

Back to the Basics: Revisiting the future, a retrospective of reminiscences

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In order to move the field of head injury biomechanics forward, it is sometimes useful to stop, reflect and ask, “how did we get to where we are?” Or, we need to ask, “how do we know what we think we know,” or “did I really say and mean that?” And perhaps more importantly, we need to know if this old stuff leaves questions unanswered that may lead to a better understanding of how mechanical energy fundamentally impairs nervous tissue function and structure. Therefore, I’d like to review some of the work of our group and reflect upon it.

I. WHAT WE THOUGHT WE KNEW

In the 1970’s we performed three groups of animate experiments that asked several questions:

The HAD-II experiments

The HAD-II experiments modified an existing Head Accelerating Device (HAD-1) [1] to provide a non-impact, distributed sagittal planar translational or angular motion [2]. The question posed was, “is there a difference in the response of the brain between the two types of motion?” The result was, “yes, angular but not translational motion was important for production of, what was then called, cerebral concussion with loss of consciousness (LOC).”

The three principal conclusions were 1) “We have...shown that rotation of the head is more likely to produce cerebral concussion than translation,” 2) “translation alone can produce visible brain lesions and thus contribute to the overall injurious effects of head impacts,” and 3) “at the levels of translation studied, concussion does not occur. *We cannot say that concussion will not occur in translation at higher acceleration levels.* These results did not conclude that brain dysfunction or any symptoms could never be produced by translational motion. In fact, we showed that there were alterations of brain structure (pathologic abnormalities) and brain electrical function (as measured by somatosensory evoked responses) after translation, but these changes were not as profound as after angulation motions [3].

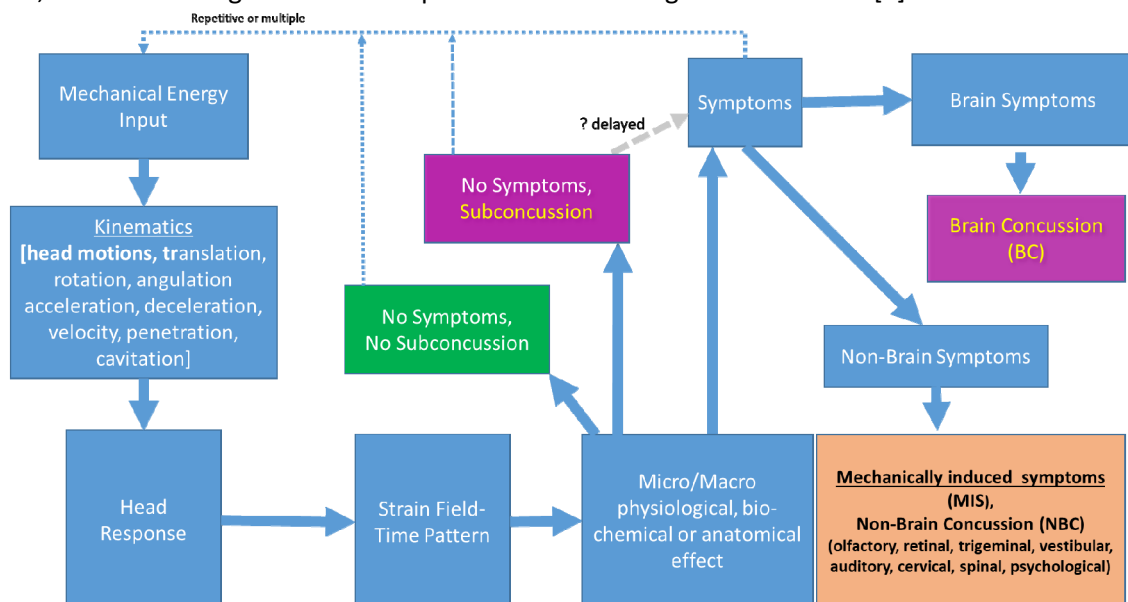


Fig. 1. A Contemporary view of Concussion.

