CEREBRAL CONCUSSION AND TRAUMATIC UNCONSCIOUSNESS

Correlation of Experimental and Clinical Observations on Blunt Head Injuries

By

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Cerebral concussion has been classically defined as an essentially reversible syndrome without detectable pathology (Denny-Brown et al., 1941) a description which finds its modern counterparts in such statements as “the loss of consciousness and associated traumatic amnesia which occurs as the consequence of head trauma in the absence of physical damage to the brain” (Ward, 1966) and “a clinical syndrome characterized by immediate and transient impairment of neural function such as alteration of consciousness, disturbance of vision, equilibrium, etc., due to mechanical forces.” (Committee to Study Head Injury Nomenclature, 1966.) This idea of concussion as an essentially physiological disturbance emphasizes the striking reversibility of the traumatic loss of consciousness and many of the effects of mechanical damage to the brain. Unfortunately, however, such definitions do not significantly advance our understanding of the syndrome beyond the level reached by the arguments of Petit over two hundred years ago. Over a decade ago Symonds (1962) reviewed the theoretical, experimental, clinical and pathological data to suggest that “concussion should not be confined to cases in which there is immediate loss of consciousness with rapid and complete recovery, but should include the many cases in which the initial symptoms are the same but with subsequent long continued disturbances of consciousness, often followed by residual symptoms—concussion in the above sense depends upon diffuse injury to nerve cells and fibres sustained at the moment of the accident. The effects of this injury may or may not be reversible.” The evolution of this modern concept of cerebral concussion has been clearly described by Hooper (1969) and has guided our own work on the mechanisms of head injury.

Recently, Walker (1973) has reviewed the varying degrees of impairment in awareness observed in “traumatic unconsciousness” (a term he prefers to concussion)
and has stated that "it seems clinical 'concussion' involves not only the brain-stem but other loci in the brain." This statement emphasizes that although falling unconscious is the most dramatic and easily detectable effect of a blow to the head which can be related to an essentially reversible effect on the brain-stem, any description of the mechanisms of head injury must explain how traumatic disturbance of consciousness or alertness relates to other effects of trauma on neural function and structure, particularly the traumatic amnesias. An important question to be answered therefore concerns the relative vulnerability of the various loci in the brain to damage in head injury, i.e. what principles underlie the distribution of focal and diffuse effects on neural tissues found in cerebral concussion. We wish to present a hypothesis for cerebral concussion which seeks to address this question and to correlate the clinical, experimental and pathological observations on blunt head injury.

A Paradigm for Head Injury Mechanics

A simplified flow diagram for the most significant events occurring in head injury is shown in fig. 1. Impairment of function and damage to neural structures can be initiated either statically (forces applied slowly, with durations >200 milliseconds) or dynamically (forces applied with durations <200 milliseconds) (Holbourn, 1943). Static loading is an uncommon cause of head injury; when brain damage does occur by such mechanism, for example, in patients whose heads are slowly crushed,
it is predominantly focal. In such cases diffuse injuries are rarely found and loss of consciousness or amnesia for the event is unusual (Russell and Schiller, 1949). Dynamic loading is the common cause of head injury and this can be initiated either by direct blows to the head (impact) or by sudden movement of the head (impulse) produced by impacts elsewhere. Brain injury by blast loading and penetrating wounds will not be considered here (Hirsch and Ommaya, 1972). Both impact and impulse inputs can injure the brain and its adnexa by the stresses and strains of inertial loading associated with the sudden changes in motion of the head; in addition, impact adds the effects of contact phenomena, which primarily consist of skull bending, fracture and wave propagation (Goldsmith, 1970).

The contribution of contact phenomena to diffuse brain damage has not yet been adequately determined. Impact to the skull will certainly produce focal effects on the brain. The extent of diffuse effects is uncertain because the duration of impact is in the order of milliseconds, that is, one order of magnitude greater than the transit time of waves passing through brain or skull (Goldsmith, 1970). The tentative nature of such effects is therefore represented with a dotted line in fig. 1. It should be emphasized that we are not minimizing the potentially crippling and even lethal effects of some focal lesions; we seek to emphasize, however, their relative simplicity of causation and their inability to explain the various manifestations of traumatic unconsciousness. Because non-impact inertial loading can produce traumatic unconsciousness and visible brain injuries, it is reasonable to assume that inertial loading is a major cause of brain damage in the majority of blunt head injuries. Until recently the relative significance of the two components of inertial loading, translatory and rotatory or angular movements of the head, was undecided. According to Holbourn (1943) shear strains generated by rotation should cause cerebral concussion as well as contrecoup contusions; translation was dismissed as being an insignificant cause of brain damage in head injury mechanics. Conversely, other workers produced experimental data suggesting that pressure gradients produced by translation contributed significantly to cerebral concussion as well as cerebral contusions (Gurdjian et al., 1966; Unterharnschiedt and Sellier, 1966; Unterharnschiedt and Higgins, 1969). Our recent experiments studying these components in relative isolation have shown that both points of view are only partly correct. At equivalent levels of input acceleration rotation of the head appears to be necessary for loss of consciousness as well as productive of diffuse and focal lesions in the brain, the main damage distribution being at brain surfaces and at zones of changes in density of the intracranial tissues. Translation of the head in the horizontal plane on the other hand produces essentially focal effects only, resulting in well-circumscribed cerebral contusions and intracerebral haematomas; such focal effects do not appear adequate for the production of cerebral concussion or other evidence of diffuse effects on the brain at head acceleration levels up to 1400 “g” in the squirrel monkey (Gennarelli et al., 1971, 1972; Ommaya et al., 1973).

