HHS Public Access

Author manuscript

JAMA Pediatr. Author manuscript; available in PMC 2019 September 01.

Published in final edited form as:

JAMA Pediatr. 2018 September 01; 172(9): 803–804. doi:10.1001/jamapediatrics.2018.1645.

Building Good Policy From Good Science—The Case for Concussion and Chronic Traumatic Encephalopathy

Christopher C. Giza, MD,
Steve Tisch BrainSPORT Program, David Geffen School of Medicine and Mattel Children's Hospital, University of California, Los Angeles;

David Geffen School of Medicine and Mattel Children's Hospital, University of California, Los Angeles.

William Stewart, MD, and
Department of Neuropathology, Queen Elizabeth University Hospital, Glasgow, United Kingdom;

Institute of Neuroscience and Psychology, University of Glasgow, Glasgow, United Kingdom.

Mayumi L. Prins, PhD
Steve Tisch BrainSPORT Program, David Geffen School of Medicine and Mattel Children's Hospital, University of California, Los Angeles;

David Geffen School of Medicine and Mattel Children's Hospital, University of California, Los Angeles.

> "CTE [Chronic traumatic encephalopathy] is real: New study finds brain disease in almost all football players tested." "Lawmakers in Illinois, New York propose tackle football bans for youth."[1,2]

Against headlines such as these proclaiming the immediate and long-lasting risks of head impacts in contact sports, what is a responsible parent, coach, or physician to do? Within this narrative, can science compete to inform policies for sports participation and brain health? These are the issues that drive youth sports participation and affect efforts to mitigate contact sports risk.

Definitions Matter

Concussion is a form of mild traumatic brain injury (TBI) resulting in the onset of a constellation of clinical signs and symptoms in the absence of macrostructural damage such as hematoma or contusion. At present, no single objective test for concussion exists, with ongoing debate about how best to make a clinical diagnosis of an otherwise invisible injury. Typically, most individuals with concussion recover completely over days to weeks, but questions still remain about persistent problems in a subset of individuals and whether repetitive concussions may initiate longer-lasting changes including neurodegeneration.

Corresponding Author: Christopher C. Giza, MD, Department of Neurosurgery, David Geffen School of Medicine at University of California, Los Angeles, 300 Stein Plaza, Room 531 Wasserman, Los Angeles, CA 90095 (cgiza@mednet.ucla.edu).

Subconcussion is a recently coined term intended to encompass the possibility that some head impacts causing no immediate symptoms are associated with cellular perturbations resulting in subclinical injuries that, with cumulative exposure, might lead to late pathology. However, while an intriguing concept, in a field where concussion already claims the title of the invisible injury, subconcussion presents even greater challenge. At what point does normal head motion become injurious?

Chronic traumatic encephalopathy (CTE) is a term applied to a neurodegenerative pathology described predominantly in autopsy cases of contact sports athletes, although similar pathological findings are also reported in late survivors of single moderate or severe TBI and in individuals without a history of TBI.[3] Preliminary neuropathologic consensus criteria exist and describe a distinctive pattern and distribution of tau protein accumulation in a complex constellation of other pathologies. Thus far, comparatively few cases in the literature, largely from convenience samples and with retrospective collection of clinical data, render meaningful clinicopathological correlation challenged. In particular, as with subconcussion, the lowest limit of tau deposition required to make a pathological diagnosis of CTE remains uncertain. Whether informing patients or reporting research results, properly defining terms and making explicit distinctions between impacts, acute injuries, and chronic sequelae is critical for clinicians and researchers.

