#### A Modern Perspective on Historical Brain Injury Research



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## The views expressed here are my own and not necessarily those of DOT



Most brain injury research papers start with a reference to the 1943 paper by Holbourn (few have actually read it – based on my personal survey)

## Holbourn (1943) is the most important paper in understanding mechanical brain injury mechanisms

### The history of brain injury research can be divided into pre-Holbourn and post-Holbourn eras

#### For Post-Holbourn Era see literature reviews

Gurdjian (1972), Hess et al. (1980), Ommaya (1984), Melvin et al. (1993), Hardy et al. (1994), McLean and Anderson (1997), Goldsmith (2001), Shaw (2002), Goldsmith and Monson (2005), Meaney et al. (2014) and many others

#### Pre-Holbourn Era (brief overview and confusions)

- The first main confusion and research focus CONTRECOUP injuries, i.e. the lesions are at the side other/opposite than the site of impact (this confusion still exists)
- The second main confusion and research focus CONCUSSION injuries, i.e. brief loss of consciousness without any lesions or sometimes death with or without any lesions (this confusion still exists)

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### Pre-Holbourn Era: Contrecoup Brain Injuries

- Fallopius (1523-62) was first to describe cerebral damage on the side of the brain opposite/other the site of impact
- 1766. The French Royal Academy of Surgery sponsored research and even set prizes for elucidation of problems concerning brain injuries. Contrecoup injuries were declared a subject of particular interest.
- 1892. Miles impact tests on animal heads (rabbits, pigs, birds) in different directions. Gave a theory of contrecoup based on a "cone of depression" forming at the site of impact that propagates to the opposite side and forming a "cone of bulging", which causes contrecoup lesions

## Pre-Holbourn Era: Contrecoup Brain Injuries

- 1940. Goggio introduced the pressure gradient theory based on a simple hydrostatic theory, where negative pressure at the side opposite to impact was proposed as the mechanism of contrecoup injuries
- 1942. Courville reviewed 206 cases of fatal brain injuries that were results of automotive collisions and falls. Made a few valuable observations that may've helped Holbourn with his theory: (1) frontal impacts – only coup contusions occurred on the basilar surface of the frontal lobe; (2) occipital impacts – only contrecoup contusions occurred at the same site as frontal impacts. Observed that the more irregular the bony walls of the skull are the more likely it is that that part will sustain coup or contrecoup contusions

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- According to Adams (The genuine work of Hippocrates), the term concussion like symptoms could be traced back to Hippocrates. One of the precepts in Hippocrates' *Aphorisms* (circa 415 B.C.) is translated as "shaking or concussion of the brain produced by any cause inevitably leaves the patient with an instantaneous loss of voice (i.e. unconscious)".
- Persian physician Rhazes (c. 853-929) considered the nature of concussion in his Baghdad clinic as the type of brain injury that could occur independently of any gross pathology or skull fracture.
- Guido Lanfranchi of Milan (?-1315) in his textbook *Chirurgia Magna* (c.1295) is often credited with being first to formally describe the symptoms of concussion.
- Circa 16<sup>th</sup> century (Capri and Pare) introduced the term *"Commotio Cerebri"* to describe the effects of injuries to the brain without skull fracture.

- 1705. French surgeon Alexis Littre reported to the Royal Academy of Surgery the case of criminal sentenced to be broken on the wheel. To escape the torture, the man has killed himself by rushing across the dungeon (15 feet across) and striking his head against the wall. Examination of the head revealed "no external marks of violence": no fracture, no lesions, etc. This has become one of the most quoted paper and stimulus for more research.
- 1828. Brodie noted that little is known about the motion of the brain during concussive injury, and it is (concussion) was regarded as a "phenomenon beyond comprehension".
- 1830. Gama the first paper on a physical model of the brain. He used Matras (a round-bottom glass flask with a long neck) filled with a gelatin like material (isinglass) with the consistency of the cerebral substance. Several strands of wires in different directions were inserted into the substance. The neck of the Matras was corked and percussed. The movement of the wires was observed, and the mechanism of concussion was linked to the vibration of the wires. The paper is very lengthy without any diagrams or any measurements (just like many others for the following 100 years or so). Nevertheless it was the most referenced paper at that time and the following 50+ years.

