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# Physics where it hurts

Impacts from bomb blasts and in contact sports can cause incurable mental problems for soldiers and athletes, with changes in the brain similar to those seen from Alzheimer's disease.

**Sidney Perkowitz** explores the physical analysis that is forming a critical part of the scientific and clinical attack on this insidious disease

In *The Hurt Locker*, the high-tension Oscar-winning 2008 film about an American bomb-disposal team in the Iraq War, team leader Sergeant Matt Thompson is seen sprinting away from an improvised explosive device (IED) when it is deliberately detonated. He is running for his life – to outdistance the IED's lethal radius of 25 m. Despite wearing a heavily armoured "bomb suit", the intense blast wave from the device sends Thompson flailing through the air. With blood splashing inside his faceplate, we realize that he is the victim of a powerful physical cause: a pulse of pressure strong enough to deal out instant death.

Although this scene (pictured above) may reflect Hollywood exaggeration, it shows how an explosive wave front can severely stress the human body and head with grave risk to the brain inside. Indeed, IEDs are a very real threat: at least 10% of the 2.3 million US soldiers who have served in Iraq and Afghanistan since 2001 are known to have suffered a traumatic brain injury (TBI) – a term encompassing any brain injury resulting from an external force.

Worries over TBI have intensified recently as it

becomes clear that even seemingly minor knocks can have serious long-term implications – a finding that dramatically expands our sphere of concern from the fate of war veterans to also include players involved in blunt impact sports. Although blows from physical objects are at first glance an entirely different mechanism from high-impact pressure waves, it turns out that these two kinds of stress can produce similar damage to the human brain. Thankfully, studies that recreate the physics of these events in labs and in computer simulations, or that directly measure the forces dealt to players on the field, are starting to shed light on this chilling disease.

## Delayed symptoms

Blows to the head that cause concussions have long been known to induce a brain disease that was called dementia pugilistica when it was thought to occur only in "punch-drunk" boxers. But there is now evidence that hard hits in American football can also induce long-term brain damage. Even more troubling, such problems can be caused as well by multi-

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**A blow to the head** John Grimsley (right), who played for the Houston Oilers and Miami Dolphins in the National Football League (NFL), in action in 1988. After his death in 2008 at the age of 45 from a gunshot accident, examination of his brain revealed clusters of the abnormal tau protein like those seen in elderly ex-boxers and characteristic of chronic traumatic encephalopathy (CTE). The brains of more than 20 other ex-NFL football players have also shown post-mortem evidence of CTE, including Dave Duerson, who committed suicide by shooting himself in the chest after writing “Please, see that my brain is given to the NFL’s brain bank” to be studied for evidence of CTE.

ple but seemingly minor sub-concussive impacts that athletes once just “walked off”. Recent suicides by American football players suffering from difficulties such as diminished memory and emotional volatility dramatize the issue and illustrate the insidious fact that the effects of TBI may take years to appear.

Post-mortem examination of the brains of football players and military veterans shows that both suffer from the degenerative condition chronic traumatic encephalopathy (CTE). Like Alzheimer’s disease, CTE is characterized under the microscope by dark clumps of abnormal “tau” protein among the brain’s neurons, and is associated with similar outcomes such as dementia and depression.

With severe and incurable mental problems at stake for soldiers and athletes, many researchers are probing the connections among impact, TBI and CTE. In addition to clinical methods, some use physical techniques to study trauma of the head and brain, from analysis of the dynamics of head movement under impact, to shock-tube and materials physics, and brain-scanning techniques such as magnetic resonance imaging (MRI). This integrated search for answers will perhaps ultimately give us a theory of how mechanical force induces neuropathology. The hope is to develop effective diagnosis, treatment and prevention of TBI and CTE, both on the battlefield and playing field – and, for that matter, wherever they occur.

### The protected brain

Evolution has seen to it that the brain – our soft centre of cognition, feeling and sensation – is armoured

within the skull. Other animals also have protected brains, some at extraordinary levels: the woodpecker, for example, has a brain that can withstand a deceleration 1000 times that of gravity,  $g$ , with every peck. Humans are more fragile than that, but – with the help of artificial support for the body – we can tolerate large forces caused by impact or acceleration. Race-car drivers routinely deal with accelerations over  $5g$  in turning or heavy braking while pilots of military jet aircraft undergo  $10g$  or more in aerial manoeuvres. In fact, tests with rocket sleds show that the human frame can tolerate accelerations of up to  $25g$  without severe injury or death.