Focal and diffuse strains developed within the head as a result of these inputs can thus result in a variable mixture of four operationally defined components of
the biological response to mechanical trauma (fig. 1). Focal concussion is defined as the reversible or irreversible disruption of function by trauma in a restricted asymmetric zone of the brain, occurring in isolation and usually cortical in location. Cerebral concussion is a similar disruption of function occurring in a diffuse symmetrical manner throughout the brain in a distribution determined primarily by certain physical rules described below. Primary brain lesions refer to visible structural disruptions of neural tissues. These may or may not correlate with the sites of concussion; contusions at the site of focal concussion are most likely to correlate with irreversible effects but the wide variation in such effects compared to the more stereotyped nature of contusions preclude a direct causal relationship. Because of the lack of data we restrict the level of such lesion visibility to that detectable by the light microscope. The fourth element, skull fracture, is self-explanatory. It is important to realize that the four components of the biological response to head injury can occur in isolation of the others under specially defined conditions (Lewin, 1966). Correlation of primary brain lesion locations with focal and cerebral concussion is perhaps most satisfactory when concussion is of such severity that a degree of irreversibility of the functional disturbance is introduced. Here too, however, it is possible to have an essentially reversible disturbance of motor, sensory and reflex function associated with a considerable degree of irreversible structural damage. What is emphasized therefore by this paradigm is the primacy of disturbance in neural functions while simultaneously recognizing that their structural substrates are only incompletely recognized by conventional light microscopy.

The severity of head injury is composed by the relative contributions of the four components in the biological response to trauma plus the added deleterious effects of the secondary responses developing after the primary events outlined above. Secondary "lesions" thus produced are not only intracranial events directly related to the primary injury (e.g. ischaemic hypoxia in a zone of traumatic haemorrhage or oedema) (Meinig et al., 1973) but also the indirect systemic consequence of the impairment in neural control mechanisms precipitated by the responses to trauma (for example hypoxia due to airway obstruction and secondary pulmonary effects in the unconscious patient) (Brackett, 1971). Post-traumatic sequels will be the result of either the extent of primary response alone in the mild case of head injury or of the combined effects of primary and secondary responses in the more severe case.

The theoretical and experimental basis for proposing the following hypothesis is derived from the physical model experiments and theoretical analysis of head injury mechanics by Holbourn (1943), the mathematical models of Advani et al. (1972) and our own work (Ommaya et al., 1964, 1966, 1968, 1973; Letcher et al., 1973). The mechanics of injury to the brain in blunt head injury revealed by such studies suggest that the distribution of damaging strains induced by inertial loading would decrease in magnitude from the surface to the centre of the approximately spheroidal brain mass. Thus at low levels of inertial loading, injurious levels of shear strain would not extend deeper than the cortex. The severity and locations of
the resultant functional disconnexions at the cortical and subcortical levels and the
degree of associated irreversible structural damage will depend to a great extent on
the material and structural properties of these tissues (Ommaya, 1968, 1971b). Similar
disconnexions at progressively deeper circumferential “layers” of the three-
dimensional mass of the brain will then occur as the shear strain input magnitude
increases. Paralytic coma (traumatic unconsciousness) is not developed until the
magnitude of shear strain is large enough to reach the well-protected mesencephalic
part of the brain-stem and thus complete the disconnexion of the alerting system of
the brain. It must be emphasized that such circumferential disconnexions are not
to be conceived as an inevitable series of “onion-peel” layers with uniform neural
disruption throughout that layer. As indicated above, material and structural
factors will influence such disconnexions. The results will be dependent in a very
complex manner on the mechanical properties of the multi-component, anisotropic
inhomogeneous brain as well as the location of bony protrusions, dural partitions,
vascular anatomy, and other sources of tissue interfaces with different densities.
Thus, it would follow that those parts of the cortex covered by smooth surfaces (e.g.
the occipital lobes) should suffer the least damage whereas those portions covered
by rough surfaces (e.g. the temporal lobes, frontal poles and orbital cortex) would
suffer the most. The contact phenomena and translatory components of inertial
loading would add to such diffuse effects by contributing focal lesion effects at
sites determined by the skull distortions and pressure gradients as shown
experimentally by Lindgren (1966). The site of impact is therefore more important
for the resultant focal effects on the brain, both by the contact phenomena and the
translatory component of inertial loading. The combination of rotational and
translational effects is possibly the reason why we have been unable to confirm
experimentally the qualitative strain distribution diagrams given by Holbourn;
there were significant discrepancies in our experimental results for the distribution
of visible brain lesions produced by inertial loading which are not simply explicable
by the difficulty in producing large strains in small animal brains (Holbourn, 1969;
Ommaya et al., 1971a). It must be noted that Holbourn’s data were based on two-
dimensional photo-elastic stress analysis in a simplified model representing only
“skull” and “brain” elements and no foramen magnum or neck.