- 1865. Alquie conducted series of experiments similar to Gama, but with a glass container filled with various fluids of various consistencies. He claimed that in every experimental setup, as long as the glass container was filled with fluid, jelly or water, no vibrations of wires occurred. Instead, there was a movement of the gelatinous mass under percussive impact. Despite disagreement with Gama, both theories were widely accepted at the time.
- 1874. Koch and Filehne produced concussion by means of repeated light blows to the head instead of a single severe blow and performed autopsies on all their animals – they did not find any gross lesions. Proposed a mechanisms of concussion to be molecular disturbance inside the cells.
- 1878. Ferrier wrote: "It is supposed that contrecoup occurs by actual concussion of the cerebral mass against the skull". This mechanism can still be found in the literature and some internet sites along with the animations

- 1892. Miles presents the point of view that symptoms of concussion are due to a profound disturbance of the circulation of the brain, and that it is due to anemia. Based on animal impact tests he observed that concussive symptoms happen so rapidly after the blow (first few seconds) that they "cannot be attributed to lesions, which, from their nature must take some time to be produced"
- 1927. Miller. Quote: "In spite of a considerable body of experimental work, a great deal of indefiniteness, not to say confusion, admittedly exists in the actual knowledge of concussion, particularly as to its physiology and pathology". Using impact tests on dogs and cats he concluded that anemia is not a factor in the causation of concussion, but rather is due to direct mechanical action on the brain cells

1941. Denny-Brown and Russell defined the word "concussion" as the state of coma, stupor, and confusion following injury to the head, and that it can occur without cerebral lesions. They used pendulum impacts on cats, dogs, and monkeys. Many observations were made: (1) the head has to move to produce concussion (as opposed to being supported on a hard surface), called it acceleration concussion; (2) impact velocity was about 28 fps to produce concussion; (3) sub-threshold blows sometimes resulted in depression of cardiac, vasomotor, and respiratory function for 10-30 seconds, occasionally longer – possible explanation of the knock-out effect in boxing; (4) death from acceleration concussion is due to failure of blood pressure; etc. Overall 21 conclusions.

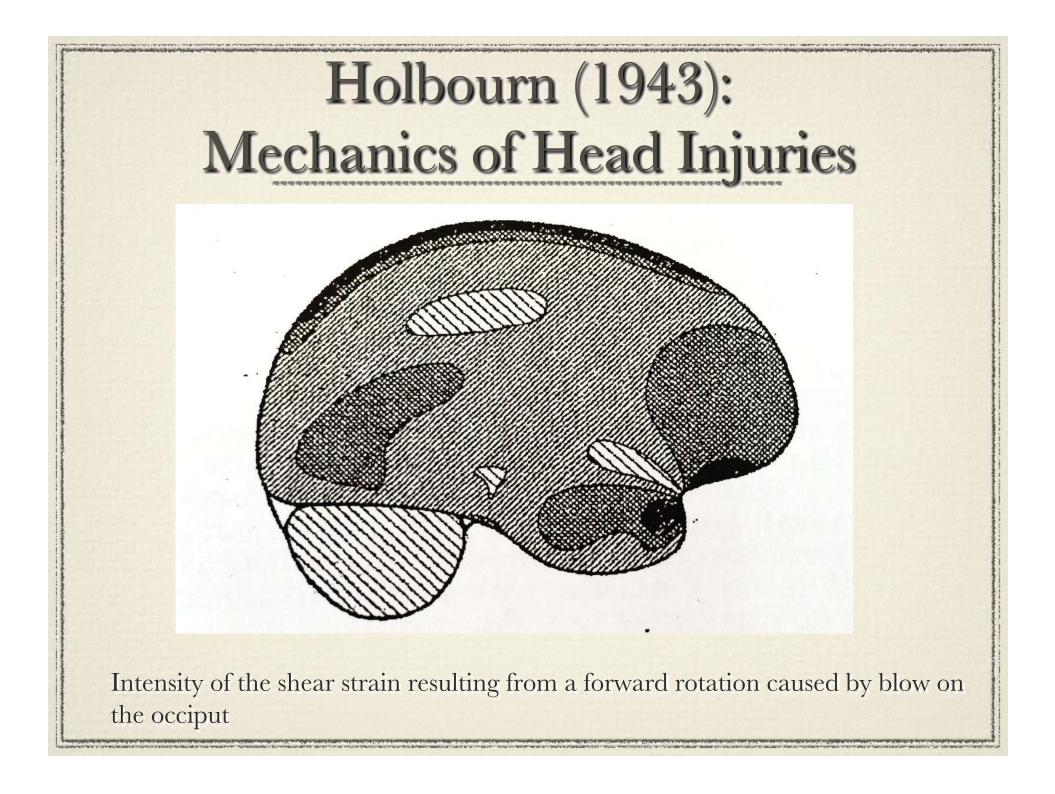
#### Pre-Holbourn Era: Pressure = - Hydrostatic Stress