But this level of resilience may not be enough for American football players, who encounter even higher stresses. The forces behind the stunningly loud “clunk” heard when two helmeted heads collide during play have been measured in real time. One landmark study, published in 2007 by Kevin Guskiewicz of the University of North Carolina at Chapel Hill and his colleagues, centred on data gathered over five football seasons from 88 college football players. Their helmets had been fitted with devices to measure acceleration in the three spatial and three rotational planes, with the data sent wirelessly to a computer.

The tested players together sustained more than 100 000 impacts, 13 of which produced concussions at high linear and rotational accelerations in the ranges of  $61\text{--}169g$  and  $163\text{--}15\,000\text{ rad/s}^2$ , respectively. (To put this in context,  $15\,000\text{ rad/s}^2$  is like revving up an electric coffee-bean grinder to its high-speed shriek in a 10th of a second.) But there was no correlation between the magnitude of the impact and the severity of the concussion, or between linear and rotational effects. In fact, large forces do not necessarily produce concussion as a clear marker of damage, according to data published in 2009 by Steven Rowson and colleagues at Virginia Tech and Wake Forest University in North Carolina. Using data obtained from 10 college football players fitted with similar helmets able to measure acceleration in six dimensions, the researchers found that of some 1700 impacts, 10% produced linear accelerations above  $40g$ , a few of which were above  $80g$ , and 8% produced angular accelerations above  $3000\text{ rad/s}^2$ . Yet none of the players sustained a concussion as clinically defined.

Such studies illustrate the intensity of the forces and the complexities of relating them singly or multiply to brain damage. Still, the data could help design better protective gear. For example, the biggest angular accelerations measured in the Virginia Tech–Wake Forest study occurred when the head was twisted about its vertical axis, perhaps because the face mask in front of the helmet projects sufficiently that any force applies a large leverage. Future helmet designs could therefore incorporate facemasks that are less susceptible to twisting forces. Another outcome might be to set standards for safe impacts on players, but as Guskiewicz noted when I recently interviewed him, any damage threshold is “probably different for every person and within players it probably changes over time” and so could not help in day-to-day play. Instead, the most useful approach may be to change

behaviour, teaching accident-prone players with what he calls a “bad hit profile” how to protect themselves in blocking and tackling.

### Shaking the neurons

Sports injuries are one thing but drawing conclusions about TBI caused by explosive blast is even harder. Impact data can be gathered from football players without increasing their risk of injury, let alone death. But for reasons of practicality and safety, blast effects on large numbers of military personnel cannot be similarly examined on the battlefield.

One alternative research approach is to replace human subjects and explosions with anaesthetized animal subjects and controlled blast simulations. In 2012 Lee Goldstein and Ann McKee of the Boston University School of Medicine (McKee also directs the Neuropathology Service for the New England Veterans Administration Medical Centers) and more than 30 co-authors reported insights into blast-induced TBI and CTE gained from this approach (*Sci. Transl. Med.* 4 134). In the first part of the work, the post-mortem brains of four US military veterans who had been exposed to blast or suffered concussion were examined. All showed signs of CTE like that found in athletes who had suffered brain damage.

To further explore blast and CTE, the researchers exposed mice to simulated IED explosions in a shock tube. Scientists have for more than a century used blast waves generated with these devices to study chemical kinetics, combustion reactions, and the behaviour of fluids and varied materials. A shock tube is essentially a cylinder several metres long in which a thin diaphragm separates a driver or compression section filled with gas at high pressure from a driven or expansion section containing gas at low pressure. If the diaphragm is suddenly burst by any of several methods, the result is a shock wave rapidly traversing the driven gas at high pressure and temperature.