HYPOTHESIS FOR CEREBRAL CONCUSSION

Let us define normal consciousness operationally as that state of awareness in the
organism which is characterized by maximum capacity to utilize its sensory input
and motor output potential in order to achieve accurate storage and retrieval of
events related to contemporary time and space (Ommaya, 1963). Our hypothesis
for cerebral concussion would then be defined as a graded set of clinical syndromes
following head injury wherein increasing severity of disturbance in level and content
of consciousness is caused by mechanically induced strains affecting the brain in a
centripetal sequence of disruptive effect on function and structure. The effects of this
sequence always begin at the surfaces of the brain in the mild cases and extend inwards to affect the diencephalic-mesencephalic core at the most severe levels of trauma. Our proposed classification of the grades of cerebral concussion thus produced is shown in fig. 2.

**Fig. 2.—Diagrammatic description of our hypothesis for the syndromes of cerebral concussion with increasing severity of primary injury causing more extensive disconnections between the cortex and the mesencephalic-diencephalic “core” of the brain. Note that Grade IV cerebral concussion is the state of traumatic unconsciousness which may be further subdivided according to duration of coma or severity of neurological sequelae.**

The extent of cortical and subcortical involvement in head injury is therefore always significant and the probability of peripheral damage increases proportionately when the amount of strain is large enough to affect the rostral brain-stem and produce the “typical” case with the paralytic coma of traumatic unconsciousness (Grade IV). Extending on either side of this level of injury severity are cases with lesser and greater damage. On the one hand may be found the less severe cases where memory disturbance occurs without loss of motor control and only partially impaired awareness (Grades I to III); in such cases we suggest that significant strains did not reach the reticular activating system. On the other hand are the more severe cases with greater degrees of diffuse irreversible damage. When such diffuse damage reaches a critical amount, and therefore not necessarily when the mesencephalon shows structural damage, the Grade V case is developed. This type of result is aptly described by the term “persistent vegetative state” as suggested by Jennet and Plum (1972).

Our hypothesis leads to three critical predictions. First, that when the level of trauma is severe enough to produce what is described as traumatic unconsciousness (shown as coma in fig. 2), the extent of simultaneous primary injury in the brain is more severe in cortical and subcortical structures (and particularly in the critically
vulnerable zones mentioned above) than in the rostral brain-stem. Secondly, it follows that because the mesencephalon is the last to be affected by trauma, primary damage to the rostral brain-stem will not occur in isolation in the vast majority of head injuries which are associated with acceleration or deceleration trauma. When a truly primary lesion of this part of the brain-stem is found at post-mortem, it should be found rarely and always in association with diffuse damage to the brain. If a patient with a lower grade of cerebral concussion dies from other causes, we would also predict that isolated primary rostral brain-stem lesions will not be found. The third prediction from the hypothesis is that although confusion and disturbances of memory can occur without loss of consciousness the reverse should never be seen; that is every case of head injury with a Grade IV cerebral concussion must have an associated period of traumatic amnesia; the mesencephalon being less vulnerable than the temporal lobes and limbic system. We wish to reiterate that these predictions will hold only for the commonly found head injury wherein the head is accelerated or decelerated after impact.

The validity of our hypothesis and the predictions from it will now be examined in the light of experimental, clinical and pathological observations.

