have memory impairment, 65 percent have emotional problems and aggression, and 40 percent have speech and gait disturbances. There are similarities and differences between CTE and Alzheimer’s: in CTE, neuropathology can involve several brain regions but only affects the hippocampus in advanced cases, whereas hippocampal atrophy begins early in Alzheimer’s; also, CTE is primarily a tauopathy, so tau deposition can occur independent of amyloid deposits (which are thought to trigger tau deposition in Alzheimer’s).

The results of a number of TBI studies suggest a positive correlation between TBI and increased risk of dementia; however, more evidence is needed to rigorously prove this and determine the factors behind the association. One possible reason could be that amyloid precursor protein levels are increased after axonal injury, which could lead to more of the toxic peptide that forms the amyloid deposits as well as trigger pathways that eventually deposit tau and destroy neurons. Studies in animal models have shown that apolipoprotein E, which is known to influence Alzheimer’s, also plays important roles in neuronal repair after TBI.

Canada is poised to take a leadership role in examining how brain injury may lead to emerging Alzheimer’s. Imaging methods and cerebrospinal fluid biomarkers can be used to identify changes in A-beta and tau, and Pittsburgh Compound-B allows positron emission tomography scanning of amyloid deposits in the living brain. To truly understand the long-term outcomes of TBI, neuropsychological scores controlled for motivational biases are needed, as are imaging methods sensitive to injury severity (including the deposition of A-beta and tau in the post-injury brain), biomarkers validated for dementia, and genetic data. Preclinical challenges include the need for model systems to control for the wide variation of TBI in human populations and for preclinical studies.
Keynote Speaker

**TBI Research Collaboration: Building Interdisciplinary Networks from Common Data Set Elements**
- Dr. Geoffrey Manley, UCSF

Although there have been significant successes in the treatment of cancer and cardiovascular disease over the past 30 or 40 years, there is a “valley of death” in translational research on TBI. TBI is the most complicated injury in the most complicated organ of the body, yet today it is classified as either mild, moderate, or severe. Recognizing that this oversimplified system misses the diversity of differences within these levels, an initiative was launched in the U.S. to improve the classification of TBI and standardize methods for collecting and analyzing data focused on best practices.

Using funding from the United States Department of Defense, the NIH, the NINDS, and the NEA, more than 150 experts assembled to discuss and forge a way forward for the effort, called TBI Common Data Elements (www.commondataelements.ninds.nih.gov). A multicenter prospective study to validate the feasibility and utility of TBI Common Data Elements, called TRACK-TBI (Transforming Research and Clinical Knowledge in TBI), has just been completed.

The NIH-funded study enrolled over 600 patients from high-volume trauma centers. A highly granular dataset was prospectively collected and included clinical features, biospecimens for proteomic and genomic analyses, advanced MRI and computed tomography (CT) imaging, and outcome measures. Early results suggest significant potential for MRI and proteomic biomarkers to improve the precision of TBI diagnosis and better stratify patients for targeted therapies.

Plans are already underway for the next grant, TRACK-TBI II. Recognizing that a much larger cohort is needed and more diverse centers representing the full range of TBI phenotypes, treatments, and outcomes, efforts are being made to bring in more high-volume centers capable of doing 3 Tesla MRIs, etc. and to leverage partners in Canada and Europe to join the study. A multi-disciplinary approach that uses TBI Common Data Elements is essential to advance knowledge in this area. As demonstrated in other diseases, a more precise classification of traumatic brain injury could revolutionize diagnosis, direct patient-specific treatment, and improve outcome.
Points from Plenary Discussion:

- Although mTBI often does not show up on a conventional CT scan, pathological lesions are now being seen in MRIs. Improving conventional imaging will make it possible to identify more “hidden” TBIs in the future.
- More bioinformatics and cutting-edge statistical collaborators need to be brought into the field to build comprehensive and cohesive diagnostic and prognostic models for TBI.
- Several studies show that if education and reassurance are provided, patients do better at 12 months than they would have otherwise. Therefore, even in the absence of targeted treatment today, preparing people to deal with the expected sequelae of TBI is helpful.
- The direct cost of this pilot study was $2.8 million; however, that did not cover all of the data analysis need to take full advantage of the rich dataset. Expanding the cohort to 3,000 patients will cost $25-30 million.
- To put the cost of this much needed research into context, a severe TBI patient has lifetime costs of over $2 million. The TRACK-TBI II funding represents the lifetime cost of only 15 patients.
Part III: Knowledge Translation
Towards Standards of Practice

Presentations

Dr. Mark Bayley, of the Toronto Rehabilitation Institute, chaired the third series of presentations on knowledge translation towards standards of practice.

*Effective Knowledge Translation: Best Practices in the Canadian Stroke Network*
- Dr. Antoine Hakim, Canadian Stroke Network

Lessons can be learned from the stroke world, which, 15 years ago, was where TBI is now. While it used to be thought that nothing could be done after a stroke to reverse the effects, the discovery that the penumbra was still viable for some time after the event revolutionized the stroke world. Since then, the use of t-PA to bust clots has made it possible to reverse some stroke symptoms if it is used within 3.5 hours of occurrence.

When the Canadian Stroke Network (CSN) came into existence, it recognized a significant lack of awareness among members of the public about what to do in the event of a stroke and a lack of knowledge among hospital caregivers on how to treat it. Working with the Heart and Stroke Foundation, the CSN developed a strategy to translate information on stroke through research, a public awareness campaign, surveillance, best practices and standards of care, and professional development.