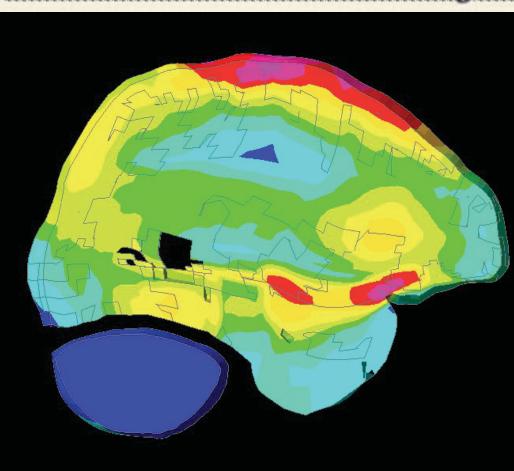
1936. Grundfest presented a study on the effects of different hydrostatic pressures upon the threshold of the frog sciatic nerve. There were minimal effects on nerve function for pressures up to 5,000 psi with only a 10% decrease in the magnitude of the action potential and immediate recovery upon release of the pressure. When higher pressures up to 15,000 psi were applied, the potential reduced further, but was reversible even after being loaded for periods up to 20-30 minutes.

- Assumed that the skull and brain behavior after the blow are governed by the Newton's laws of motion and physical properties of the brain:
  - 1. Uniform density of the brain, blood and CSF are approximately the same and equal that of water
- 2. Extreme incompressibility of the brain, e.g. the brain doesn't change its size when subjected to hydrostatic pressure (very high bulk modulus)
- 3. Very small modulus of rigidity (same as shear modulus), e.g. it offers very small resistance to changes in shape compared to resistance to changes in size (very small ratio of shear to bulk modulus)
- 4. The rigidity of the skull is much greater than that of the brain
- 5. The shape of the skull and brain are important in deciding the location of injuries.
- 6. The brain is injured when its constituent particles are pulled apart and do not join up again when the blow is over. The amount of pulling is proportional to shear strain

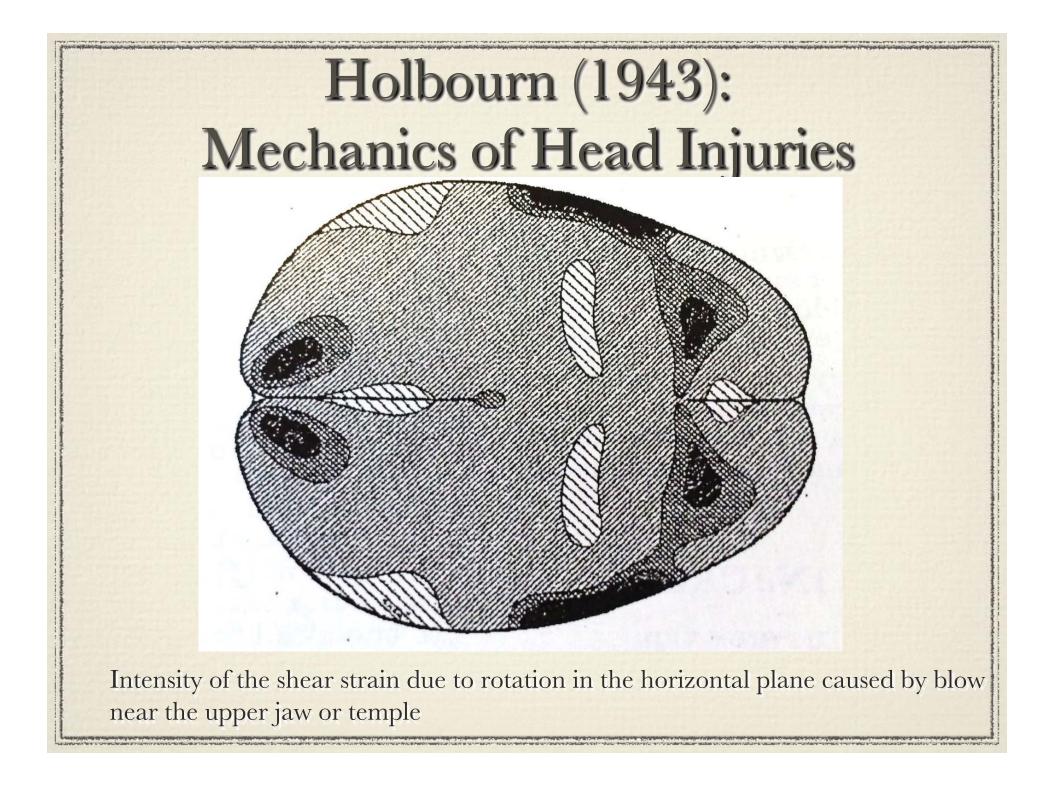
- Based on these 5 properties of the brain-skull system predicted the location of injuries from various blows
- Based on the same 5 properties proposed and explained that there are only two possible brain injury mechanisms: (1) injury to the brain due to skull deformation (this includes skull fractures); and (2) injury to the brain occurring whether or not the skull is deformed (due to change in linear and rotational velocity)
- Explained further that based on the listed brain properties, "change in linear velocity tend to produce compressional or rarefactional strains, which have no injurious effects. The shear strains, which are also produced by linear acceleration, are small. They are produced mainly in the neighborhood of foramina where tissue has a tendency to be extruded or sucked in, and in the neighborhood of ventricles owing to the slight difference in density between CSF and brain tissue. These shear strains produced by linear acceleration are small compared to those produced by rotational velocity."

