

initial analytical brainstorming but did not participate in data analysis; thus she is not listed as a co-author of this paper. Also, we thank Michelle Stone, BS, and Kimberly Hartz, MS, for their administrative assistance. These individuals were not compensated for their contributions.

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## Invited Commentary

## Assessing Subconcussive Head Impacts in Athletes Playing Contact Sports—The Eyes Have It

Ann C. McKee, MD; Michael L. Alosco, PhD

**Converging research** has shown that subconcussive head impacts are a substantial source of acute and chronic structural and functional changes in the brains of contact sport athletes. Subconcussive head impacts involve the transmission of mechanical energy to the head from a force sufficient to cause neuronal injury or dysfunction, but they do not result in immediate overt clinical symptoms. From high school through professional play, athletes playing contact sports can experience hundreds of unrecognized subconcussive impacts in a single season, through which they continue to play, seemingly unharmed. Although large prospective studies are needed to understand this phenomenon, the frequency of subconcussive head impacts has been correlated with acute microstructural changes in cortical and deep gray matter structures of the brain,



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as well as impairments on neuropsychological testing in various samples of athletes playing contact sports, including football, soccer, and ice hockey.<sup>1</sup> Growing evidence, primarily in former football players, further suggests that repetitive exposure to subconcussive impacts can lead to long-term neurobehavioral disturbances,<sup>2</sup> including those from the neurodegenerative disease chronic traumatic encephalopathy (CTE).<sup>3,4</sup> Recent experimental models of unilateral impact injuries that replicate subconcussive hits, not concussions, are associated with neuropathological changes resembling CTE in the brains of wild-type mice, including a progressive spread of focal tau accumulation to bilateral, widespread brain involvement.<sup>5</sup> Given that millions of individuals play contact sports each year, it is paramount that we understand the associated risks of subconcussive head impacts.

The article by Zonner et al<sup>6</sup> provides additional evidence of brain alterations secondary to subconcussive impacts from high school football, this time as oculomotor dysfunction. Oculomotor dysfunction has been reported in the setting of acute concussion, and it is thus an intuitive next step to determine if such clinical phenomena can occur in the setting of subconcussive impacts. Zonner et al<sup>6</sup> conducted a prospective study of the near point of convergence (NPC) values among 12 high school football players. The football players completed a total of 14 NPC evaluations, including preseason, in-season, and postseason assessments. The number of head impact incidents was measured by the Vector mouthguard (Athlete Intelligence). A total of 8009 hits were recorded in the sample over the course of a single football season. The longitudinal data showed that the frequency and magnitude of the subconcussive hits was associated with a transient, maximal increase in NPC from baseline to game 3. However, NPC values began to normalize compared with preseason baseline at midseason and fully recovered by the postseason measurement. Previous studies have shown similar increases in NPC in collegiate football players<sup>7</sup> and soccer players<sup>8</sup>; however, the tantalizing aspect of this study was that the impaired NPC response slowly returned to baseline during the last half of the season despite continued exposure to subconcussive hits. The reason for the oculomotor recovery despite ongoing exposure is a novel finding that, as the authors note,<sup>6</sup> warrants further investigation into the nature and underlying pathophysiology of this adaptive response.

The small sample size, lack of assessment of brain structure and function, and lack of a comparison group to determine the clinical meaningfulness of NPC changes are limitations of this study.<sup>6</sup> Yet the prospective design, including serial NPC assessments, measurement of frequency and

magnitude of head impacts (via mouthguard), and novelty of the study are important strengths. Overall, it is an important preliminary study that will lay the foundation for future clinical and experimental research on oculomotor function in the setting of exposure to repetitive subconcussive head impacts.

The eye is part of the central nervous system and is complex in its neuronal architecture and function; it also offers a practical and noninvasive approach to potentially detect various neurologic disorders, including CTE and other long-term neurologic consequences associated with repetitive subconcussive head impacts. Extant research supports the usefulness of optical coherence tomography in the detection of Alzheimer disease and associated disorders. iPad-based sideline tests of rapid eye movements can accurately detect oculomotor dysfunction associated with concussion. It is possible that eye-based biomarkers may be sensitive to the detection of neuronal injury and dysfunction associated with subconcussive head impacts. Potentially, in the future, examination of the eye and retina may permit the detection of phosphorylated tau or transactive response DNA binding protein 43-kDa proteins as a way to diagnose CTE in living individuals.

There have been many advances in the detection, management, and treatment of concussion. Subconcussive head impacts have been given less attention as a public health concern. The current study adds to the growing efforts to better understand the effects of subconcussive head impacts in athletes who play contact sports and to improve our ability to detect these ambiguous injuries. The long-term future of athletes who play contact sports and potentially contact sports themselves depends on taking active steps for the detection and management of subconcussive impacts to allow for early intervention.

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