Several studies have been undertaken as part of this effort. One, in which volunteers took people’s blood pressure at local pharmacies, talked to them about results, and contacted their doctor if the level was moderately elevated, was very relevant to stroke prevention. As a result, the total incidence of stroke, heart attack, and heart failure in participating communities decreased nine percent within a year—and discussions are underway to expand the initiative.

Public education has been carried out through media, websites, and other means on how to recognize stroke and reduce risk by cutting back on sodium—which has an impact on blood pressure and, as a result, cognitive function in older age. To foster professional development, best-practice guidelines have been developed, courses are offered, and an annual Canadian Stroke Congress is held. Today, only facilities that pass tight criteria with regard to processes and equipment used in the care of stroke
patients are designated as comprehensive stroke centres. Working with Accreditation Canada, the CSN also has an accreditation process in place that is being adopted by other countries and is the only one accepted by the World Stroke Organization.

Although risk factors for strokes are more prevalent and increasing, the stroke initiative has had demonstrable results—including a dramatic increase in the percentage of people who make it to stroke centres within the critical timeframe for treatment (from less than 10 to over 40 percent).

Towards a National Strategy on Clinical Practice Guidelines in Canada: Recent Progress
- John Abbott, Health Council of Canada

There is growing recognition of the need for more effort by all parties on both the clinical and policy sides, including governments, to develop an approach for the development, dissemination, and uptake of clinical practice guidelines (CPGs). CPGs are linked with overarching policy goals, such as performance measurement, quality improvement, and efficiencies.

In its 2010 report, the Health Council of Canada (HCC) flagged CPGs as critical to improving patient care and accountability for clinical decision-making. This concept has been supported by the Premiers, who have directed the provincial Health Ministers to work in consultation with experts on this initiative. A Health Care Innovation Working Group, struck to focus on the subject, is working closely with the Canadian Medical Association (CMA) and will deliver its first report in July 2012.

In the meantime, the HCC, CMA, and other partners have been working on the issue within a larger policy context and, in November 2011, convened a Clinical Practice Guidelines Summit to discuss it in more detail. Consensus was that a concerted national approach to CPGs was needed to ensure the availability of high-quality CPGs to all patients and providers in all settings. The consideration of national CPGs already in place in other countries (e.g., New Zealand, Scotland, UK, USA, and Australia) was encouraged as part of this effort.

Researchers, clinicians, governments, and patients all have important roles to play in determining the topics of future CPGs and coordinating with other CPG initiatives to ensure that those developed form an integrated series of guidelines. Canada is at a
breakthrough point in moving forward on CPGs, and the convergence of interests in forging a national approach should be harnessed.

**Points from Plenary Discussion:**

- One of the challenges is that health care is delivered provincially—and there is a lack of standardization of approaches even within provinces. Provincial governments need to be at the table and agree to commit the necessary human and financial resources to deliver on guidelines.
- Governments rely on clinical expertise. TBI experts need to work together to develop the guidelines first, then go to the administrator or government and put something concrete on the table that they want endorsed/supported.

**Full Spectrum of Military Service-Related TBI: DND and VAC Perspectives**

*Canadian Forces Perspective*
- **Dr. Bryan Garber, Canadian Forces**

The Canadian Forces (CF) provides full spectrum health care and a number of other health-related services, including workplace compensation and extended healthcare coverage to all CF members. It works collaboratively with Veterans Affairs Canada (VAC) and other academic organizations involved in research on TBI. This is an issue of particular importance to the CF because the demographic of the military is primarily young men, who are a key risk group for head injuries both in garrison and on deployment.

While TBIs do occur in garrison and are likely of greater public health impact, much attention has been placed on TBIs that occur on deployment, particularly as a result of exposure to blasts. Epidemiologic surveillance data of CF members returning from a six-month deployment to Afghanistan show that about five percent report having suffered an mTBI. Most of these were as the consequence of a blast, and most were on the mild end of the spectrum.

To address the problem, the CF struck an expert panel in 2008 to come up with reasonable guidelines for both the primary care of mTBI in an operational setting as well as the post-deployment management of those reporting a history of mTBI during deployment. These guidelines were created by expert consensus and adapted from existing sports injury and US military guidelines. There are, however, unique
circumstances in a military operational setting that do not exist in the case of a sports concussion. Since none of these guidelines have undergone rigorous validation in a deployed setting, their true value in optimizing patient management remains in question.

Knowledge opportunities in acute mTBI management include the creation of objective diagnostic field-based tests, evidence-based criteria for return to duty decisions, and CT scan protocols for “complicated” mTBI in military settings. Individuals who have persistent symptoms following mTBI after combat deployment represent a complex clinical picture because of the lack of specificity of so-called post-concussive symptoms and their overlap with other conditions such as post-traumatic stress disorder (PTSD) and medically unexplained physical symptoms that are well documented consequences of combat exposure.

This supports the need for additional research on late mTBI management, including studies on the clinical significance of subtle changes on functional imaging and electrophysiologic studies, RCTs on the efficacy of therapies targeted at persistent symptoms, and studies to improve understanding of potential long-term effects and late consequences. Knowledge opportunities in this area of TBI rehabilitation include the timing and intensity of in-patient rehabilitation, optimal care pathways, stem cell research, and alternative therapies.