Acute-Chronic Pathophysiological Linkages: A Role for Basic Science

While basic science can help inform some of our understanding of concussive and subconcussive brain impacts, such as the threshold of force below which a neurometabolic cascade is not initiated[4] or sex differences in biomechanical thresholds for axonal stretch injury,[5] it is also important to recognize the limitations of preclinical studies in terms of providing clinically actionable data for humans. In contrast to humans, rodent brains have no gyri, little white matter, and a different orientation of the neural axis. As a result, translation of research findings across species is challenging. Further, deposition of neurodegenerative proteins does not occur in the rodent brain in a manner seen in humans, so other strategies are needed (eg, transgenics), but this adds another layer of separation between what we learn in the laboratory and what may be happening in humans. A final, critical point is that scientists need to be very cautious when taking clinical definitions and translating them into animal models; subconcussion in a rodent is even more vaguely defined than in a human. Likewise, applying terminology, such as CTE, to rodent models is likely to further confuse the discussion, particularly when the definition in humans is still being delineated.[6]

Nevertheless, under these limitations, carefully designed preclinical platforms can still inform the basic biology of TBI. Models are designed to study specific elements of injury (rather than the entire biologic process) and can offer distinct advantages when examining factors such as impact interval or long-term changes. Impact intervals can be standardized in the experimental design, which cannot occur in human studies; although determining how time intervals in animals correspond to humans must still be considered.[7] Rodent models can also examine long-term (lifespan) changes more rapidly than prospective longitudinal studies in humans and therefore may offer us a preview of mechanisms to pursue and translate to our human studies.[8,9]

Finding a Balance

Opinions that contact sports associations are to concussion and long-term health what “Big Tobacco” might have been to smoking and lung disease are disingenuous and serve only to polarize debate rather than advance it. There are clearly risks of sport participation, as there are in many human activities, and some activities carry greater relative risks than others. Many of these can be quantified, and we have learned to discourage early sports specialization, encourage multiple sports, avoid unnecessary impacts, use proper protective gear, and enforce rules to reduce likelihood for injury while retaining the physically challenging nature inherent to sports competition.

However, there are considerable benefits to sports participation, some of which have been demonstrated objectively, which should not be lost for fear of risk. Recess is associated with better attention in the classroom in young students. Lower body mass index is associated with better cognitive scores. Many studies support the long-term cognitive benefits of physical activity, and adult levels of physical activity are strongly influenced by activity in youth. Youth participation in sports decreases their risks to numerous other greater risks associated with adolescence.[10] This is where understanding of relative risks has not been fully appreciated.

Furthermore, in the absence of good data and thoughtful discussion, uninformed policy even with the best intentions will have unintended consequences. Our society is perhaps the most sedentary ever, with obesity rates exceeding one-third of the young population: what long-term cognitive consequences will this have? What is the best way of promoting safe physical activity without discouraging active lifestyles? If organized sports are not yet safe enough, does banning them ensure that young people will not engage in risky activities, or will these activities just occur even further from rules and oversight? If uncertain connections are prematurely made between a common occurrence (such as mild TBI) and an untreatable degenerative disorder, what happens to the individuals who have symptoms or disorders amenable to intervention but conclude that nothing can be done?

Using Science to Develop Informed Policy

It is no easy task to read beyond headlines in newspapers or in scientific journals. Clinical and basic scientists need to push for an objective discussion of the facts, interpret data within the context of the research, recognize a study’s limitations, and appreciate differences in the quality of data, while also diligently avoiding confirmation bias. Public health policies, patient care decisions, and sports participation of course are all happening in real time, and nothing will wait for the perfect, definitive answer at some undetermined future point. But to tackle challenging problems, such as the long-term effects of head impacts and the role of team sporting activities, requires an open forum: freely discussed issues, balanced review of information, and a willingness to determine the underlying truth of nature. All stakeholders, including athletes, health care professionals, policymakers, scientists, journal editors, and reporters, should be aware of these issues to contribute meaningfully to this discussion.

