Advances in Imaging Technology Developed at BWH Reveal “Invisible Injuries” in Football Players

The long-term neuropsychiatric consequences of repeated mild traumatic brain injury, and specifically sports-related concussive and sub-concussive head impacts, to football players has been an active area of research at the lab of Martha Shenton, PhD, Director, Psychiatry Neuroimaging Laboratory, Department of Psychiatry, Brigham and Women’s Hospital. For decades, she and her colleagues have been investigating the role of brain abnormalities in schizophrenia, post-traumatic stress disorder (PTSD), traumatic brain injury (TBI), attention-deficit hyperactivity disorder (ADHD), velocardiofacial syndrome, and William’s syndrome.

In a study published online in the Journal of Neurotrauma (J Neurotrauma, 2015 Sep 25), Dr. Shenton, Inga Koerte, MD, and Julie Stamm, PhD, conducted brain imaging of former National Football League (NFL) players between the ages of 40 and 65. The goal of the study was to examine the relationship between age of first exposure to repeated head injuries through tackle football and later-life corpus callosum microstructure. They found that former NFL players who started playing tackle football before the age of 12 were found to have a higher risk of altered brain development compared to those who started playing at a later age. The study is the first to demonstrate a link between early exposure to repetitive head impacts and later life structural brain changes.

To examine brain development in the players, the research team used diffusor tensor imaging (DTI), to look at the movement of water molecules along white matter tracts. They found that the research participants who started playing football before age 12 were more likely to have alterations of the white matter tracts of the corpus callosum.

Age When Players Begin Playing Football Was Key Factor in Impact of Injuries

“Our was the first study to show that when you start playing football matters,” Dr. Shenton said. “There was an association between early exposure to repetitive head impacts and structural brain...”
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changes later in life.” The researchers found the bigger risk of alterations in brain development for players who played tackle football between the ages of 10 and 12, a critical window in the development of a child’s brain, than for those who waited longer to start playing the game. A separate study published in the *Journal of Neurotrauma* (*J Neurotrauma*, 2015 Sep 23) by the same group of researchers found that men who started tackle football before age 12 were more likely to struggle with fundamental cognitive function – like memory, reasoning and planning. They were also three times more likely to face “clinically-meaningful depression.”

This study was conducted as part of the *Diagnosing and Evaluating Chronic Traumatic Encephalopathy using Clinical Tests (DETECT)* project¹, funded by NIH. In a statement on the study, the researchers said “these abnormal neuroimaging findings are not necessarily indicative of chronic traumatic encephalopathy or CTE. While this study adds to the growing concern that exposing children to repetitive hits to the head in tackle football may have long lasting consequences, there are likely other contributing factors that contribute to overall risk for CTE.”

In addition, the Psychiatry Neuroimaging Laboratory has received funding from the Department of Defense for a positron emission tomography (PET) study to investigate the role of tau pathology in living retired NFL players. Dr. Shenton is also studying the effects of subconcussive blows to the head in elite professional soccer players as well as university hockey players.

**Advances in Neuroimaging Make Possible Better Diagnosis and Treatment**

“All of these advanced neuroscience studies utilize tools and technologies developed in the PNL,” said Dr. Shenton. “They include a multi-tensor tractography algorithm (developed by Yogesh Rathi, PhD) to trace white matter pathways in the brain; a free-water imaging technique (developed by Ofer Pasternak, PhD), which provides information about the structure of the tissue; an algorithm to measure the geometry of white matter fibers (developed by Peter Savadjiev, PhD), and a compressed sensing-based algorithm for faster acquisition of diffusion MRI scans. Without these advances in imaging technology our neuroscience studies would not be possible.”

“Our studies speak to the importance of advances in neuroimaging technology. We now have many imaging tools available to us to improve our understanding of concussions and traumatic brain injuries and help the clinicians who treat patients,” said Dr. Shenton. “These were previously ‘invisible’ injuries, but now they are visible and we can track them and learn more about them and better help those who suffer these injuries. This to me is the ultimate importance of our work.”

Growing concern about repetitive hits to the head during sports and the short-term and long-term effects is warranted. “We are encouraged by the increased awareness of the acute and long-term consequences of repeated concussive and subconcussive head trauma as well as proposed legislation intended to protect youth and adolescent athletes,” she concluded.

¹Led by Robert Stern, PhD, professor and director of Boston University Alzheimer’s Disease and CTE Center's Clinical Core

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Comprehensive Examination of Antidepressant Use in Pregnancy Results in New Findings about Risks to Newborns

Researchers at Brigham and Women’s Hospital (BWH), led by Krista F. Huybrechts, PhD, MS, an epidemiologist in the Division of Pharmacoepidemiology and Pharmacoeconomics at BWH, have published several large population-based studies examining the safety of antidepressant use during pregnancy.