Points from Plenary Discussion:

- The mechanism is not understood by which a blast wave could create brain injury in the absence of force sufficient to injure lung or ear—nor is it known whether it is possible in humans. Most injuries that occur likely have direct impact on the head similar to motor vehicle collisions. Moreover, when soldiers present with late symptoms, these could be attributable to head injury, PTSD, or unexplained physical symptoms. In the absence of objective diagnostic tests that can reliably discriminate these, the CF takes a symptom-based approach to management that is consistent with guidelines published by the ONF.
- The CF is relatively small (80,000 people in Canada); however, there would be a willingness on behalf of the military to contribute to research (e.g., through the enrollment of subjects in studies) that is well aligned with the CF’s priorities and addresses questions of value in managing TBI from a clinical perspective.
Veterans Affairs Canada (VAC) provides assistance to military veterans with TBI-related health conditions and disability—some of whose injuries date back to World War II and the Korean War. Those who are eligible receive case management and physical and mental health support. Some of the challenges around TBI, from the VAC’s perspective, include the recognition, diagnosis, and attribution of symptoms (e.g., there is no gold standard for diagnosis, particularly for mild traumatic brain injury); that TBI symptoms are often non-specific; that TBI is an acute injury and what follows is not "TBI" but a more specific state; and that medical records might not provide sufficient information, especially when personnel do not access healthcare services. Other challenges related to the management of symptoms that might be attributable to prior TBI are related to access to effective care in life after service and the siloing of physical and mental health in the civilian world. Complex, competing paradigms are at play.

A history of prior TBI, especially mTBI, invokes a broad differential diagnosis of physical and mental health conditions other than but possibly including ongoing brain damage related to a prior TBI. Compensation is available for service-related injuries and illness, and the tendency for people to seek explanations for their symptoms makes it natural for released personnel who develop non-specific symptoms later in life to relate them to prior service.

The common goals of all involved include recognition, appropriate diagnosis, optimal treatment and management of health impairments related to TBI, equal access to health care, and sound and timely knowledge synthesis and exchange—including emerging findings from research. Knowledge exchange is an important challenge, as there is a great deal of inconclusive science, variable expert opinion, and media sensationalism (e.g., “invisible wounds of war” and "signature injury") around mTBI. In addition to better diagnostic tests, a common conceptual framework with standardized terminologies for health, disability, injury, disorder, symptoms, and other terms is needed to clarify issues for veterans, families, policy writers, and practitioners.

Points from Plenary Discussion:

- Better tools are needed to recognize and diagnose ongoing brain changes attributable to prior TBI, especially mTBI.
• There is clear need for sound and timely information for veterans, families, and healthcare providers based on latest research findings.
• The overall goal is to optimize well-being for veterans and their families. This requires optimum recognition, diagnosis, and treatment of health problems; minimizing disability when veterans with TBI-related impairments encounter barriers internally (adaptive coping) and externally (social and physical environments); and ensuring access to sufficient determinants of health.
• People recover differently with the same pathology, so a biopsychosocial approach is important.
Part IV: Identifying Opportunities and Priorities

Concurrent Brainstorming Sessions

The second day of the workshop was composed of concurrent think-tank sessions and had the following three main objectives:

- to identify promising opportunities in TBI research that might benefit from new networking and partnership activities;
- to determine how to better align pre-clinical and clinical TBI research with the most pressing clinical needs; and
- to find ways to ensure that research findings influence best practices in the recognition, prevention, and treatment of TBI.

Participants were divided into pre-determined groups, each with an appointed facilitator and a note-taker, to brainstorm on specific questions (see Appendix III) under five key themes:

1. **Addressing the unique challenges of paediatric TBI**: injury to the developing brain
2. **Harnessing new technologies**: biomarkers, imaging, and patient stratification
3. **Implementing best practices in neuro-rehabilitation**: innovation and efficacy
4. **Improving the understanding and treatment of TBI comorbidities**: mental health and addiction
5. **Moving research into practice**: translation of new findings

Group members were reminded to consider the entire spectrum of TBI—across the lifespan and spectrum of care, and in both a civilian and military context. Highlights of their discussions were presented in plenary, followed by comments and questions from other participants. The detailed outcomes of their discussions are provided here.
1. Addressing the Unique Challenges of Paediatric TBI

Existing Gaps

- Effective methods/tools for diagnosing and measuring outcomes of mTBI and TBI.
- Distinction between different severities of injury.
- Mechanisms of TBI (mTBI, in particular), the behaviors that lead to it (e.g., risk taking), and its natural history/evolution across time and developmental stages.
- Scientifically supported guidelines for existing treatments, especially chronic symptoms after mTBI.
- Information on co-morbidities.
- Information on functional outcomes.
- Information about long-term follow up.
- Information on effective prevention strategies.
- Information on current practices.
- Evidence to better standardize education about consultation.
- Information on those who come to emergency departments (EDs) versus those who do not consult or consult only at a later date.