Subsequently, others interpreted what they thought we said, and therefore, concussion has been defined (refined) differently; first by realizing that LOC need not be present but that some alteration of brain function

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must occur (such as confusion or amnesia) [4-5]. Now, further modifications of the definition of concussion include non-brain symptoms in its definition and show the complexity of concussion and other mechanically induced symptoms (MIS) (see Fig. 1) [6]. We propose that some of these MIS may occur from translational or from angular motions, or both. Therefore, *not everything that occurs after a head strike or a head motion is necessarily due to angular head motions*. The future will tease out the specific mechanisms, tolerances and injury risks of whatever the components of concussion will be further defined.

The Penn-I experiments

The Penn-I experiments asked whether increasing the magnitude of non-impact, distributed sagittal planar angular motion could produce prolonged traumatic coma associated with the pathological findings described by Stritch [7-8]. The result was, “no, they could not, but instead these conditions could produce large acute subdural hematomas (ASDH) due to bridging vein rupture” [9].

This somewhat unexpected finding provided a mechanism for one of the most important causes of head injury deaths and disability [10] and so, the clinical importance of ASDH prompted ourselves and others to study the mechanics of bridging vein rupture [11-14].

To date, ASDH remains a serious cause of human death and disability especially in car crashes, assaults and helmeted American high school footballers. Although some work has demonstrated general tolerance levels for ASDH, specific injury curves for ASDH at different ages have not been established (see below).

Indeed, as shown in Fig. 2, the clinical interactions of concussion, ASDH and brain swelling are complex, and our experiments left the biomechanics of these complexities to future investigators.

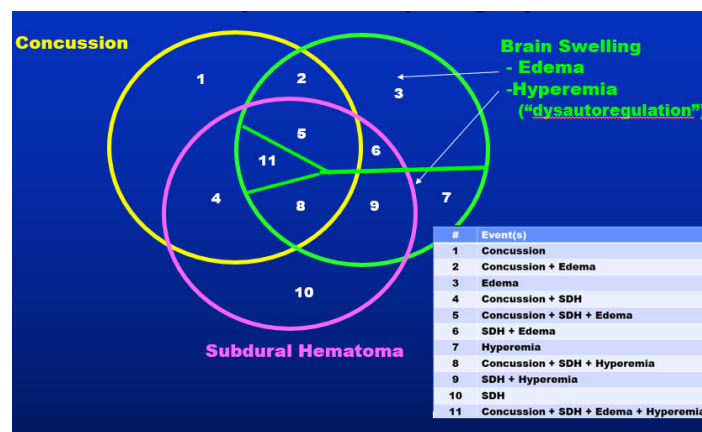


Fig. 2. Consequences of an impact in sports.

The Penn-II experiments

The Penn-II experiments asked whether prolonged coma could be produced by increasing the pulse duration of the angular motion pulse and by changing the direction of motion from sagittal plane to coronal plane motions. The result was, “yes, the condition of prolonged coma with lesions scattered throughout the brain’s white matter, corpus callosum and dorsolateral quadrant of the midbrain, a condition we subsequently named diffuse axonal injury (DAI) could be produced” [15]. That DAI in animals matched exactly the pathological changes in injured humans was encouraging that the mechanism of this common human tragedy had been established [16]. This finding of severe DAI being due to lateral head motions ultimately led to the implementation of side airbag protection which diminished vehicular-induced DAI.

These experiments also

- defined the importance of input direction with coronal motions being more injurious than horizontal than sagittal angulations, [17]
- indicated to us that blood vessels (as in ASDH) were more susceptible to injury at short pulse durations and that axons (as in DAI) were more susceptible to injury at longer pulse durations, and
- implicated the axon as a locus of brain damage due to these input conditions. However, we never concluded that the axon was the *only* site of injury. Nonetheless, many researchers, including our own team, began to focus on what happened to the axon and neurons after injury [18-21].