In the tube used in the Goldstein–McKee work, a polyester membrane separated compressed nitrogen from air at atmospheric pressure. When the membrane burst, that generated a blast designed to mimic a 120 mm mortar round detonating 5.5 m away. (With the explosive power of 4.5 kg of TNT, these rounds are often used in IEDs.) The blast impinged on an anaesthetized laboratory mouse held in the expansion chamber with its head free to move. A suite of instruments to measure pressure and velocity recorded the blast parameters and the mouse’s reactions.

A single blast was found to be enough to create brain deficiencies in mice. Within two weeks after a blast, exposed mice displayed reduced learning and memory capacities as they negotiated a laboratory maze – symptoms that persisted for at least the month that the study continued. Most significantly, post-mortem examination of the mice’s brains showed the tau protein clumps indicative of CTE, as well as injured neurons and axons (the slender fibres that carry nerve signals).

These signs of blast-induced pathology were augmented by physical analysis showing that the damage was not the result of blast pressure in the



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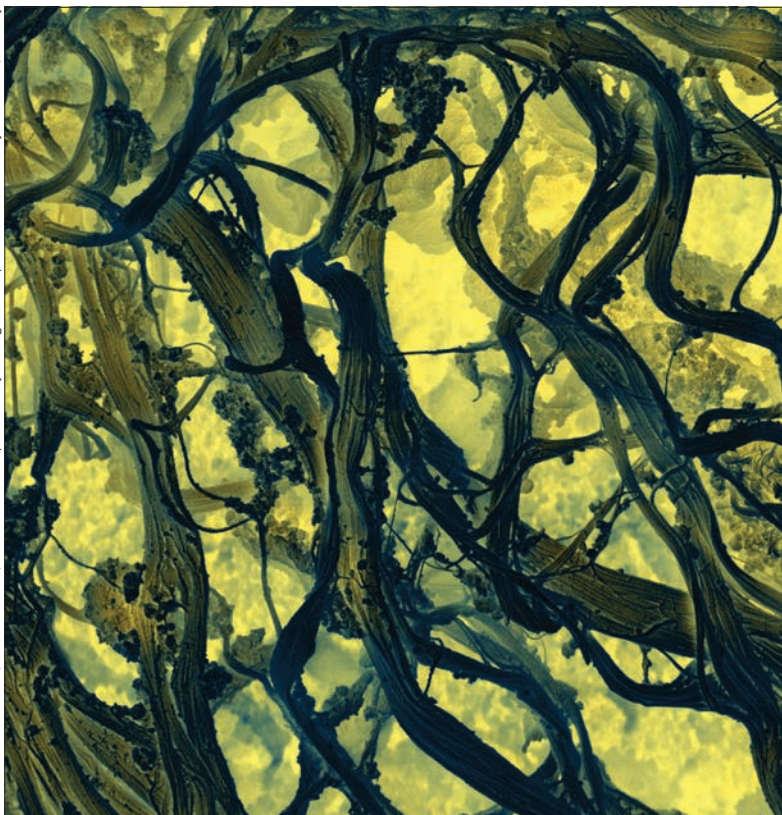
**Handle with care** Ann McKee at the Edith Nourse Rogers Memorial Veterans Hospital in Massachusetts studies athletes’ brains in her research into trauma caused by head injury.

brain, which was measured as below tissue-damage thresholds. Also, travelling at 1.3 times the speed of sound, the supersonic blast front traversed the brain too quickly to create a damaging pressure differential. But high-speed videography showed that the blast and its following blast wind rapidly whipped the mouse’s head side to side and up and down, with peak angular acceleration over 900 krad/s<sup>2</sup> (blast wind is the countervailing rush of air after the blast passes, in this case at 150 m/s). Confirming the hypothesis that this violent shaking damaged the brain, the researchers found that mice exposed to the blasts with their heads immobilized continued to negotiate the maze with normal brain capabilities.

This research links CTE to rapid head oscillations caused by blast, but as the researchers note (and as is typical in animal studies), the mouse model cannot automatically scale to humans. Nevertheless, the physical analysis of animal data makes this research potentially an important step toward understanding the links between mechanical trauma and neural impairment in humans.