Needs and Next Steps

- Review and come to consensus around definitions of TBI to inform diagnoses and enable informed decisions about the timing and type of interventions.
  - Determine partners.
  - Consult existing models of functioning, such as the WHO’s International Classification of Functioning, Disability, and Health Model, and existing literature (e.g., paper on moderate-severe TBI in the Journal of Neurotrauma).
- Define common data elements/variables, so they are collected in a standardized/uniform way and at appropriate points in time, and develop a national registry to house them. This would enable both prospective and retrospective studies.
  - Identify, tap into and incorporate existing networks, registries, in various specialties (e.g., pediatrics).
  - Include a consultation registry.
• Use new networks (e.g., mTBI-specific/national), teams, and research money (e.g., capacity building RFA) to motivate multi-disciplinary team research and build capacity.
  o Key enablers could be sport organizations, private clinics, industrial partners, etc.
  o Learn from network examples (e.g., CCTG, PICU, ER).
• Undertake research/RCTs to address gaps in diagnoses, treatments, and outcomes.
  o Identify best methods for diagnosis (e.g., a number of neuropsychological tests are available, but there are insufficient data to support their efficacy; issue of context specificity).
  o Determine efficacy to guide best practices and create treatment guidelines.
  o Consider social integration.
  o Identify gaps in the knowledge of family physicians and the best ways to educate them.
  o Determine current practices (e.g., surveys, ABIKUS, current vs. EBM gap analyses in diagnoses).
  o Recognize age-specific differences.
  o Improve understanding of impact of rest following mTBI.
  o Determine which education programs are most effective and the most efficacious way of getting messages out to the necessary audiences.
  o Improve understanding of the natural history of TBIs.
  o Improve understanding of the role of the developing brain in diagnoses and the evolution of injury following TBI.
  o Research-based evidence to inform prevention programs and education and determine the most efficacious way of getting messages out to audiences (e.g., public, coaches, therapists).
    ▪ Explore the potential role of technology (e.g., smart phone apps).
• Standardize procedures for diagnosis and treatment.
  o At the time of the injury by those involved (e.g., coaches, parents, therapists).
  o At concussion clinics (e.g., McGill and Toronto as models)
  o At EDs (to decrease the number of missed cases)
2. Harnessing New Technologies

Existing Gaps

- Capacity: Canada has an estimated 160 researchers working in the field of focused TBI research, which is a small number for an area that is a major burden on health and disease.
- Poor communication among researchers (e.g., basic scientists, clinical scientists) working in TBI.
- Disparities in funding between clinical and basic research (may be due to different grant review cycles and changes in panel of reviewers).
- Support for innovation (which is not time-bound).
- Translation of research into medicine (expensive, time consuming, ethical and regulatory issues specific to new technologies).
- Large-scale longitudinal studies.
- Guidelines for research and specific therapeutic strategies.
- Standardized definitions (e.g., persistent TBI, biomarkers).

Needs and Next Steps

- Standardize definitions to enable the creation of a standardized pathway for TBI research.
- Translate research into practice: bench to bedside and beside to bench (e.g., also take clinical ideas back to the lab and find the mechanism/physiology behind them).
- Have CIHR serve as a medium to bring together provincial, federal, private-sector, and industrial partners to share their ideas with researchers in TBI and form a funding infrastructure. Invite bodies that are more liable to invest in TBI research (e.g., NHL); provide incentives to take part.
- Have CIHR work as a facilitator to bring together researchers of all types, so they communicate more.
- Create a research network with a nationwide standardized databank and networking space to enable the sharing of samples, biospecimens, results, technologies, human resources, and ideas.
- Hold another meeting to establish common data elements. Include stakeholders, donor bodies, research partners (including graduate students and post-doctoral trainees), etc. (e.g., Dahlam meeting in Germany).
Leverage existing funds and strategies and attract more funding partners, so the field can become more self-sustaining.

Build on existing strengths: adapt existing infrastructures/models from other fields (e.g., PURE-MRI) and add new ideas and technologies using a phased-in approach.

Encourage innovation and build infrastructure to support it over the long term.

Create a nationwide database to inform future guidelines for research direction and management, translation, and therapeutic strategies.

Encourage community and researchers to grow, explore, and evolve in different directions within TBI.

Improve classification beyond mild-moderate-severe; be inclusive of other parameters (e.g., biomarkers, imaging) for measuring severity of TBI.

Undertake longitudinal studies.

Utilize innovations from elsewhere and make it work in the setting of TBI research (e.g., stroke and tPA).

With regard to the potential for the application of biomarkers, imaging, and patient stratification in TBI,

- first, identify new biomarkers beyond those that are already known (e.g., S100B, ubiquitin hydroxylase), and
- second, conduct experiments to use these biomarkers as a toolset when merged with magnetic resonance imaging. Study designs for pre-clinical and clinical translation can be planned accordingly.

Biomarkers are key elements for stratification/characterization. All types should be integrated, coupled with longitudinal designs, for assessment of early severity as well as for prognosis and monitoring (e.g., pre- and post TBI at different timeframes). Categories of biomarkers include

- clinical variables,
- imaging studies,
- electrophysiological assessments and signals (passive and evoked),
- biochip assays for serum biomarkers, and
- cerebrovascular reserve measures (e.g., blood flow velocity, oxygenation, pressure).
3. Implementing Best Practices in Neuro-Rehabilitation

Existing Gaps

- RCTs for interventions
- Evidence of what works
- Timing of treatment
- Elements needed to determine efficacy of treatment:
  - Clear definition of recovery using behavioural, functional criteria (baseline, natural history of recovery)
  - Factors underlying variability (individual difference) and influences on best treatment (limits placed on RCTs)
- Description of systems of care in Canada and their variability
- Potential of biological markers in selecting optimal rehabilitation interventions
- Meaningful outcome measures
- Funding for research on TBI rehabilitation