**Experimental Observations**

In our first model for experimental head injury we discovered that wearing a collar protected the brain during impact to the head (Ommaya et al., 1964, 1966). On examination of the mechanism for this protective effect we found that the collar did not reduce either stretching of the neck or translation of the head. So by exclusion, head rotation was suggested as being the key factor in producing diffuse shear strains in the brain and that it was the reduction of the angulation of the head on the neck by the collar which minimized the shear strains in the brain during impact (Ommaya et al., 1966). In further experiments aimed at testing Holbourn's hypothesis we established that inertial loading without head impact, as produced in experimental whiplash, was capable of producing experimental cerebral concussion and superficial vascular lesions in the brain but the distribution and nature of such lesions did not fit Holbourn's predicted lesion distributions precisely. We did confirm that this response was sensitive to the velocity change experienced by the head at short durations of impact (<50 milliseconds) as predicted (Ommaya et al., 1968, 19716; Holbourn, 1969). Holbourn's main prediction that the head rotation was the critical factor for both cerebral concussion and contrecoup lesions and the opposing contention that translation also played a role was not tested critically in these experiments. Measured levels of head rotations at which cerebral concussion occurred in rhesus monkeys receiving occipital head impacts were approximately half that required when the head was accelerated without direct impact in experimental whiplash (Ommaya et al., 1971b). This observation supported the idea that components other than inertial loading were significant in the genesis of cerebral concussion. In the chimpanzee, however, with a brain to head mass ratio much smaller than that
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of 1:5 found in the rhesus and man, the levels of rotation at which concussion occurred were similar in direct and indirect impacts (Ommaya et al., 1973). This was attributed to the thick scalp and skull and short muscular neck in this species, factors which would tend to minimize the contact phenomena of impact, thus making inertial loading the prime injury mechanism. We assumed that the rotational component was critical for the diffuse effects of head injury and on the basis of these data were able to develop a tolerance curve predicting the injurious rotational acceleration threshold for man (Ommaya et al., 1970, 1971b).

In order to test this assumption and further our understanding of the mechanisms of head injury, we have recently completed experiments wherein pure inertial loading

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Fig. 3.—Head Accelerating Device (HAD-II) used to test the rotational and translational components of inertial loading separately. Note the helmet (shown also in insert) which eliminates the contact phenomena of impact. When the rotation arm B is disconnected from the helmet the head-helmet “rigid body” is moved in pure translation (for about 1 inch travel of the centre of gravity) by the translation arm A. Fixation of the Rotation arm (at the level of Ti) causes the translation arm to angulate the head-helmet combination at the Ti junction over an angle of 45°. The acceleration wave forms thus produced are reproducible, being determined by the speed of the cam and the profile cut into its edge, into which a solenoid switch drops a pin connected to the linkage driving the translation arm.
was examined more precisely and its components definitively compared. In these experiments we have also developed a quantitative and objective index of cerebral concussion to supplement clinical neurological examination; this is the somatosensory evoked response at the skull surface to median nerve stimulation at the wrist (Gennarelli et al., 1972; Ommaya et al., 1973). The device in which we compared the two components of inertial loading directly enable the production of either pure translations or rotation of the head through 45 degrees; in both cases the centre of gravity of the head moves approximately one inch (fig. 3). Identical levels of input accelerations independent of the effect of impact contact phenomena could thus be compared while varying the effect of one variable only, such as rotation. Serial neurological examinations of the animal before and after trauma were recorded on video-tape with split-screen imaging of the simultaneous EEG and other physiological variables (Parsons and Ommaya, 1969). A PDP-12 computer enabled on-line monitoring of the somatosensory evoked responses (SER) generated by stimulation of the median nerve at the wrist. Comparison of the video-tape data and SER facilitated critical on-line correlations between the neurological and electrophysiological data (Gennarelli et al., submitted for publication). All the animals in the rotated group exhibited neurological evidence of experimental cerebral concussion defined as the sudden onset of paralytic coma or traumatic unconsciousness. In contrast, none of the translated group showed this effect. All animals were sacrificed after twenty-four hours and the location of lesions in both groups were compared. These data are shown for each animal in Tables I and II; and the distribution of gross primary lesions is summarized in fig. 4. The species used in this series of experiments was *Samiri sciureus* (squirrel monkey).

<table>
<thead>
<tr>
<th>Monkey No.</th>
<th>Peak positive acceleration*</th>
<th>Cerebral concussion</th>
<th>Brain lesions</th>
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<tr>
<td>SR-1</td>
<td>1025</td>
<td>+</td>
<td>+ SDH + SAH - CC - ICH + ICPH - BSH</td>
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<td>402</td>
<td>+</td>
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<td>SR-12</td>
<td>783</td>
<td>+</td>
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+=Lesion present. -=Lesion absent. *In “g” (resultant of the measured tangential and radial components).

SDH=Subdural hæmatoma. SAH=Subarachnoid hæmorrhage. CC=Cortical contusion. ICH=Intracerebral hæmatoma. ICPH=Intracerebral petechial hæmorrhages. BSH=Brain-stem hæmorrhages.
<table>
<thead>
<tr>
<th>Monkey No.</th>
<th>Peak positive acceleration*</th>
<th>Cerebral concussion</th>
<th>SDH</th>
<th>SAH</th>
<th>CC</th>
<th>ICH</th>
<th>ICPH</th>
<th>BSH</th>
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<td>SL-2</td>
<td>1230</td>
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</table>

+ = Lesion present.
— = Lesion absent.
*In “g”.

