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"Improving Sports Safety: A Multifaceted Approach"

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Chairman Terry, Ranking Member Schakowsky, and Members of the Subcommittee, I am honored to have this opportunity to appear before you today.

My remarks focus on the radiological research on sports-related concussion and subconcussion. I specifically address the evidence resulting from the use of advanced neuroimaging techniques, particularly diffusion magnetic resonance imaging (dMRI) which, unlike conventional magnetic resonance imaging (MRI) and computed tomography (CT), is sensitive to diffuse axonal injury, the most common injury observed in mild traumatic brain injury (mTBI) (e.g., see review in Niogi and Mukherjee, 2012; Shenton et al., 2012, included in supporting documentation).

Executive Summary: The following will be reviewed:

1) The magnitude of mTBI as a health problem in this country, what we know about mTBI, and why it has been difficult until quite recently to find radiological evidence.

2) Evidence from post-mortem findings of CTE from previously retired professional football players from Ann McKee and colleagues' work (McKee et al., 2009; 2013).

3) Evidence of the effects of repetitive brain trauma from blast injury, which looks quite similar to the CTE findings in athletes (Goldstein et al., 2012).

4) The importance of repetitive mTBI, particularly in sports-related injuries and how repetitive injuries may increase the risk of neurodegenerative disorders, once referred to as "punch drunk" or "dementia pugilistica" in boxers, and now referred to as chronic traumatic encephalopathy (CTE).

5) Evidence from our group, using diffusion MRI, that shows brain alterations in university hockey players in Canada from pre- to post-season, including three subjects who experienced a concussion during the season (Koerte et al., 2012a, included in supporting documentation), followed by a comparison of symptomatic retired professional football players and matched controls that demonstrates cortical thinning and accelerated thinning with age in retired, symptomatic professional football players compared with controls (Koerte et al., unpublished data).

Finally, evidence from our group of brain alterations, from a study of elite soccer players from Germany who were selected for having no symptoms and no history of concussion, and had only experienced subconcussive blows to the head (Koerte et al., 2012b, included in supporting documentation).

This evidence, taken together, suggests that there are some individuals who are at increased risk for brain changes that may lead to neurodegenerative disorders such as, but not likely limited to, CTE.

The question to be addressed is why some individuals develop long-term consequences of brain trauma while others do not.

First, sports-related mTBI, also known as concussion, affects between 1.6 million and 3.8 athletes in the United States each year (Langlois, Rutland-Brown, and Wald 2006). The number of sports-related concussions in youth has also increased in recent years (Gilchrist et al., 2011). Moreover, the incidence of repetitive subconcussive blows (i.e., hits to the head with enough force to have an impact on neuronal integrity, but without associated symptoms) is even greater. For example, a recent study by Broglio et al. (2011) found that the average high school football player receives 652 hits to the head per season that exceed 15 g's of force. Further, a recent study from our group (Koerte et al., 2012b; included in supporting documentation) describes structural changes to white matter in soccer players with extensive histories of heading the ball but *without* known symptoms or history of concussions, i.e., only subconcussive blows to the head.

The number of mTBI and sports-related mTBI reported each year in the United States is, however, likely a gross underestimate since it does not include those who seek treatment in private clinics, those seen by primary care physicians, or those who do not seek treatment at all. For this reason, and based on the large number of unknown cases, mTBI has been called a “silent epidemic” (Goldstein, 1990).

Fortunately, for the most part the news is positive in that most who suffer from a single mTBI recover within days to weeks. For a minority of those afflicted (15-30%), however, persistent post-concussive symptoms continue for months and even years (e.g., Bigler 2008; see also reviews in Shenton et al., 2012; Levin and Robertson 2013), with some going on to permanent disability, and 20% not returning to work (Nolin et al., 2006). This “miserable minority” (Ruff et al., 1996) often evinces persistent post-concussive symptoms that include dizziness, headache, irritability, sleep disturbances, depression, impulse control problems, and deficits in attention, concentration, memory, executive function, and speed of processing (e.g., Bigler 2008).