Key Themes

1. Identify the elements required to determine the efficacy of TBI rehabilitation interventions.
   a. Biomarkers for characterization of dysfunction in various systems, natural history of recovery, identification of meaningful patient outcomes
   b. Active ingredients of rehabilitation that continue in real life, generalizability to real world
   c. Commonly agreed-upon definitions
2. Identify the optimum models for testing treatment interventions.
   a. E.g., national database; RCTs; conventional studies; community-based low-cost models
   b. Prioritize imaging studies that can quantify treatment models.
   c. Establish a foundation for clinicians and researchers for prioritization of issues.
   d. Emphasize the importance of working with consumers to help shape research.
3. Identify a model that could frame TBI research.
   a. E.g., medical, disability, biopsychosocial
   b. May need to revise models of care in acute rehabilitation (e.g., early supported discharge in home setting)
4. **Identify the best interventions.**
   a. Long-term treatment models
   b. Ecological treatments
   c. Based on theoretical framework, knowledge of mechanisms of injury (where, what, when, how), observable mechanisms demonstrated using neuroimaging, biomarkers, neuropsychological testing
   d. Specific skills could be targeted (e.g., cognitive, sensory, motor)
   e. Based on solid understanding of patient’s problems

**Needs and Next Steps**

- Examine what is happening to the brain in treatment and in rehabilitation.
- Look at things from a disability model rather than a medical / disease model.
- Promote international collaboration and use it as a stepping-stone to creating a national TBI network founded on the link between clinicians and researchers for the translation of research into practice.
  o Approach CIHR for funding (e.g., Signature Initiatives, SPOR).
  o Link to successful international networks (e.g., UK and Australia).
- Consider developing a National Centre of Excellence for the Study of TBI.
- Create a visible national platform, communities of practice, and networks founded on the utilization of best technologies for treatment, education, and delivery (e.g., “the stroke engine” platform for communication, practice, job creation, knowledge translation).
- Promote greater collaboration between neuroscience and rehabilitation researchers to link the findings of neuroscience to the clinical application of these findings with patients in rehabilitation, and between researchers/clinicians to prioritize and achieve important outcomes.
- Work with consumers so that they can help shape and prioritize research.
- Come to consensus on the best evidence available from research and use it to develop practice guidelines for implementation.
- Put TBI rehabilitation on the national research agenda (policy makers; funding agencies).
- Determine whether to focus rehabilitation research on moderate/severe TBI or TBI at all levels, taking into consideration efficiency and cost.
- Use low-cost technology (e.g., web platform) to improve treatment/education to remote communities (e.g., First Nations).
- Document (e.g., using a database) what is currently being done in clinical practice to further develop individualized or personalized rehabilitation.
• Optimize outcomes by encouraging interdisciplinary treatment, a personalized approach, and consideration of individuals’ living environment, and by including clinicians in research to collect data.
• Develop a clinical model system of care (e.g., study subsets of patients, look at outcomes that deal with participation/burden of care, use a hypothesis-driven dataset).
• Demonstrate the importance of using more elaborate outcome measures that consider all the complexity of everyday functioning in real-world environment and their pertinence to basic neuroscience researchers (create a loop in the research cycle).
• Develop more meaningful outcome measures (not just questionnaires but naturalistic observations).
• Track the trajectory of change to see what is working.
• Develop non-traditional and resource-efficient treatments to help people cope with life.
• Determine which treatments promote generalization to everyday life.
• Develop appropriate long-term models for monitoring outcomes (e.g., Australia monitors outcomes over lifespan, post-injury).
• Develop models of care for long-term treatment that
  o are low-cost,
  o are community-based,
  o utilize low-cost technology (e.g., tele-rehab; partnership with Bell?),
  o involve case management,
  o adapt chronic self-management programs,
  o develop self-efficacy,
  o develop new neuropharmacological treatments,
  o prevent further neurodegeneration,
  o develop appropriate mechanisms for the maintenance of motivation/engagement,
  o incorporate information about co-morbidities,
  o are multidisciplinary, and
  o are ecologically valid.
• Think outside the box, particularly with regard to acute care, while still being resource efficient (e.g., Early Supported Discharge in Calgary has resulted in improvements in outcomes).
• Develop common data elements, including biomarkers, physiological indices, environmental characteristics, and individual characteristics of patients.
4. Improving the Understanding and Treatment of TBI Co-Morbidities

Existing Gaps

- Registry and surveillance data across settings and jurisdictions, lifespan of development, age, sex and gender, SES, and on factors such as sleep, mental illness, and addiction.
- Longitudinal data to improve understanding of the etiology, natural history of co-morbidities.
- Understanding of mechanisms (biological, psychosocial, and environmental) to facilitate early and secondary prevention.
- Research strategies that consider the heterogeneity of the population and multiple phenotypes.
- Contextual information (e.g., effective measurement of environments, individual interaction).
- Research on quality of life and the “right” outcome.
- Objective measures of dysfunction.
- First-person (survivor’s) perspective on the phenomenology of multiple co-morbidities.
- Access to therapies.
- Funding for longitudinal studies.
- Application of technology.
- Translation of interventions into real-life settings.
- Understanding of function vs. morphology.
- Information on sleep and fatigue: psycho-social impacts and interventions to address them (promoting quality of life and community re-entry).
- Classification of TBI, so information can be applied to appropriate populations.
- Information on return to work and return to school (particularly in mTBI).
- Well-developed, evidenced-based treatments across the lifespan.
- Information on prevention (including secondary).
- Information on the impact of TBI on marriage/family.
- Information on protective factors to prevent degradation of social supports.