Table II. — Effects of Head Shaking—Translation

SDH = Subdural haematoma.
SAH = Subarachnoid haemorrhage.
CC = Cortical contusion.
ICH = Intracerebral haematoma.
ICPH = Intracerebral petechial haemorrhages.
BSH = Brain-stem haemorrhages.

It became clear that a greater number of such lesions occurred in a more diffusely widespread symmetrical manner in the rotated group whereas only a few asymmetrically placed focal lesions developed in the translated group. Intracerebral haematomas occurred exclusively in the translated group but in only 2 out of 12 animals. These were unique lesions in one occipital lobe producing a striking separation of the grey-white interface (fig. 5, Plate XXXVI). Conversely, petechial haemorrhage at grey-white interfaces were present in a bilaterally symmetrical fashion in every member of the rotated group, but in only two of the translated group in a sparse asymmetrical fashion. These lesions are illustrated in fig. 6. Cortical contusions were found at approximately the same frequency in both groups but those seen in the translated group were characteristically discrete, involving only the outer cortical layers in a somewhat excavated fashion. Haemorrhages in the brain-stem were remarkably scarce, occurring in only 2 of the rotated animals and in none of the translated animals. Both of the rotated animals in which primary brain-stem haemorrhage was seen were very severely concussed with diffuse lesions throughout the brain, one dying shortly after the trauma and the other remaining in a prolonged state of depressed responsiveness to stimuli. Thus at the levels of acceleration tested (up to 1230 “g’s”), it was possible to produce cerebral concussion only when the moving head was allowed to angulate or rotate. When rotation was prevented and the head allowed to translate only (movement in a straight line), cerebral concussion did not occur. Conversely, evidence of focal
primary brain damage, for example gross structural failure of tissue, could be produced independent of diffuse lesions or loss of consciousness under conditions of pure translation. These facts, coupled with the association of diffuse surface as well as deeper lesions with cerebral concussion only in the rotated group, support our hypothesis that cerebral concussion of a severity great enough to produce paralytic coma requires shear strains occurring in a widespread and diffuse manner involving the cerebral cortex and deeper structures with brain-stem involvement being primarily a reversible affair. In the more severe case, the diffuse damage with or without the brain-stem effects are essentially irreversible; if a patient in such a category survives, it will be with varying degrees of neurological and behavioural deficits, one class of which is seen in the persistent vegetative state.

Analysis of the electrophysiological data obtained with the somatosensory evoked response (SER) technique also supports our interpretation of the biomechanical, neurological and pathological data (Gennarelli et al., submitted for publication). In the squirrel monkey the P\(_1\) component of the SER represents conduction in primary lemniscal afferents whereas the P\(_2\) component represents the cortically
recorded signal of sensory inputs travelling via the extra-lemniscal pathways. Alterations in $P_2$ therefore provide an objective sign for adequacy of conduction through what may be considered to be the alerting system in the rostral brain-stem reticular formation in mesencephalic and diencephalic structures. Abolition of the $P_2$ wave at the cortex (recorded with extradural electrodes) was found to coincide

![Graph showing serial display of somatosensory evoked response (SER) to median nerve stimulation in a rotated animal.](image)

**Fig. 7.**—Serial display of the somatosensory evoked response (SER) to median nerve stimulation in a rotated animal. Note the pre-impact components which are all obliterated at impact. This animal remained unconscious for seven minutes and the return of the second positive wave ($P_2$, representing conduction in the non-specific pathways) coincided precisely with the arousal of the animal from unresponsive coma. The animal remained somnolent for over six hours after impact and at 220 minutes the SER component had not yet returned to normal. The SER display in this and the next two figures is shown in two time scales with the longer display on the right.
precisely with the onset of paralytic coma and its return with the restoration of the animals' responsiveness and motor performance (fig. 7). In the translated animals $P_2$ was always preserved and none of these animals were concussed (fig. 8). The hypothesis that the paralytic coma of cerebral concussion is associated with failure of activity in the mesencephalic reticular formation is thus supported.

Fig. 8.—The SER in a translated animal. Note that in comparison with fig. 7, only decreases in amplitudes with no loss of the signal components is seen. This animal, like all in the translated group, showed no clinical impairment of the pre-impact alert state of awareness.
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(Ward, 1966; Walker, 1973; Gurdjian et al., 1966). We also found, however, that irrespective of such effects of trauma on the brain-stem, definite and more long-lasting effects were also demonstrable at the level of the cerebral cortex. The time taken for the $P_2$ wave to travel from one hemisphere to the opposite side

![Diagram showing electrical activity over time](image)

**Fig. 9.**—The SER in a rotated animal concussed for 60 seconds with delayed secondary loss of consciousness after a "lucid interval." This was reflected in the secondary loss of the $P_2$ component, returning again at 5½ minutes when the animal awoke a second time. This animal had a large subdural hematoma more on the left side. The changes in the SER always preceded the changes in the EEG.
CEREBRAL CONCUSSION