### Simulating and scanning

Further progress in understanding how physical impact relates to brain injury may come from computer modelling of the human brain under blast conditions. Successful modelling of this type requires realistic values for the brain’s physical make-up, but unfortunately these are not easy to come by. The brain is inhomogeneous, combining isotropic grey matter made of the bodies of neurons with white matter made of axons that tend to be directionally



**One direction** The vine-like structures shown here are axons in a colorized scanning-electron-microscope image (at 3500 $\times$  magnification) of white matter from porcine brain tissue, which is similar to human brain tissue. The tendency of axons to be directionally aligned complicates the material physics of the brain, which for researchers makes understanding traumatic brain injury all the more challenging.

aligned. It is also deformable and viscoelastic – like Silly Putty, the brain responds differently to forces applied quickly or slowly – which greatly complicates its dynamic reactions. As a consequence, measurements on brain tissue under varying conditions have given different results.

Still, simulations based on available data can potentially be useful, as shown in 2009 by William Moss and Michael King of the Lawrence Livermore National Laboratory and Eric Blackman of the University of Rochester, both in the US. They modelled the brain simply as a featureless viscoelastic ellipsoid, surrounded by a layer simulating the fluid that cushions the brain, all within an elastic ellipsoid representing the skull. The model showed that a non-lethal blast from 2.3 kg of the plastic explosive C4 could still deform or ripple the skull sufficiently to create harmful pressure in the brain – data that could help in the design of military helmets. But in 2010 and 2011 Raúl Radovitzky and co-authors from the Massachusetts Institute of Technology and the Walter Reed National Military Medical Center drew a different conclusion about the value of a face shield in helmet design from a different simulation.

Besides full anatomical data, simulations that reliably predict the medical effects of trauma need realistic values for the material properties of neural tissue, as studied by Michael Gilchrist, Badar Rashid and Michel Destrade of University College Dublin (Destrade is also at the National University of Ire-

land, Galway). In work reported in 2012 and currently in press, they examined porcine brain tissue, which resembles human brain tissue. Their quantitative results for the response of the tissue under compression during time scales characteristic of blunt impact are expected to significantly improve modelling.

However, Gilchrist thinks that methods to examine the human brain *in vivo* such as diffusion tensor imaging – a form of MRI that displays the anisotropy of the brain’s white matter – will further illuminate the properties of brain tissue and may lead to “customized” personal predictions for TBI. Brain scanning may also for the first time provide early detection of CTE in living subjects: a group under Gary Small at the University of California, Los Angeles has just reported directly observing tau protein clusters in the brains of five retired professional football players using positron emission tomography (PET) scanning.

### Science, medicine and policy

Among the reasons to continue studying TBI and CTE are the serious policy issues they raise. These include whether young people, many of whom participate as amateurs and whose brains are especially vulnerable, should play contact sports such as American football, rugby, karate and soccer – with multiple “headers” being the concern in the latter. Older professional American football players are deeply concerned as well: nearly 4000 of them have brought legal challenges against the governing National Football League (NFL), claiming it has long denied evidence of serious brain damage. The majority of these lawsuits remain in progress, but in the meantime the NFL has introduced a series of rule changes in an attempt to prevent players from getting hit above their shoulders – for example, if a player loses his helmet, a whistle is sounded and play ceases immediately. We also need to do more to protect soldiers from blasts and care for the large numbers already afflicted. But TBI also deserves attention in infants in the tragic form of shaken baby syndrome. Indeed, anyone can be injured by accidents on the road and in the workplace, where TBI is a major cause of death and disability.

Furthermore, not every researcher is satisfied that even the basic issues are fully settled. Guskievicz, who pioneered the scientific study of football injuries, thinks that cause and effect between sub-concussive impacts and CTE is so far unproven. Other researchers, meanwhile, call for more evidence that blast causes CTE in humans and for long-term tracking of the evolving outcomes of TBI over time.

At a recent conference about TBI, McKee, who is a lead researcher in the mouse blast work and an expert in brain damage in football players, was quoted as noting that so much is unknown about the outcomes of TBI that “for us to try to grapple with all of the variables is impossible”. Medical solutions will require, she thinks, an understanding of the microscopic and molecular physical changes that TBI induces in the brain. Among other things, that is a call for more physical analysis as a critical part of the scientific and clinical attack on TBI and CTE. ■