**Needs and Next Steps**

**Building Capacity**

- Conduct *in situ* outcome and implementation studies.
- Identify vulnerable individuals from a biological/genetic and psychological perspective.
- Develop alternatives to RCTs for research on co-morbid conditions (e.g., single subject/qualitative) that take into consideration all contributing factors (e.g., severe cases are often early injury with complex psychosocial situations).
- Identify modifiable factors.
- Study and adapt existing treatment protocols.
- Study protective factors (e.g., to prevent the degradation of social supports).
- Undertake projects that include co-morbid populations and program evaluation.
- Promote the reporting and sharing of data (e.g., for use in meta-analysis).
- Examine how needs are fulfilled and services delivered in different regions (within and across provincial boundaries) and communities (e.g., urban/rural, remote, multi-cultural, aboriginal).
- Harmonize program outcomes and the evaluation of current service systems across jurisdictions.
- Increase use of public health records.
- Harmonize strategies for databases and surveillance.
- Leverage use of the Health Care in Canada Survey and other databases and registries (e.g., WSIB, insurance companies, driver’s license) and influence data collection, where possible.
- Leverage existing methodologies, such as model systems programs in the US.
- Coordinate efforts with existing longitudinal studies (e.g., aging, homelessness).
- Establish research chairs (possibly regional) in brain injury and mental health to capitalize on existing mental health research (could be in centers of excellence in Mental Health; military rehabilitation chair a potential model).
- Launch team grants and target career awards beyond new investigator awards (e.g., intermediate and senior).
- Provide funding for post-doctoral researchers.
- Support clinicians to do research (release time).
- Examine possible funding opportunities arising from popular press on sports figures.
- Build on existing strengths (e.g., ABI population-based data set, ONF-supported research).
• Include brain injury in the Canadian Survey of Neurological Conditions.
• Model systems-type funding in Canada.
• Launch an initiative to improve common data elements and modify them for mTBI and sports.

Moving Research into Practice

• Target PR at physicians (e.g., conference).
• Gear KT efforts toward mainstream providers (e.g., similar to stroke strategy): provide education (e.g., simple recommendations) for general practitioners, mental health providers, public health nurses, and all others who serve clients.
• Raise public awareness of common issues across the lifespan.
• Link those involved in prevention and treatment.
• Use the stroke strategy as a model to identify appropriate messages, audiences, and delivery/dissemination methods.

International Context

• Collaborate with other jurisdictions on population-based health; compare outcomes based on systems of care.
• Record and facilitate international contacts.
• Promote the exchange of information with collaborators from other countries.
• Promote funding for joint research programs.
• Address the potential for serendipitous findings (e.g., cross cultural/SES differences) related to social issues.
• Use “wait list”, which occurs in Canada but no other jurisdictions (e.g., bootstrap a Canadian study to the American military studies, using the same methodologies).
• Examine differences attributable to health care systems and societal factors.
• Create standardized protocols/measures (parallels to NIH civilian outcomes).
• Look to funding agencies for assistance reporting on the Canadian context and coordinating efforts with international researchers (e.g., Canada has something unique to offer in terms of its health care record).
5. Moving Research Into Practice

Existing Gaps

- Public awareness.
- Strategies for engagement (e.g., consumers, healthcare practitioners, potential partners).
- Knowledge translation to policy makers.

Needs and Strategies Moving Forward

Building Capacity

- Create an overarching framework similar to the “stroke engine”.
- Hospital accreditation (HIPE project underway; early collaboration with Accreditation Canada).
- Advocate for a national clearinghouse.
- Develop and implement national guidelines (incorporate existing ones, such as DND, mTBI, BTF, ABIKUS).
- Prioritize “actionable nuggets”.
- Engage users/consumers extensively. Conduct cross-system reality checks: is what is being proposed meaningful, feasible, and acceptable?
- Harness public awareness of concussion to increase recognition of mTBI (e.g., policy makers, military/veterans, sports, consumers).
- Get to the Premier’s table (prioritize TBI).
- Tie best practices to performance measures (bench to bedside).
- Focus on comparative effectiveness research and advocate for a national state of affairs (possible assistance from Accreditation Canada, health services organizations).
- Examine different models of care and take a systems approach to putting guidelines into practice (e.g., engage nurse practitioners; paramedics/OT/PT; paramedics in this discussion).
- Foster dialogue around centralization and regionalization and how to tweak the system to identify and manage the high-risk patient.
- Create partnerships for both funding and delivery (e.g., information technology; app developers; computer science undergrads; colleges; family practice research database; data centre; aboriginal groups [e.g., through remote follow-up; engage
Institute of Aboriginal Health); insurance companies; WSIB; hospital foundations; sports groups; manufacturers).

- Create a development strategy and the infrastructure to build a network for crafting the research to translate into practice guidelines and for supporting their translation and implementation. Focus on performance measures that capture patient outcome as well as the performance of providers and their organizations.
- Identify and utilize champions (e.g., premiers, sports, consumer groups).
- Look to other areas of innovation that may have commercial spinoffs, such as biophysics.