PPHN and Antidepressants
Published in the *Journal of the American Medical Association* (JAMA. 2015 Jun 2;313(21):2142-51.), the team’s study of antidepressant use late in pregnancy and the risk for pulmonary hypertension of the newborn (PPHN) included 3,789,330 pregnant women enrolled in Medicaid from two months or less after the date of their last menstrual period through at least one month after delivery. Among these women, 128,950 (3.4 percent) filled at least one prescription for an antidepressant late in pregnancy (102,179 used an SSRI, and 26,771 used a non-SSRI antidepressant). The reference group consisted of women without exposure to antidepressants at any time during pregnancy. After restricting the cohort to women with depression and adjusting for confounding variables, the adjusted odds ratio was 1.10 (95 percent CI, 0.94-1.29) for SSRIs and 1.02 (0.77-1.35) for non-SSRIs. Upon restriction of the outcome to primary PPHN, the adjusted odds ratio for SSRIs was 1.28 (1.01-1.64) for SSRIs and 1.14 (0.74-1.74) for non-SSRIs.

“We found no significant association between the use of antidepressants and previously suspected cardiac defects, including paroxetine use and right ventricular outflow tract obstruction and between sertraline use and ventricular septal defects.”

Clinical Significance
At BWH, experts in maternal-fetal medicine and women’s mental health collaborate to deliver expert care for women with psychiatric conditions before, during, and after pregnancy. Women are provided with consultation and treatment for a variety of mental health concerns that can arise during pregnancy or the postpartum period or may predate pregnancy. They can be seen during the course of prenatal care in an obstetric, primary care or psychiatric clinic, or even within the Neonatal Intensive Care Unit (NICU), for consultation and evaluation. Based on the latest research findings, women are routinely counseled on the benefits and risks of the use of psychiatric medications during pregnancy, including the risks of untreated mental health symptoms, including depression and anxiety, during pregnancy.

“Our goal is to help our patients make informed choices about the use of antidepressants and other psychiatric medications during pregnancy alongside non-medication treatment options,” said Leena P. Mittal, MD, Director of the Reproductive Psychiatry Consultation Service within the Department of Psychiatry at BWH. “We rely on large-scale studies such as these to provide valuable data and guidance for patients trying to make choices that will optimize their mental health and the wellbeing of their growing families.”

Dr. Huybrechts and her team are currently studying the safety of other types of psychiatric medications, including antipsychotic medications, mood stabilizers, and stimulants, during pregnancy.

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Clinicians regularly face challenges delivering comprehensive psychological and medical care to patients with complex conditions, such as delirium, alcohol withdrawal, suicide risk, and potential harm to others (DASH). Although these problems can affect patients at any age, they are particularly common among the elderly.

Brigham and Women’s Hospital (BWH) has achieved measurable improvements in reducing readmission rates among this population with the development of a multidisciplinary effort led by the departments of medicine, nursing and psychiatry to improve care and outcomes for patients admitted as inpatients. David F. Gitlin, MD, Chief of the Division of Medical Psychiatry at BWH, was a key driver of this initiative.

“Some of the recurrent issues our patients presented with was this cluster of problems including delirium, alcohol use disorders, suicide risk and violence potential, and we are at an increased risk for higher-than-average readmission rates due to misdiagnosis, we focused our efforts on earlier detection and treatment,” Dr. Gitlin said.

Dr. Gitlin was an author of the Joint Commission Journal on Quality and Patient Safety titled A Population-Based Care Improvement Initiative for Patients at Risk for Delirium, Alcohol Withdrawal, and Suicide Harm (Jt Comm J Qual Patient Saf. 2015 Jul;41(7):291-302). Barbara E. Lakatos, DNP, PCNS-BC, APN, Program Director of the Psychiatric Nursing Resource Service at BWH and BWH hospitalist Adam Schaffer, MD, were co-authors.

In their publication, the BWH team reported that implementing an interdisciplinary care improvement initiative at BWH for patients at risk of negative outcomes related to certain mental or behavioral health conditions reduced the preventable 30-day hospital readmission rate of patients by nine percent over three years.

**Reducing Readmission Rates is a Hospital-wide Effort**

In an effort to reduce readmission rates caused by mental health problems, Dr. Gitlin and his colleagues used a comprehensive, population-based effort, implemented across all departments at BWH, to enhance screenings for these conditions. The DASH initiative involved enhanced screening and the introduction of new care management guidelines and order sets pertaining to the DASH diagnoses.

With the exception of neonatal and hospice patients, all BWH inpatients were included in the study. After screening and care guidelines were developed, the team embarked on a hospital-wide effort to integrate them into the clinical workflow in 2010. Training videos, resource manuals and role-playing workshops were developed and assessment tools were embedded into nursing and medical workflows. The effort started with pilot units and were later adopted across the entire hospital.

The care improvement process consisted of four phases: development of guidelines; implementation/rollout; integration into practice; and sustainability, including ongoing practice development and evaluation. The implementation outcomes were evaluated using eight parameters: acceptability; adoption; appropriateness; feasibility; fidelity: implementation cost; penetration and sustainability.

The assessment showed the volume, average length-of-stay, clinical service line, discharge location and 30-day admission rate of DASH patients. The researchers found that while the DASH population increased by one percent from 2012 to 2013, the 30-day readmission rate decreased by nine percent from 2010 to 2013 approaching the hospital’s overall rate of 13.3 percent.

Dr. Gitlin said, “A key reason for these positive results is that our DASH program was embedded in the clinical culture across the hospital. Close nurse-physician collaboration, including joint leadership and simultaneous rollout for nurses and physicians, contributed to the initiative’s effective implementation. The nursing staff education, under the leadership of Barbara Lakatos, was critical to reducing readmission rates.”