Articles

Concussion in Sport

The Unheeded Evidence

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Abstract: Patients with repeated minor head injury are a challenge to our clinical skills of neurodiagnosis because the relevant evidence objectively demonstrating their impairment was collected in New Zealand (although published in the *BMJ* and *Lancet*) and, at the time, was mired in controversy. The effects of repeated closed diffuse head injury are increasingly recognized worldwide, but now suffer from the relentless advance of imaging technology as the dominant form of neurodiagnosis and the considerable financial interests that underpin the refusal to recognize that acute accelerational injury is the most subtle and insidiously damaging (especially when seen in the light of biopsychosocial medicine), and potentially one of the most financially momentous (given the large incomes impacted and needing compensation) phenomena in modern sports medicine. The vested interests in downplaying this phenomenon are considerable and concentrated in North America where diffuse head injury is a widespread feature of the dominant winter sports code: Gridiron or American Rules football. The relationship of this to shattered lives among the brightest and best of young men and the relatively dated objective evidence are a toxic mix in terms of ethical analysis and, therefore, there is a malignant confluence of social forces that tends toward minimizing the injury.

Keywords: concussion; brain function; neuropsychology; the politico-economic environment of health ethics

The current saga of head injury in sport, played out in popular and medical media, has all the ingredients of a tragedy: action, scope, a plot, a unity of concern, seriousness, and a denouement in which all is revealed. Some of these are common to a good detective novel or even a short story (such as those of Sherlock Holmes). But as we trace out the sports concussion story it emerges that the denouement is unsatisfyingly incomplete (and therefore has a weakness in its structure). I will argue that this defect is in part contributed to by the producers and impresarios, not the story itself, and, as audience, we are being denied in a way that is becoming familiar from all too recent and even current situations in which biopower and transparency are at odds with each other. The evidence that sports concussion and subconcussive injury significantly and cumulatively damages the brains of some of our brightest and best is compelling, but elements that make it so have been unheeded or systematically suppressed because of a misapplied ethics of evidence inappropriate to the case in point. That evidential path, initially suggestive but now undeniable, began in the 1960s and has the form not of a simple-minded exposé of an independent variable causally implicated as would be a clinical intervention, but of an etiological synthesis bringing together in an intelligent way, clinical psychology, neurophysiology, neuroimaging, neuropathology, and clinical observation. That is the kind of reasoning we teach our medical students, but as a scientific endeavour, we seem in danger of losing sight of it, and with it, one of the pillars of scientific and ethical medicine.

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Delayed Recovery of Cognition I

The first set of observations was by neurosurgeons, neurologists, and clinical neuropsychologists who noted that some of their young patients who had suffered "minor" head injuries not thought to amount to significant "concussion" could not properly perform their normal duties because of poor concentration, fatigability, and headache. This did not happen to all, and the injuries showed no consistent pattern nor did the bedside neurological evaluations that formed the criteria for hospitalization and clinical concern. The problem became the site of a debate between those who ascribed it to neurosis or a psychogenic impairment and those who thought that the "commotion of the brain" (which did not seem neurologically severe) had been a significant injury.

The first objective evidence for the latter view was published in 1974[1] and clearly showed a reduction in the information-processing rate on a test that simulated complex cognitive performance under pressure: the Paced Auditory Serial Addition Task (PASAT). The test proved a highly reliable measure of central processing speed in moderately complex cognitive operations: that of adding a single digit number to the one prior to it in a sequence that was played to the subject over the course of a trial and for which the timing (interstimulus interval) could be varied. As one of the original healthy subjects on which the test was developed, I can attest to the stress involved as the speed of presentation was increased.

The first article was quickly followed by a second showing the cumulative effect of multiple minor concussive injuries, with slower and less complete recovery of information- processing rate in subjects who had had multiple injuries.[2]

The test and its stressful effects on those who did poorly were noted, and even though the neural hypothesis explained the data much better than did the psychological one, debates about compensation, liability, sick leave, and other broader sociopolitical issues added fuel to the fire. It was time for further information, but "the game was afoot."

Delayed Recovery of Intellectual Function II

It is worth jumping forward in time to adduce further evidence that information processing is slowed in the brains of subjects who have had multiple minor concussions before we clinch the case that this is a neural rather than a psychological phenomenon.

On the basis of a review of evidence, a group of clinical neuropsychologists using a battery of tests noted the absence of conventional neurological abnormalities, and yet the presence of subtle and cumulative cognitive effects of concussion.[3] These included less practice effect improvement.

The authors conclude their review of the many strands of neuropsychological evidence with a striking claim that they have exposed in such patients "subtle cerebral dysfunction that precludes them from mustering the cognitive resources needed to overcome the increased demands of stressful situations."[4] Neurophysiological elucidation of what was going on was indicating exactly the same conclusion.

Neurophysiology

A study of evoked potentials (EPs) and event related potentials (ERPs) measuring sensory and cognitive processing in multiple traumatic brain injury (TBI)[5,6] showed

significant alterations in the late phases of information processing in the brain. The findings included the following.