Moving Research into Practice

- Get the facts out.
  - Actionable Nuggets Project:
    - Identified 20 mobilizable practices
    - Piloted in Ontario/Newfoundland (Australia)
    - Involved prioritization
    - Single website
    - National guidelines group (Clearinghouse)
- Take lessons from existing KT activities.
  - Concussion strategy:
    - Awareness
    - Recognition
    - Diagnosis (updated WHO systematic review)
    - Early care
    - Rehabilitation
    - Reintegration
  - ABIKUS (moderate and severe BI):
    - Implemented at four centres
    - Guidelines needed to be very clear and explicit
  - Cognitive rehabilitation audit tool:
    - Collaboration with Aussies
    - Ability to check adherence
  - ICU Guidelines (Martin Chapman, Sunnybrook):
    - Addressed poor adherence to ICP monitoring and high variability in ICU care
    - Launched neurocritical care
    - Created an algorithm of care
New Opportunities in Traumatic Brain Injury Research
Draft: June 14, 2012
Leslie Jones Communications

- Used Geoff Manley and Brain Trauma Foundation
- Highlighted importance of engagement in network
  - SCI Knowledge Mobilizations Network:
    - Includes guidelines and performance measures
    - Engaged organizations willing to collect outcomes/process measures
    - Engaged practitioners in narrowing focus
    - Focused on users

International Context

- Ensure alignment with other chronic disease groups.
- Learn from mental health models.
- Align with initiatives such as SPOR.
- Put Canadian strengths on the international table:
  - National network of collaborators
  - Alignment with international guidelines and standards
  - Centres of excellence
  - Core datasets that are part of international data elements
  - Effectiveness research
  - Neuroimaging repository (treatment effects)
  - Biophysics (innovation)
Closing

Summary

Mr. Bassett-Spiers provided a high-level summary of the workshop discussions, highlighting collaboration, cooperation, and integration as three main themes that had emerged. Advocacy and getting a clear and sustained message out to consumers, policy-makers and other stakeholders, he said, was essential—as was bringing in other partners, engaging the broader community, leveraging funding, and addressing the disproportionate burden of TBI on aboriginal, homeless, and other vulnerable populations.

He emphasized that the workshop was not an ending but a beginning, and that those involved were committed to working together to take advantage of national and international opportunities in TBI research. While Canada already had some capacity in this area, he said, more thought was needed around technologies and other methods of connecting with one another—perhaps through the creation of a clinical research network. He thanked the CIHR for organizing the workshop and serving as an umbrella under which the many groups assembled could come together.

Next Steps

Dr. Phillips closed by thanking everyone for attending, the speakers for contributing context to the discussions, and those involved in the organization of the workshop for their efforts in bringing the event to fruition. He acknowledged that it would take some time to digest the many ideas and opportunities brought forward over the past few days and for the group itself to coalesce. He urged participants to use the momentum initiated at the workshop to reach out to their communities and bring in other key players, as making this a fully inclusive process was essential moving forward.

Dr. Phillips explained that CIHR and other potential funders were not going to impose a research agenda on those involved; rather, it would be defined by the national strategy. The onus, he said, was on all players to come together as a group to determine priorities and opportunities and the resources needed to achieve them—including some issues that could be tackled in the near term. He stressed the need, for example, to put more effort into addressing the tremendous burden TBI puts on vulnerable populations.
Obtaining meaningful information on TBI, he commented, required “large N’s”—and the best way to achieve them was to be part of international efforts to standardize data collection and management through consensus on common data elements. Working effectively in collaboration with colleagues in the U.S. and Europe, said Dr. Phillips, required both self-awareness and awareness of what was happening elsewhere in the world. An important starting point, he suggested, would be to assess Canada’s current resources, capacities, and areas of strength, expertise, and opportunity—to ensure alignment with rather than duplication of existing work.

For INMHA in particular, he said, the international initiative also represented part of a much larger opportunity to better understand the brain and the impacts of damage to the brain on human health. He stressed the importance of encouraging two-way communication between the clinical and pre-clinical community, and the potential benefits of identifying some biomarkers to predict responders and non-responders.

Dr. Phillips cited the lack of funding for pediatric TBI in individual research institutions as reflective of a nationwide problem, adding that partnerships aimed at leveraging existing funds were necessary to advance TBI research. Given the importance of TBI to DND and VAC, he said, partnership opportunities were being explored in which CIHR could potentially serve as a broker in providing new innovations and interventions that would directly improve the health and wellbeing of their staff.

The business community, said Dr. Phillips, had to be informed about the impact of brain health on commercial productivity and the overall economic health of the nation. Provincial health authorities, he said, also had to be educated about the benefits of investing in TBI research—and that message had to be reiterated to consumer groups, Members of Parliament, and other decision makers. As the field continued to advance and there were more opportunities to demonstrate its impact, he hoped a case could be made for TBI to become a SPOR network. In the same vein, he suggested, a Networks of Centres of Excellence program could be developed to link the TBI community.