Because conventional CT and MRI do not generally show brain injury in mTBI, and because the symptoms are non-specific (i.e., they are also observed in depression and post-traumatic stress disorder, as well as other disorders), it is has been a challenge to diagnose mTBI. There are, in fact, some who believe that if you remove the effects of depression and PTSD, mTBI does not exist, or the origin may be psychological in nature. I do not share this belief.

Radiological evidence has been slow in coming, but with more sophisticated imaging techniques such as diffusion MRI, more recent radiological evidence has shown subtle brain alterations in mTBI that has not heretofore been detectable. This work is, as noted above, more recent, with the first studies beginning in only 2003 (see review in Shenton et al., 2012). Understanding the mechanisms that determine a good versus a poor outcome, however, remains to be determined, and is an important area of scientific inquiry.

Second, there is evidence that those who experience repetitive brain trauma over a period of time may be at risk for developing

chronic traumatic encephalopathy (CTE). This condition is most commonly observed in athletes who experience repetitive symptomatic concussive or asymptomatic subconcussive trauma, such as boxers, football players, or hockey players. The term first used to describe the long-term consequences of repetitive head trauma was dementia pugilistica or “Punch Drunk,” in reference to boxers who experienced cognitive impairments and changes in mood, motor problems, impulsivity, and other impairments (Martland, 1928; Millspaugh 1937; Corsellis, Bruton, and Freeman-Browne 1973). This term, along with the term CTE, describes a neurodegenerative disease believed to be caused, at least in part, from repetitive brain trauma, including repetitive mild traumatic brain injuries (mTBI).

CTE has, nonetheless, also been observed in service members returning from Iraq and Afghanistan (Goldstein et al., 2013), where between 2000 and 2012, 253,330 service members had sustained at least one mTBI (DoD Worldwide numbers for TBI, 2011). The frequency of these injuries has led to TBI being called the “signature injury” of war (Okie et al., 2005). Of further note, as of June 30, 2012

(2000 to 2012), over 266,810 service members were screened for sustaining at least one concussion (Defense and Veterans Brain Injury Center, 2012, at www.dvbic.org/dod-worldwide-numbers-tbi). A most disturbing possible consequence of these "invisible" injuries is the increased rate of suicide among veterans. More than 1,100 veterans took their lives between 2005 and 2009 (DOD Worldwide Numbers for TBI, 2011), more lives than were lost from combat during this same time period.

Third, the estimated cost of mTBI is enormous to the person, to his/her family, and to the larger community, with overall healthcare costs estimated to be $60 billion per year for TBI in general (Finkelstein et al., 2006) and $17 billion for mTBI (CDC, 2003).

Fourth, and in summary, it is only recently that radiological evidence has been available to detect brain alterations in mTBI, including in athletes playing football, hockey, and soccer. Post-mortem evidence of repetitive brain trauma in former professional football players shows clear changes in the build up of tau proteins in the brain

(e.g., McKee et al., 2009; 2013). However, before even considering such long-term effects it is important to be aware of the brain alterations observed in *living* players who do not show clinical or cognitive symptoms, nor even have a history of concussion, but nonetheless evince brain alterations as was observed in the Koerte et al. (2012) study of soccer players with only subconcussive blows to the head. Might some of these individuals progress to neurodegenerative diseases such as CTE? We don't know the answer here. But, if we can detect subtle changes early, and we can follow the impact of concussion over time using imaging, we might be able to predict what kind of changes lead to recovery, and what kind of changes lead to persistent post-concussive symptoms, and perhaps to a further cascade of changes in the brain, ultimately leading to major changes in personality, mood, and cognition as observed in CTE. Further, if we can detect changes sufficiently early, then can we find interventions that will prevent progression to CTE and other neurodegenerative diseases?