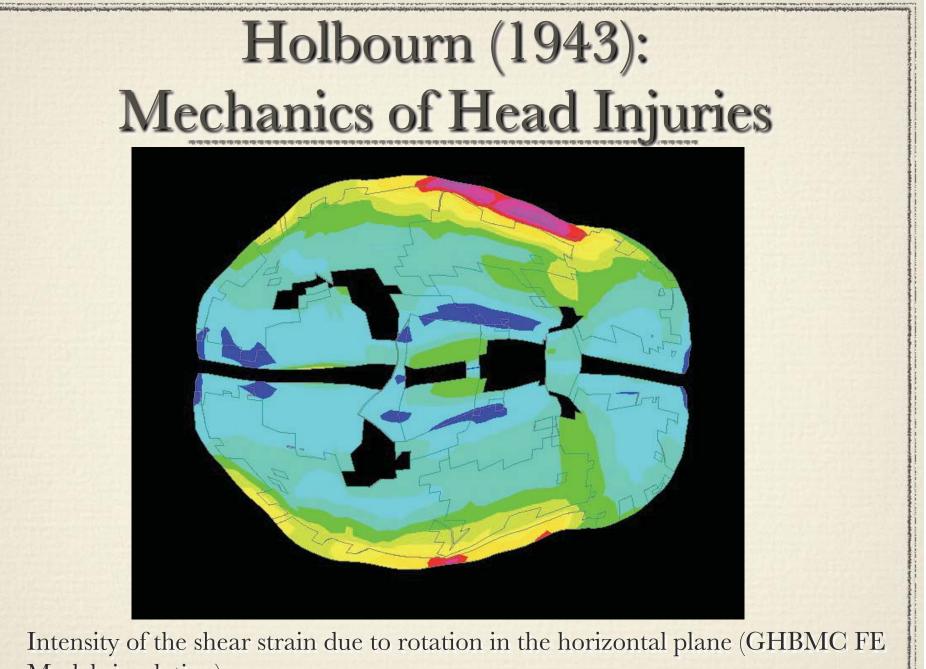
- Developed a physical model of the brain (5% gelatin and 0.5% formalin) and skull (made out of paraffin wax), applied rotation to it and measured (calculated) shear strain using a circular polariscope.
- Described that for a system with the properties 1-5 above the theory of contrecoup is "without physical foundation". The so-called contrecoup injuries are really rotational injuries.
- Based on the results of Denny-Brown and Russell research explained that concussion is also a rotational type injury.
- For blows of long duration the shear strains in the brain are proportional to the force, hence the injury is proportional to the acceleration, or the rate of change of velocity of the head.
- For very short blows the injury is proportional to the force multiplied by the time for which it acts, hence the injury is proportional to the change of velocity of the head and not the rate of change, i.e. the acceleration. For this reason the term "acceleration concussion" is misleading.