This focus on the axon was useful and fruitful but did not answer the many questions of how mechanical energy ultimately puts into play the several known cascades of cellular damage that can eventuate in the ultimate outcome after brain injury (the purple arrow in Fig. 3) [22]. So, as shown in Fig. 3, ionic, oxidative, inflammatory or messenger-related mechanisms of cellular damage may initiate reparative or deleterious effects, with or without gene modulations, on not only axons, but also on other neural elements or on vascular, mitochondrial, or glial elements in the brain. *Whether the link between these conditions of potentially progressive damage and the primary effects of injury is mechanical or biological is yet to be determined.*

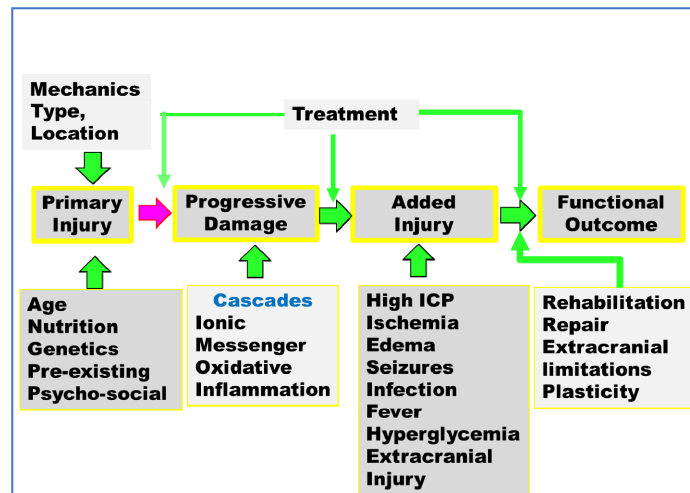


Fig. 3. Influences on Head Injury Outcome

Further, whether these cascades of cellular damage act in a serial or a parallel manner is unknown (see Fig. 4). Does mechanical energy elicit axonal damage and the attendant ionic cascade of events eventuate in oxidative, messenger and inflammatory cascades? Or, alternately, does mechanical energy damage one or more cellular elements independently, and, in turn, each of these initiates potentially damaging cellular cascades?

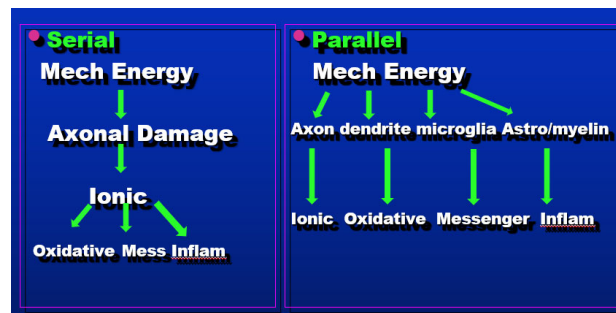


Fig. 4. Possible Mechanisms for Mechanisms of Damage

II. RE-ANALYSIS OF OLD DATA

Current analysis of the input conditions of these three groups of experiments leads us to contemporary concepts that differ somewhat from what we originally proposed.

Effect of wave shapes

The wave forms of our Had-II, Penn-I and Penn-II experiments that produced cerebral concussion (with LOC), concussion-plus-ASDH, and DAI respectively are shown in Fig. 5. Several observations comparing these three can be made:

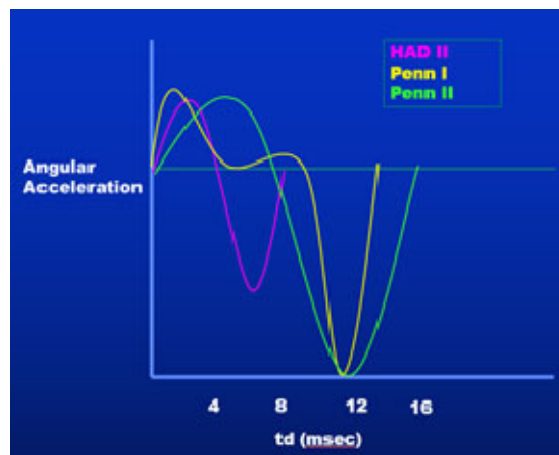


Fig. 5. Waveforms of the Had-II, Penn-I and Penn-II experiments

- The three have approximately similar acceleration magnitudes but differ in deceleration amplitude and in duration. *The pathophysiological effects of other amplitude-duration pulses are not known.*
- As can be seen in all three, the acceleration and deceleration phases are asymmetrically sinusoidal and not separated, except perhaps for a few milliseconds in the Penn-I system. This is due to the short anatomic distance required to move the head of the subject within its anatomic limits. Thus, these pulses do not mimic the common human conditions of 1) a fall or pedestrian in a car crash with long low acceleration phase followed later by a sharp deceleration, or 2) an assault or sport injury with an abrupt acceleration followed later by a slow deceleration.
- To relate these animal injury thresholds to the human situation we used Holbourn’s inverse scaling principals and arrived at human tolerances as shown in Fig. 6. The maximum brain strain values are from Margulies and Thibault [23]. Superimposed on these strain values are the HIC=1000 curve and the thresholds for ASDH from Meany and Thibault (the unconnected red dots) [24].

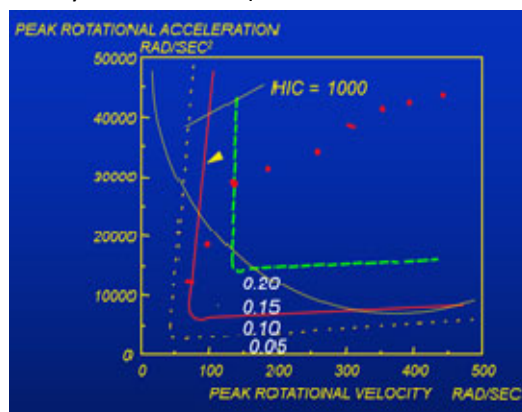


Fig. 6. Critical strains for concussion (0.05-0.1), DAI (0.15-0.20) and ASDH (red dots).

What we do not know is what the brain strain-time pattern and the brain’s response would be 1) if other pulse shapes were utilized, or 2) if a more complete matrix of other single or multiple directional vectors were used.

However, we had to consider modifications in these and our other proposed tolerances after we investigated the potential effects of additional waveshapes on brain strain [25]. Fig. 7 shows the effect of separating the acceleration and deceleration pulses by various time intervals in three brain regions. Brain strain increases with separation intervals from 0 to 20-25msec, after which it is same as single pulse. At zero separation where we conducted most of our experiments, strain is 30-50% of that of single (acceleration or deceleration) pulse. Thus, we concluded that if single pulse or widely separated pulse is more realistic in humans, our initially reported tolerances are 30-50% of what they should be! Consequently, injury thresholds for the set of diffuse brain injuries needed to be modified as shown in Fig. 8 [26].

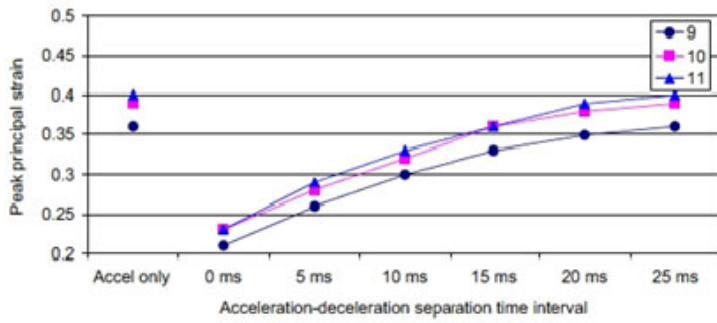


Fig. 7. Effect of separation of acceleration and deceleration pulses on brain strain