(1) Longer P3 latencies in those with more concussions in which P3 latency is "a measure of widespread processing for stimulus evaluation and categorisation— i.e. thinking."[7] And the authors noted that such a finding is expected from damage to larger-caliber axons connecting disparate areas of the brain.
(2) The diffuse injury inferred was not evident in structural imaging, particularly at mild levels of original traumatic effect, but the authors remarked that the electrophysiology was sufficiently clear that a psychogenic hypothesis of postconcussion syndrome was not supported, and concluded that there was incomplete recovery of damage to a significant number of neurons.

Sophisticated techniques of functional neuroimaging provided more compelling evidence of what was going on: (1) diffusion weighted imaging demonstrates shearing injuries; (2) functional MRI (fMRI) shows more widespread activation attributed to "cognitive-load induced recruitment";[8] and (3) the authors noted that collated functional imaging using EP, ERP, and magnetic source imaging (MSI) show subtle changes in cerebral function. The last of these is particularly informative because it integrates anatomical data from brain areas with neuromagnetic data from dendritic networks measuring functional gathering of information for use in the cerebral cortex,[9] and therefore gives a dynamic anatomical and physiological profile of what the PASAT is measuring.

Neuropathology

The initial comprehensive pathology of closed head injury was published by Sabina Strich in 1961 and showed diffuse axonal shearing injury, axonal retraction bulbs, and microglial clusters caused by rotational forces.[10] The head injuries that Strich studied were severe such that all patients were unconscious from the time of injury, and suffered long-term effects rendering most of them severely demented or vegetative (the term was not in use at the time). The crucial evidence implicating mild head injury in a similar range of pathological changes was published by Oppenheimer (in 1968) who, after Strich, set out to show "tiny lesions" that "might throw useful light on acceleration injuries to the brain."[11] The remarkable feature of his article was "that in five of the cases in which microglial clusters were observed the cerebral injury was clinically trivial" and the patients died of other causes.[12] Microglial clusters are characteristic of diffuse axonal injury and are part of the characteristic neuropathology now recognized as typical of the distinctive pattern of neurodegeneration induced by chronic traumatic encephalopathy (CTE)[13] even though the later distinctive microscopic changes in neurons and the demonstrable abnormal proteins shared by CTE and Alzheimer's disease were not amenable to the technology available to Strich and Oppenheimer.

Neurofibrillary tangles, glial tangles, tau amyloid (cf. Alzheimer disease), and multiple widespread neural disconnection[14] with associated degradation of callosal white matter (diffusion tensor imaging [DTI]) are the pathological changes that one might expect to see with the progressive deterioration in connectivity and processing speed associated with concussion. The authors of these studies repeatedly

stress that the effects of TBI are more devastating on cognition and personality if the injuries occur during youth.

The Consensus Statement (2016)[15]

The current major consensus statement on sports related concussion is interesting in what it includes and excludes. It notes that "For most injured athletes, cognitive deficits, balance and symptoms improve rapidly during the first 2 weeks after injury" (at 843). It mentions the general inconclusiveness of neuroimaging, but states that "The strongest and most consistent predictor of slower recovery from SRC is the severity of a person's initial symptoms in the first day, or initial few days, after injury" (at 843).

The neuropsychological testing in the statement mentions computerized testing and psychometry, but makes no mention of PASAT, and therefore neglects the most sensitive and convincing measure of central processing time, a measure closely correlated with postconcussive work performance in everyday occupations, and a good candidate for the missing "gold standard" to use along with "subjective symptom scores and imperfect clinical and NP testing"(at 843).

The electrophysiological evidence relating to late waves in the EP and ERP is also mentioned along with imaging modalities, fMRI, and electrophysiology, all of which are problematic because of variations in study design and "physiological and clinical recovery" (at 843–4).

When the document discusses postconcussive syndrome (with persistent symptoms) it remarks that those symptoms are not specific to concussion and explicitly recommends considering other diagnoses and preinjury conditions such as "mental health problems" or migraines (at 843). Throughout, we find disclaimers about the evidence even though repeated concussion may be significant, and the impacts required may be less but cause progressively slower recovery, particularly where the patient is less than 18 years old (at 843).

The link to CTE is again mentioned, but it is arguably somewhat tentatively related to pathophysiology and neuroimaging and to a lack of evidence of causality from concussion in contact sports; the well-documented and reproducible PASAT data are not cited.