In his final words, Dr. Phillips expressed confidence in the advancement of TBI research in Canada and internationally. He said that a major objective had already been achieved by holding the national workshop and, thereby, recognizing an area of unmet need that CIHR and its partners were prepared to address together. One of the goals of the funders’ meeting to follow, he said, would be to identify a path forward, including ways to keep the group connected and informed about developments in the international collaboration and opportunities arising from it.
## Appendices

### Appendix 1: Agenda

#### DAY ONE: Thursday April 12, 2012

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<th>Time</th>
<th>Session</th>
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<td>08:30-09:00</td>
<td>Welcome and Opening Remarks</td>
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| 09:05-09:35 | TBI: Incidence, Vulnerable Populations & Economic Burden in Canada  
Dr. Michael Cusimano, St. Michael's Hospital |
| 09:35-09:55 | Towards a TBI Research Strategy for Canada: Report from the ONF-BIAC Advisory Committee  
Dr. Grant Iverson, UBC |
| 09:55-10:15 | Overview of the EU-NIH-Canada “International Initiative for Traumatic Brain Injury Research”  
Dr. Anthony Phillips, CIHR-INMHA |
| 10:30-11:00 | Management Best Practices: Guidelines for mTBI and Persistent Symptoms  
Dr. Shawn Marshall, MD MSc University of Ottawa |
| 11:00-11:30 | Child and Youth TBI: Incidence, Treatment Best Practices, Clinical Perspectives  
Dr. Jamie Hutchison, Sick Kids |
| 11:30-12:00 | Post-TBI: Clinical, Cognitive/Imaging Research  
Dr. Alain Ptito, MNI |
| 12:00-12:30 | From phenomenology to mechanism: Integrating clinical and pre-clinical concussion research  
Dr. Cheryl Wellington and Dr. Alex Rauscher, UBC |

12:30-13:30 LUNCH AND NETWORKING
13:30-14:15 KEYNOTE SPEAKER Introduced by Dr. Sam Weiss, Hotchkiss Brain Institute

Dr. Geoffrey Manley, Professor and Vice Chairmain of Neurosurgery, UCSF
“TBI Research Collaboration: Building Interdisciplinary Networks from Common Data Set Elements”

PART 3 KNOWLEDGE TRANSLATION TOWARDS STANDARDS OF PRACTICE
Chair: Dr. Mark Bayley, Toronto Rehab

14:15-14:50 Effective KT: Best Practices in the Canadian Stroke Network
Dr. Antoine Hakim, CEO and ScientificDirector, CSN

14:50-15:25 Towards a National Strategy on Clinical Practice Guidelines in Canada: Recent Progress
Mr. John G. Abbott, CEO, Health Council of Canada

15:40-16:40 Full Spectrum of Military Service-Related TBI: DND and VAC Perspectives
Dr. Bryan Garber, Canadian Forces and Dr. Jim Thompson, Veterans Affairs Canada.

18:00-22:00 RECEPTION, KEYNOTE SPEAKER, AND DINNER

19:00-20:00 Keynote Address Introduced by Dr. Anthony G. Phillips
Dr. Adrian Owen, University of Western Ontario
Brain Imaging in the Vegetative State

DAY TWO: Friday April 13, 2012

08:30-14:30 CONCURRENT BRAIN STORMING SESSIONS: IDENTIFY OPPORTUNITIES AND PRIORITIES

08:30-08:45 Overview of Day 2: Approach and Objectives
Dr. Elizabeth Theriault, CIHR-INMHA

08:45-10:15 CONCURRENT BRAINSTORMING SESSIONS:
1. Address the unique challenges of paediatric TBI: injury to the developing brain
2. Harness new technologies: biomarkers, imaging and patient stratification
3. Implement best practices in neuro-rehabilitation: innovation and efficacy
4. Improve understanding and treatment of TBI co-morbidities: mental health and addictions
5. Move research into practice: translation of new findings

10:30 -12:00 CONCURRENT SESSIONS CONTINUED

12:00-13:00 LUNCH AND NETWORKING
13:00-14:15 Reports from Concurrent Sessions
10 minutes each, 5 minutes for questions

14:15-14:25 High Level Summary
Mr. Kent Bassett-Spiers

14:25-14:30 Conclusions and Next Steps
Dr. Anthony Phillips

CLOSED SESSION: FUNDING AGENCIES NETWORKING

15:00-17:00 Facilitated Discussion: Refining the Elements of a Canadian TBI Strategy
PANEL: Kent, Sam, Tony, Remi, DND/VAC, others

National TBI Research Strategy: Investment and Funding Opportunities
Role for Canada in the International TBI Initiative: Preparing for InTBIR
Opportunities for New National Partnerships
Steps Forward: Timelines and Responsibilities
Closing Remarks
# Appendix 2: List of Participants

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<td>Department of Critical Care, St. Michael's Hospital</td>
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<td>5 Barlow</td>
<td>Karen M</td>
<td>Co-chair</td>
<td>Alberta Children's Hospital Research Institute Behaviour and the Developing Brain Theme Group</td>
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<td>Erik</td>
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<td>Partnership &amp; Citizen Engagement, Knowledge Translation, Canadian Institutes of Health Research</td>
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## New Opportunities in Traumatic Brain Injury Research

**Draft: June 14, 2012**  
Leslie Jones Communications

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Appendix 3: Questions for Brainstorming Sessions

1. Building on the Environmental Scan conducted by ONF/BIAC and the content of the scientific presentations at this workshop, what are the major gaps in TBI research, what are the strategies that would best fill those gaps, what is Canada’s capacity in the area, and how would we move forward?

2. How could Canada build its capacity in these areas?

3. What would be required to successfully address these gaps: e.g., clinical research networks, research and clinical registries or common data elements/data sets, industry participation or other key enablers?

4. What are the strategies necessary to move this research into clinical practice?

5. How would Canada position this research and knowledge mobilization strategy in an international context consistent with the NIH-EU-CIHR-led initiative?