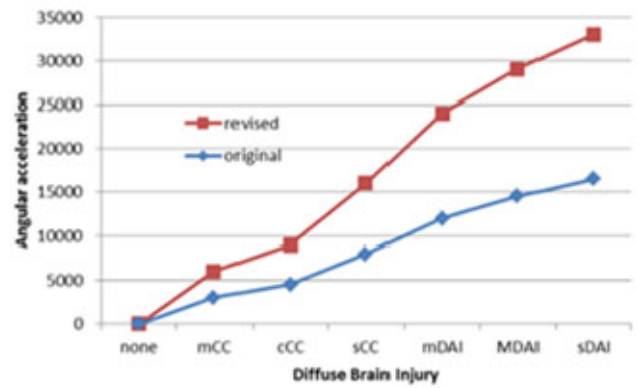


Fig. 8. Revised tolerances for human diffuse brain injuries (mCC=mild cerebral concussion, cCC=classical cerebral concussion, sCC=severe cerebral concussion, mDAI=mild DAI, MDAI=moderate DAI, sDAI=severe DAI)

Effect of angular velocity or pulse duration on concussion, concussion-with-ASDH and DAI

- Going from HAD-II to Penn-I, we attributed the injuries changing from the production of concussion to concussion-with-ASDH to the increased magnitude of the deceleration pulse in the later.
- Going from Penn-I to Penn-II, we attributed the injuries changing from the production of concussion-with-ASDH to DAI to the increased duration (or increased angular velocity) of the deceleration pulse in the later.
- This led us to a qualitative relationship of tolerances shown in Fig. 9. We proposed this construct based on the clinical observations 1) that ASDH could occur without concussion, 2) that ASDH and DAI could occur independently or in combination and 3) that DAI was similar to but more severe than concussion.

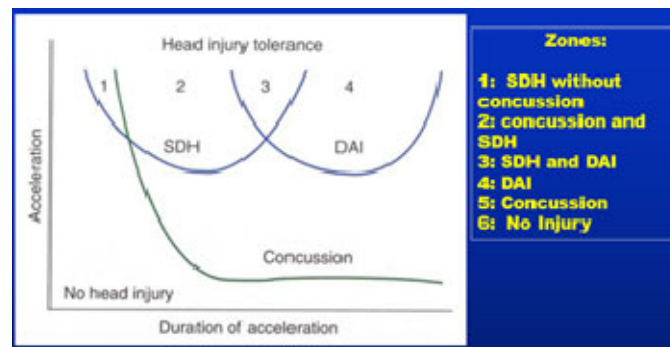


Fig. 9. Theoretical Construct of Injuries Due to Angular Acceleration

- Although this construct seemed to fit the clinical situation, the “U-shaped” tolerances for ASDH and DAI were not consistent with most biomechanical principles.
- Thus, it seemed reasonable to update this construct to fit better with quantitative contemporaneous data and thus Fig. 10 was produced where the lines represent approximately 50% probability of producing each particular injury. It is understood that the x-axis could have been just as easily designated as “angular velocity.” Here, the Ommaya data for human concussion [27], a derivation of the Lowenhielm-Depreitere-Lloyd [11-14] data for ASDH and the Margulies-Thibault data for DAI [22] are shown together.