CONTRALATERAL TO IPSILATERAL LATENCY DELAY $P_2$

Fig. 10.—Latency of contralateral to ipsilateral conduction of $P_2$ plotted as a function of time after impact for the two groups of animals. This reflects interhemispheric cortical functional integrity. The data clearly shows the marked increase in per cent delay of $P_2$ conduction in the rotated group as compared to the unimpaired translated group. This increased latency moreover persists far longer than either the $P_2$ conduction deficit noted in fig. 7 or the duration of loss of consciousness. These data suggest that cortical injury is more significant than brain-stem injury at this level of traumatic input and also that pure translation does not produce any significant diffuse effects at either brain-stem or cortical levels at the levels of acceleration tested (up to 1230 “g”).

Plotted as a percentage of the time taken to make the same transfer before impact is shown in fig. 9. Note the marked slowing of such interhemispheral cortico-cortical transfer found only in the rotated group and absent in the non-concussed translated group; this impairment of cortical (+subcortical) function persists long after the return of $P_2$ indicated adequate conduction through the reticular formation. This would suggest that cortical (or telencephalic) effects of such head injury are widespread and possibly more severe than the brain-stem effects. The hypothesis that cortical involvement is always significant in cerebral concussion is thus also supported (Denny-Brown and Russell, 1941; Symonds, 1962; Hooper, 1969; Walker, 1973; Ommaya et al., 1970, 1973).

CLINICAL OBSERVATIONS

The complex patterns of clinical behaviour after head injuries are well recognized (Hooper, 1969; Walker, 1973; Lewin, 1966). It is possible, however, to discern a general pattern of recovery in many patients after severe but relatively uncomplicated head injury which is important to recapitulate (Hooper,
1969). The patient falls unconscious and remains for a while in an unresponsive, immobile coma. Emerging from this state of paralytic unconsciousness the patient successively passes through stages of stupor, confusion with or without delirium and finally, an almost lucid phase with automatism before becoming fully alert. Stated in another way, return of awareness to stimuli usually precedes motor and sensory recovery which in turn recover before restoration of memory and other cognitive functions. It is of great interest that this sequence of reintegration of normal consciousness is similar in a wide spectrum of head injuries and correlates with the severity of injury only in being much slower in cases with prolonged coma, such patients being of course more liable to have residual symptoms. The common element in such severe cases is that alertness always returns before full return of memory functions. Another feature of the "recovered" case of severe head injury is the association of a labile effect with the difficulty in learning new material (Ommaya, 1966). These observations support the idea of a greater vulnerability of the cortex and particularly of the limbic and fronto-temporal cortices which occupy zones of great structural irregularity and variation in tissue density.

A large number of clinical observations at the less severe end of the spectrum of cerebral concussion syndromes can also be explained by our hypothesis. The lesser grades of cerebral concussion (I to III) are quite common, particularly in contact sports such as American football and boxing. The majority of such concussions do not produce paralytic coma or traumatic unconsciousness; instead, confusion and amnesia are usually seen. It is a common experience for patients who have been briefly "dazed" or confused to continue well-coordinated sensorimotor activity after a sports accident without subsequent recall of the episode (Ommaya et al., 1973). Yarnell (1970) and Yarnell and Lynch (1973) have recently reported a group of such mildly concussed patients examined immediately after impact who were confused and disoriented in time but possessed intact recall of events immediately before impact; retrograde amnesia did not develop until five to ten minutes after the impact. Yarnell also described further cases similar to that reported by Fisher (1966) in which the occurrence of severe amnesia after head impact was not associated with a loss of alertness. In the latter report the author writes: "It must be concluded that a traumatic insult to the memory mechanisms can occur with complete sparing of the neural basis of alertness," and again: "In moderate to severe concussion, although both systems are usually affected together, they are not equally vulnerable, for alertness is restored first as a rule, while impaired memory almost always persists for a longer period. It might be expected therefore that amnesia would occur in the presence of retained alertness (Fisher, 1966).

Our hypothesis offers a reasonable explanation for the greater vulnerability of memory and the lesser vulnerability of alertness in head injury. In a recent study on memory mechanisms in man, we presented data to support the hypothesis that it is the hippocampal gyri rather than the hippocampus per se which form the brain structures critically involved in coding experiences for retrieval
from storage via the associative neocortex (Ommaya et al., 1972). It would follow that if the hippocampal mesocortex and temporal neocortex bear the main brunt of the cortical damage, then the recovery of alertness should precede the return of telencephalic integrative functions controlling motor and sensory mechanisms, with memory mechanisms being restored last of all. The observation by Torres and Shapiro (1961) that EEG abnormalities occurring in a group of patients after non-impact inertial loading of the head ("whiplash injury") were similar in nature and incidence to those seen after impact produced head injury is inexplicable, except by invoking the common role of inertial loading with maximal effect on the cortex in both conditions.