Early detection of changes to the brain could help us address other questions as well. For example, why do some athletes develop a neurodegenerative disease while others do not? What are the predisposing factors? Exposure? Genetics? How can we facilitate brain recovery? If, initially, mTBI has a neuroinflammatory response, would anti-inflammatory medications assist in recovery? What supports and what hinders regeneration and recovery? These are all questions that need to be answered. What we do know is that diagnosis is critical for mTBI, and it is now more possible to reach a diagnosis in a clinical setting when techniques such as diffusion imaging are used.

Imaging tools must be sensitive and applicable to living individuals. And once they are widely available, we will be able to follow recovery and degenerative processes in a manner that gives us more information about prognosis. With accurate diagnoses that detect individually specific brain regions that are affected, treatment can then be developed to intervene prior to the possible cascade of degenerative changes.

In conclusion I believe that the subcommittee's focus on sports safety, and in particular sports-related brain injury, is warranted. Safety in high-impact sports *should* be a major focus of attention, as there is clear evidence of changes to brain where there is increased risk of head trauma. Policies, such as return to play restrictions, which govern what happens following an injury with observable evidence of brain trauma, should be highly protective of brain health. And individuals crafting such policies should keep in mind just how much we are learning right now about sports related brain injuries – and how much more we are likely to learn in the years to come.

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Witness Background Statement.

Dr. Martha E. Shenton is Professor of Psychiatry and Radiology, and Director of the Psychiatry Neuroimaging Laboratory (http://pnl.bwh.harvard.edu), Brigham and Women's Hospital, Harvard Medical School. She is also a Health Scientist at the VA Boston Healthcare System. Her laboratory has pioneered in development of neuroimaging tools to understand brain alterations in disorders such as schizophrenia, traumatic brain injury – including sports-related brain trauma – posttraumatic stress disorder, William's syndrome, and Velocardiofacial Syndrome. She received her A.B. degree in Psychology from Wellesley College where she graduated Durant Scholar (Summa cum laude) and was elected to the Eta Chapter of Phi Beta Kappa. She received her Ph.D. in Psychology from Harvard University, with a post-doctoral fellowship in Biological Psychiatry at Harvard Medical School.

The research conducted in her laboratory is interdisciplinary and includes a diverse number of experts including neuroradiologists, psychiatrists, psychologists, computer scientists, biomedical engineers, biochemists, and geneticists, all of whom bring unique skills and knowledge to developing and applying novel imaging techniques to elucidate neuropsychiatric disorders. She has been the recipient of several career awards from the National Institute of Mental Health, including a K01 Mentored Award (1988-1993), two K02 Independent Investigator Awards (1994-1999, 1998-2004), and a K05 Senior Scientist Award (2004-2009). Her research has also received recognition in the form of being the recipient of the Joseph Zubin Memorial Fund Award for Research in Psychopathology, the William Silen Lifetime Achievement Award for Mentoring, and by a Distinguished NARSAD Award. She has also served on numerous study sections at the National Institute of Health and has authored more than 350 peer-reviewed empirical articles and proceedings, as well as authored multiple books chapters and one book entitled *Understanding Neuropsychiatric Disorders: Insights from Neuroimaging*, Shenton ME and Turetsky BI (Editors), Cambridge University Press, 2011. She is Associate Editor of *Brain Imaging and Behavior*, and field editor for the *International Journal of Neuropsychopharmacology*, and is on the editorial board of *Schizophrenia Bulletin*, *Schizophrenia Research*, and *Psychiatry Research: Neuroimaging*, as well as being a frequent reviewer on many journals. She has served on multiple committees including being an invited member of a the committee, "Developing Standards for Diffusion Tensor Imaging (DTI) and Diffusion Spectrum Imaging (DSI) through Public-Private Partnerships", sponsored by the Institute of Medicine's Forum on Neuroscience and Nervous System Disorders, Health Arm of the National Academy of Science (see Curriculum Vitae).