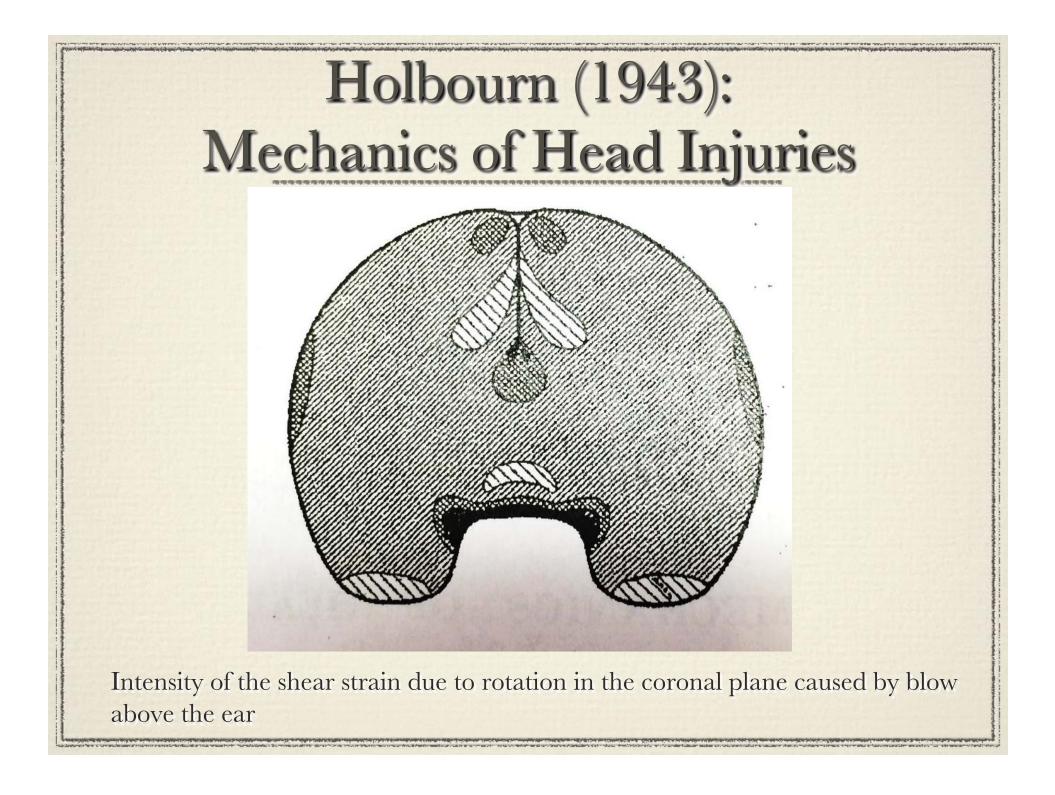


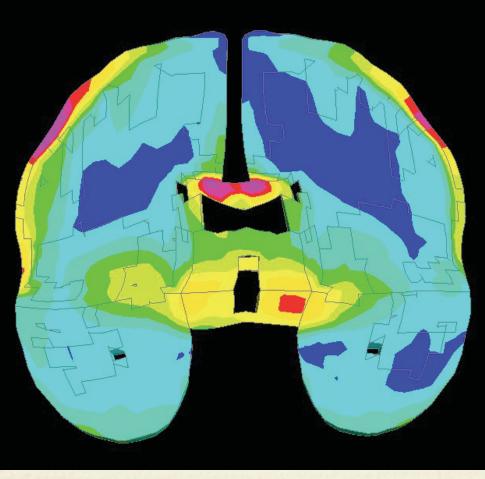
Intensity of the shear strain resulting from a forward rotation (GHBMC FE Model simulation)





Model simulation)





Intensity of the shear strain due to rotation in the coronal plane (GHBMC FE Model simulation)

### How Does it All Relate to Brain Injury Criteria?

- The mechanism of brain injuries is shear strains due to ROTATION (not translation)
- It is rotational VELOCITY (not acceleration) that is proportional to strains for shorter pulses
- Brain Injury Criteria formulation should be based on the rotational velocity, and perhaps on rotational acceleration for longer pulses