Conflict of Interest Disclosures:

Dr Giza is a consultant for the National Football League Neurological Care Program and the National Hockey League Players' Association. He serves on the advisory panel for LoveYourBrain, Major League Soccer, National Basketball Association, National Collegiate Athletic Association, and the United States Soccer Federation. He reports book royalties from Blackwell Publishing for *Prioritized Neurological Differential Diagnosis*. Dr Giza receives Grants/Research Support: National Institutes of Health National Institute of Neurological Disorders and Stroke (R01 NS27544), National Collegiate Athletic Association, US Department of Defense, University of California, Los Angeles (UCLA) Brain Injury Research Center, UCLA Faculty Grants Program, UCLA Steve Tisch BrainSPORT program, Easton Clinic for Brain Health, Avanir (research grant 2017–2018), National Institute of Neurological Disorders and Stroke Neural Analytics Small Business Innovaton Research grant (NS092209 2016–2018). Dr Stewart is a consultant for the Football Association and receives grants/research support from the National Institutes of Health (R01NS03814 and R01NS094003), National Health Services Scotland Career Research Fellowship, Glasgow Children's Hospital Research Fund, and the Football Association. Dr Prins receives grants/research support from the National Institutes of Health National Institute of Neurological Disorders and Stroke (R01 NS27544), UCLA Brain Injury Research Center, UCLA Faculty Grants Program, UCLA Steve Tisch BrainSPORT program, and Easton Clinic for Brain Health. No other disclosures are reported.

REFERENCES

1. Associated Press. CTE is real: new study finds brain disease in almost all football players tested http://www.cbc.ca/sports/football/cfl/cte-concussion-study-finds-brain-disease-football-players-1.4221276. Published July 25, 2017. Accessed May 31, 2018.
2. Kenning C. Lawmakers in Illinois, New York propose tackle football bans for youth. Reuters. https://www.reuters.com/article/us-football-youth-tackle/lawmakers-in-illinois-new-york-propose-tackle-football-bans-for-youth-idUSKBN1FF09V. Published January 15, 2018. Accessed May 31, 2018.
3. Hay J, Johnson VE, Smith DH, Stewart W. Chronic traumatic encephalopathy: the neuropathological legacy of traumatic brain injury. Annu Rev Pathol. 2016;11(1):21–45. doi: 10.1146/annurev-pathol-012615-044116 [PubMed: 26772317]
4. Katayama Y, Becker DP, Tamura T, Hovda DA. Massive increases in extracellular potassium and the indiscriminate release of glutamate following concussive brain injury. J Neurosurg. 1990;73(6): 889–900. doi:10.3171/jns.1990.73.6.0889 [PubMed: 1977896]
5. Dollé JP, Jaye A, Anderson SA, Ahmadzadeh H, Shenoy VB, Smith DH. Newfound sex differences in axonal structure underlie differential outcomes from in vitro traumatic axonal injury. Exp Neurol. 2018;300(November):121–134. doi:10.1016/j.expneurol.2017.11.001 [PubMed: 29104114]
6. Tagge CA, Fisher AM, Minaeva OV, et al. Concussion, microvascular injury, and early tauopathy in young athletes after impact head injury and an impact concussion mouse model. Brain. 2018;141(2):422–458. doi:10.1093/brain/awx350 [PubMed: 29360998]
7. Prins ML, Alexander D, Giza CC, Hovda DA. Repeated mild traumatic brain injury: mechanisms of cerebral vulnerability. J Neurotrauma. 2013;30(1):30–38. doi:10.1089/neu.2012.2399 [PubMed: 23025820]
8. Grant DA, Serpa R, Moattari CR, et al. Repeat mild traumatic brain injury in adolescent rats increases subsequent β-amyloid pathogenesis. J Neurotrauma. 2018;35(1):94–104. doi:10.1089/neu.2017.5042 [PubMed: 28728464]
9. Mouzon BC, Bachmeier C, Ojo JO, et al. Lifelong behavioral and neuropathological consequences of repetitive mild traumatic brain injury. Ann Clin Transl Neurol. 2017;5(1):64–80. doi:10.1002/acn3.510 [PubMed: 29376093]
10. Pate RR, Trost SG, Levin S, Dowda M. Sports participation and health-related behaviors among US youth. Arch Pediatr Adolesc Med. 2000;154(9):904–911. doi:10.1001/archpedi.154.9.904 [PubMed: 10980794]