A critical question which remains to be resolved is the relative contributions of primary and secondary effects to the ultimate outcome in surviving patients. A recent report by Overgaard et al. (1973) is relevant here: they found that the first neurological examination (within six hours of head injury in 70 per cent of patients) was reliably predictive of the final outcome with only three sets of clinical variables being recorded, i.e. the level of consciousness, motor functions and neuroophthalmological signs. Their data would support the hypothesis that the critical damage was primary rather than secondary in survivors and that the cortex rather than the reticular formation bore the brunt of irreversible damage. They also noted that episodic systolic hypertension was significantly correlated with a poor prognosis. This suggests that the secondary factors of cerebral oedema, vascular congestion and possibly increased CSF volume due to impaired absorption may be the prime cause of the ischaemic hypoxia which adds further brain damage to the primary insult. In coping with these added volumes, the lack of significant correlation between prognosis and intracranial pressure or regional cortical blood flow may well be due to the lack of correlated information on the critical rate of such intracranial volume changes (Bruce et al., 1973). We have shown therefore that, while relatively high rates of mass expansion in the head produce a classically exponential P/V curve, slower rates (<0·02 cc/mm in the rhesus monkey) fail to evoke a Cushing response, do not produce a rise in ICP but still cause brain death at the same volume of added mass as at the higher rate (Nakatani and Ommaya, 1973). Presumably this is by the same mechanism; failure of adequate vascular perfusion of the control centres for the vital functions in the brain-stem.

**Pathological Observations**

In spite of many detailed pathological studies, a completely adequate description of the relative three-dimensional distribution of all primary lesions throughout the brain at known intervals of time after head injury is not yet available, either in man (where it will probably never be completely obtained) or in experimental animals (Unterharnscheidt and Higgins, 1969; Ommaya and Corrao, 1970; Strich, 1969; Zulch, 1969). Such a study is urgently required, data being needed in cases sustaining injury at three levels of injury severity, that is, with reversible deficits, with irreversible deficits but survival and with irreversible deficits plus
death. Review of available data, however, does enable certain aspects of the hypothesis to be examined. The observation that the prime location of contusions is in the temporal and frontal regions irrespective of the site of impact has not been satisfactorily explained by previous hypotheses (Ommaya et al., 1971a). The occurrence of subdural haematomas after falls on the buttocks and after whiplash injury alone is of course more easily attributable to the rotational components of inertial loading (Ommaya and Yarnell, 1969). In a recent review of the pathology of brain damage in blunt head injuries, Strich (1969) has emphasized the diffuse nature of histological changes in axons, microglial stars around tissue tears as reported by Oppenheimer and the neuronal changes found by many investigators. Grcevic and Jacob (1965) have reported preliminary facts on a serial-section study in fatal human head injuries showing diffuse lesions in a rostral periventricular pattern. Although cell-counts from controlled experiments in animals have been reported for a few locations, the available evidence does not enable us to decide on the relative vulnerability of cortex and subjacent white matter to mechanical trauma, nor is it yet possible to envisage the three-dimensional distribution of the diffuse lesions (Windle and Groat, 1945). An important study by Mitchell and Hume Adams (1973) on the incidence of primary brain-stem lesions in patients dying after head injury supports the idea that such lesions probably do not occur in head injuries without severe damage elsewhere. Our hypothesis that the brain-stem is the least vulnerable part of the brain for primary damage is thus not refuted.

The difficulties in interpretation of pathological material from experimental studies have been pointed out on numerous occasions (Ommaya and Corrao, 1970; Strich, 1969). Because of the smaller mass of brain in animals and the restriction implicit in impact techniques, it has not been possible to duplicate all the clinical and pathological observations made in man (Ommaya et al., 1970, 1971a, 1973; Gennarelli et al., submitted for publication). Critical review of the experiments claiming that primary brain-stem damage and even primary rostral cervical cord damage are the substrate of acceleration concussion suggest that the data may equally well be interpreted as a consequence of the method used (Ommaya et al., 1966). It is important to stress that interpretations of experiments must provide satisfactory explanations of the clinical observations on cerebral concussion. This point was also made by Denny-Brown (1961) who, in reviewing the work of Friede, pointed out the lack of immediate disturbance of consciousness and of traumatic amnesias in contusions to the medulla or upper cervical cord in man.