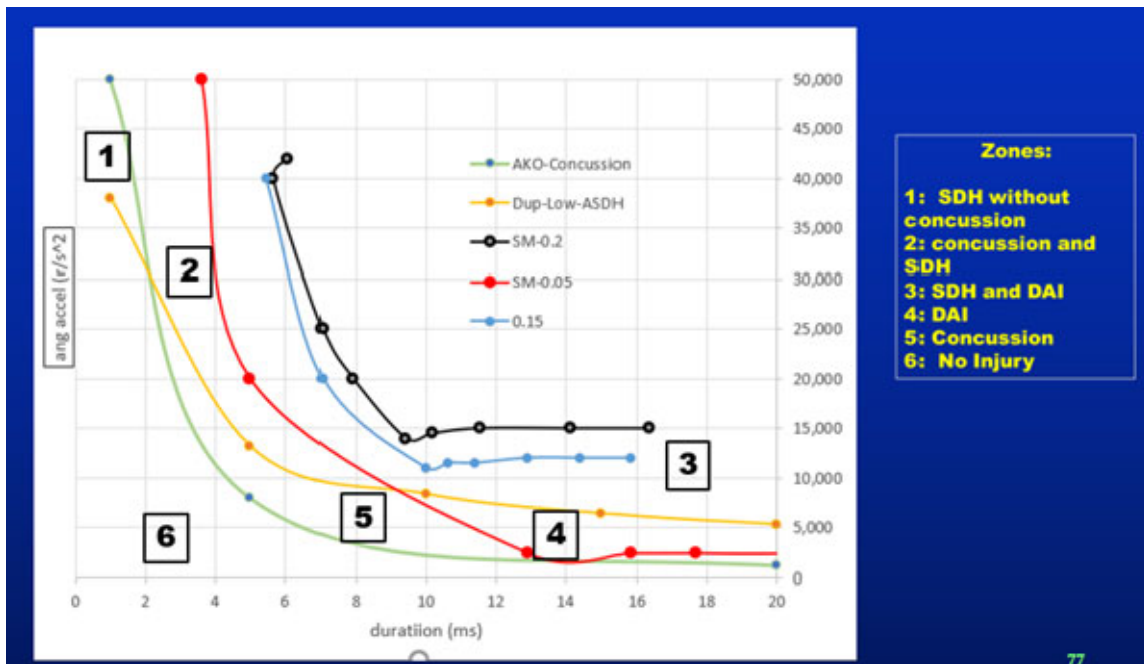


Fig. 10. Current Quantitative Construct of Injuries Due to Angular Head Motions

- The approximate formulae that describe the tolerance curves are:

$$\text{Concussion: } \alpha = 43900d^{-1.04} \quad (R^2=0.9596) \quad (1)$$

$$\text{ASDH: } \alpha = 38040d^{-0.658} \quad (R^2=0.99) \quad (2)$$

$$\text{DAI (strain=0.20): } \alpha = 578.79d^2 - 14758d + 104465 \quad (R^2=0.8901) \text{ or } 19570 * d^{-1.019} \quad (R^2=0.7189) \quad (3)$$

where α is angular acceleration (r/s^2) and d is duration (ms). Certainly, this construct will be fine-tuned as further data is produced in the future.

Finally, we must return to the proposition that mechanical energy applied to the brain may be the independent determinant of initiating the several cascades of cellular dysfunction that may occur. Thus, we are left with conjectural regions in Fig. 10 where these events may be found. The real Fig. 11 is left to future investigation.

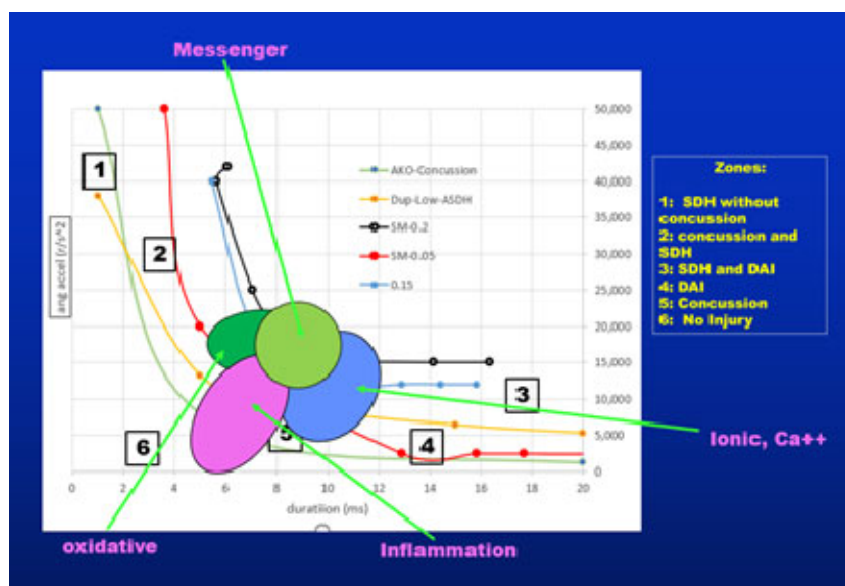


Fig. 11. Biomechanical tolerances of the future?

III. CONCLUSIONS

- It has been my humble privilege to present this lecture in Bertil Aldman's honor.
- Contemporary evaluation of your old data can provide new insights and a roadmap for potential future research questions.

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