The tone of this document is therefore to downplay the reality and evidence of a major health problem that is increasingly suspected to play a significant role in post-sports career life for those affected, and that was thoroughly documented by a neurosurgeon and a neuropsychologist in the 1970s using a reliable and inexpensive assessment tool.[16]

Show Me the Evidence

Contemporary medicine rightly stresses quality of evidence in adopting new remedies for disease but the hierarchy of evidence in which well-organized prospective, randomized, double-blind, controlled trials are the gold standard is not as applicable to historical truths such as the cause and epidemiology of a particular multifactorial problem at a given time and depending on a complex set of social, economic, and political (anthropological or ecological) contingencies. Sports concussion is just such a phenomenon. Ideally we could conduct a large inclusive trial of young people entering sport, document their health status so as to include the

elements of the syndrome we are interested in, and then reassess them periodically, carefully contrasting the affected (injured) group with their cohort of (possibly matched) controls. But we also have a long history of an alternative style of investigation, as in the famous campylobacter and gastric ulcer case in which a form of "causal proof" clinched the pathophysiological synthesis. Such causal proofs can be traced back to Koch and transmuted for the noninfectious case as a set of claims that: (1) the etiological condition is clearly found in cases in which the disease is seen but not in healthy subjects, (2) there is a positive identification of the etiological mechanism by pathology and objective scientific testing, (3) there is a plausible pathophysiological causal pathway linking the mechanism and the disease syndrome, and (4) one can identify the mechanism in new instances of affected (previously healthy) individuals.[17] Where a causal mechanism is relatively simple, the etiological problem to be solved may be straightforward, even if as it arises in the patient population at large in the midst of a multistranded causal nexus (involving youth, lack of self-care, recklessness, substance abuse, and all the ills that sportsmen are prone to) such that a great deal of synthetic work is required to untangle the pathogenesis. But in such cases a reliance on a simple conception of empirical evidence is not going to be what is required.

Applying a more complex version of Koch's reasoning requires that we have a clear demarcation between those affected and their healthy peers in terms of a robust functional verification or characterization of the phenomenon at the heart of the story—here impaired central processing (as, par excellence, revealed by the PASAT test), an indication of the pathophysiology and the way the causal story works, and convincing evidence that the same independent event type (a concussive injury or multiple such) engenders the same condition in previously unaffected individuals. A convincing etiological story of that type can be, and has been, confirmed at key points in a consistent strand of evidence spanning the last 40 years, but is still disparagingly held up against an unrealistic stereotype of biomedical evidence. Why is that?

Biopower and the Hippocratic Professional

Concussion in sport seems to be another case where we, as responsible health scientists, are conned by the nay-sayers who are driven by vested financial or other political interests. We have seen this happen in relation to tobacco and cancer, the food industry and cardiovascular disease, and diabetes and obesity, as well as in relation to the diseases strongly correlated with poverty and inequality. In each case, the bleating about lack of convincing evidence in relation to sport and concussion looks to be not the kind of science on which we would normally base policy in delivering good healthcare designed to keep people from harm. Having said that, there is a significant question about how we should act.

A blanket ban on contact sports seems counterproductive given the immense benefits of vigorous sport in terms of fitness levels, diversion from the social pathologies that arise in the absence of the plausible benefits of sport for life and maturation, and the community and social significance of sports and sporting culture. It also seems unwarranted that we should deprive some people of the chance to do things they enjoy in the interest of paternalistic judgments about their well-being; but aside from those restrictive measures, certain responses seem not only fitting but also to serve the wider agenda of the healthcare professions as caregivers for the societies that they arise in.

First, it seems that sportspeople ought to be warned about the true risks, including the balance of probabilities affecting health and well-being, and informed about the true nature of the conditions that they run the risk of developing and suffering from if they become casualties. Many will elect to take those risks, because that is a trade-off that they are prepared to make, but just as with miners and those who clean windows on skyscrapers for their living, some reasonable and realistic provisions should be made to minimize injuries based on a clear understanding of the genesis of cumulative postconcussive encephalopathy (or CTE). This will allow both a reasoned assessment of the condition and its prevention or at least mitigation, and a clearly informed choice about participation by those who get involved. Who should provide such information and in what setting? Sports physicians may well be the best placed to understand, weigh, and deliver such information, but concern properly exists as to whether they may be subject to a conflict of interest resulting from employment expectations.[18,19] Some would say that the mechanisms of and uncertainties about multiple TBIs are such that it is too much to expect athletes to understand them. This makes it particularly important to be responsible about conveying the risks to them. Over 2,000 years ago, the pundits of the profession remarked "Although it were no easy matter for common people to discover for themselves the nature of their own diseases and the causes they get worse or better, yet it is easy for them to follow when another makes the discoveries and explains the events to them."[20] Those of us who have lived through the revolution in patient autonomy and informed consent have, as they say, heard all that before.

Second, it seems that we should impose the true costs of any activity primarily on those who profit by that activity, just as we should have imposed the health burden resulting from smoking on those who manufacture and sell tobacco products, and should have imposed costs or penalties on the food industry for their wholesale promotion of unhealthy eating. These steps constitute removing, at a societal level, practices engaged in unjust enrichment at the expense of a community that has to deal with the ramified and extended costs of profiteering.

Third, we need to further build in adequate mechanisms of identification, care, and restoration of concussed individuals based on sound research that takes the problem seriously and unpacks the complex biopsychosocial phenomena involved in producing, exacerbating, and relieving the traumatic consequences that we have no ethical justification for downplaying or ignoring. They will not go away if we neglect them, in fact they will get considerably worse because of that neglect (at multiple levels).

Notes

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