In this review we have not considered the cumulative effect of multiple impacts and the relation of late effects of head injury to our hypothesis (Unterharnscheidt, 1966, 1969). These important problems must be assessed but it is unlikely that further advances can be made in these areas if a deeper level of understanding of injury mechanisms to the brain after a single controlled input for trauma is not attained. Only in this way can we separate the primary from the secondary effects of mechanical insult to the brain.
DISCUSSION

The mechanisms of head injury cannot be understood by studies in man alone. A model for inertial loading of the brain in head injury enables the investigator to overcome the limitations in developing adequate correlations between functional and structural changes imposed by impact methods hitherto used almost exclusively in such studies. The contact phenomena of impact are probably also best studied in isolation. In order to test our hypothesis, measured biological responses after head injury must be shown to occur in the distribution and directions predicted. Such measurements could profitably include \textit{in vivo} tests of neural functions (for example the SER) which in turn must be correlated with neurological and behavioural effects of the trauma as well as with the subsequent neuropathological data on structural tissue failures at sites of predicted maximal strains. A useful technique would be to validate such experimental models by utilizing them as "white boxes" and seek to match their observed responses to known inputs with those observed in the "black box" of human head injuries using identical diagnostic techniques for non-invasive measurement (Gennarelli \textit{et al}., 1972; Letcher \textit{et al}., 1973; Ambrose and Hounsfield, 1973; Ommaya, Corrao and Letcher, 1973). Scaling of data from animals to man is possible using a variety of available physical and mathematical models or by developing such models to meet particular problems (Goldsmith, 1970; Ommaya \textit{et al}., 1967). Mathematical and physical models can serve two very important uses in addition to scaling requirements. First, they may provide 3-dimensional quantitative maps of the loci for stresses and strains in the brain under a variety of stimulated impact conditions; the physiological and pathological "maps" of functional and structural effects of such strains may thus be compared to the theoretical predictions. Secondly, such models (once they have been validated) may be the most effective tool in testing the quality of safety devices and protection systems by simulating more efficiently the entire system in a computer programme. In patients an immediate need is to recognize the extent of primary damage as well as the exact sequence of development of secondary lesions; prevention of the potentially reversible secondary lesions from adding to the irreversible damage produced by the primary mechanical insult would be facilitated.

Finally, it may be noted that we have described so far what may be called the macroscopic approach to understanding head injury mechanisms. A precise understanding of such mechanisms also requires the development of hypotheses and techniques for what may be called micro-trauma experiments. These should seek to establish the physicochemical basis of reversible and irreversible damage to neural tissues by mechanical trauma at the cellular and molecular level. Because this approach necessarily can progress only as far as our current incomplete understanding of the structural correlates of normal function in the nervous system, it will be readily realized that head injury research in its broadest sense is also research at the frontiers of neurobiology (Cohen, 1973).
SUMMARY

A new paradigm for cerebral concussion is proposed which is not refuted by the available clinical and experimental knowledge on head injuries. It is suggested that rotational components of accelerative trauma to the head produce a graded centripetal progression of diffuse cortical-subcortical disconnexion phenomena which is always maximal at the periphery and enhanced at sites of structural inhomogeneity. The translational components of such trauma are significant for the production of focal injuries only. In this hypothesis the rostral brain-stem (mesencephalon and caudal diencephalon) is the least vulnerable part of the brain and its involvement in the paralytic coma of head injury is always associated with significant injuries to more peripheral parts of the brain. Observations on traumatic amnesias, coma and lesion distribution after head injury are shown to be consistent with the predicted pattern of relative vulnerability of brain regions in head injury.

ACKNOWLEDGMENTS

This paper is based on an address given to the first meeting of the International Research Committee on the Biokinetics of Impact (IRCOBI) held in Amsterdam, November 1973. The work reported herein has been supported by Contract No. DOT-HS-081-1-106-1A awarded by the Bureau of Highway Safety, Department of Transportation and by the National Institute of Neurological Diseases and Stroke, National Institutes of Health. Gratitude is expressed to Mr. Larry Thibault for invaluable assistance in the engineering and experimental aspects of this research and to Mr. Arthur Hirsch for his unfailing support of our work.

REFERENCES


(Received April 17, 1974)

LEGENDS FOR PLATES

PLATE XXXVI

Fig. 5.—Macroscopic and microscopic views of the occipital lobe of one of the two translated animals in which an asymmetrical intracerebral hemorrhage was produced without any other significant surface hemorrhage or cerebral contusion elsewhere. Note the peculiarly “clean” splitting of the grey-white interface suggesting the sudden production of an intracerebral cavity with subsequent hemorrhage. This type of lesion was not seen in the rotated animals. (Hæmatoxylin-eosin.)

PLATE XXXVII

Fig. 6.—Microscopic view of the petechial hemorrhages seen in all the rotated (and concussed) group of animals. These lesions varied in size but tended to be more prominent at grey-white interfaces and were always diffusely and symmetrically placed. Similar lesions were not found in the translated group except for one doubtful case where two minute clusters of red cells in a frontotemporal location were noted.
To illustrate article by Ayub K. Ommaya and T. A. Gennarelli.
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