Experimental Primary Fatal Head Injury Caused by Linear Acceleration—Biomechanics and Pathogenesis

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Summary

The present experiment was undertaken to clarify the pathogenesis of primary fatal head injury due to impact and further to obtain a severity index denoting the relationship between the magnitude of impact and the severity of head injury in animals with experimental blunt head injuries caused by simplified impact upon the cranium.

The experiment was conducted on Ketalar-anesthesized rhesus monkeys. Impact was imparted to the animals by means of a 12 in. HYGE impact tester. Before and after the impact the animals were subjected to a series of examinations at intervals, including respiration, ECG, blood pressure, cerebral circulation, partial pressure of blood gases, acid-base equilibrium and EEG. Pathological examination, measurements of lactic acid and monoamine contents in various portions of the brain were also made.

An impact upon the head, at an acceleration in the horizontal antero-posterior direction of 1000-1500 G and a duration of 3-4 msec, proved fatal invariably in animals weighing more than 8 kg (body weight x effective acceleration above 30 kg). In dead animals, primary injury consisting of narrowing of lumen and stoppage of blood flow in perforating arteries of the brain-stem and small hemorrhages in the same areas was noted. It was demonstrated that these changes give rise to central dysregulation of the circulatory (including heart) and respiratory systems which in turn acts on cerebral circulation and metabolism.

This fact not only proves the existence of a primary fatal head injury and further clarifies its mechanism of development but also suggests the possibility of grading the severity of head injury by simplified impact and also by expressing the relationship between the magnitude of impact and the severity of brain damage as a severity index.

Key words: head injury, biomechanics, primary death, ischemic damage, serotonin, microangiogram

Introduction

Ever since study efforts by Gurdjian et al. (1943), have been made to investigate the fastness of the living body against head injury by expressing the force of impact in terms of acceleration and action time it has lead to the obtainment of a threshold curve for concussion (Patrick et al., 1963; Ommaya et al., 1973) stated in their recent report that rotational acceleration also comes into play in the occurrence they estimated a threshold for concussion. On the other hand studies have also been made on the physical properties of the scalp, cranium and brain (Melvin 1971, Masuzawa 1972) and an attempt was made to develop a model formulae to estimate the damage sustained by the brain in head injuries (Hayashi 1969).

However, various injury scales for the expression of the degree of damage to the living body caused by impingement (Severity Index proposed by Gadd, Damage Index advocated by Brinn et al.), are still in use, by different investigators even at present and accordingly no established or standardized method of figuring the severity of injury on a quantitative basis is available as yet.

Before such a method of quantification can be made available, it is, therefore, necessary to work out the biomechanics and pathogenesis of fatal brain damage caused by impact (as an ultimate form of head injury). A review of data involving clinical cases of fatal head trauma (Nakamura 1974.) revealed that death from brain damage is brought about by three essen-
ially different mechanisms. To be more specific, 20% of such fatalities are accounted for by immediate death caused by injuries to the brain-stem or extensive damage to the brain, 70% are due to brain-stem disorder resulting from increased intracranial pressure and consequent incarceration of the brain, and the rest are deaths from profuse blood losses due to open brain injury. This is one of the reasons why any system of clinical classification of head trauma cannot be based on a single scale.

In order to obtain a unitary system of scale for the severity of brain injury, it is desirable, therefore, to conduct experiments in which fatal brain damage is induced by a dynamically simplified injuring force without concurrent skull fracture, damage to cervical spine and intracranial bleeding.

Using a 12 in. HYGE impact tester, we succeeded in causing fatal brain injury that satisfies these requirements in experimental animals. In the present study, the mechanism of development and pathophysiology of such brain injuries were investigated in an attempt to unify scales for evaluating brain injury.

**Material and Methods**

An impact of blow was given to the frontal region of 14 rhesus monkeys under anesthesia with intramuscular Ketalar (10 mg/Kg) by means of 12 in HYGE impact tester.

Two accelerometers (ST. AH6, full scale 3000 G) for the measurement of acceleration in line of the longitudinal and antero-posterior axes were set on the parietal and occipital regions of each animal. Burr holes were made in the frontal and occipital regions and in the posterior fossa. A pressure senser (ST. PM6H, full scale 10 Kg/cm²) was placed in the epidural space, then fixed and sealed tightly with cement for dental use. Four screws were implanted in the skull to serve as electrodes for recording EEG in bipolar lead. Electrodes for recording ECG were implanted into the subcutaneous tissue of the precordium and were fixed there. Catheters were inserted into the femoral artery and vein and held in place, through which blood pressure was measured and arterial as well as venous blood samples were drawn.

Before and immediately after impact and at 5-minute intervals during ensuing periods, the animals were measured for partial pressures of blood gases and acid-base balance by the Astrup method. Blood pressure, respiration and pulse were recorded on oscillograph in a continuous manner.

In order to prevent the impactor from directly striking the face of rhesus monkey and also to permit acceleration in the horizontal direction only, a mask deep enough to cover 1/3 of the antero-posterior axis of head was prepared for individual animals. Masks were made by pressing the head of animals into plaster filled in a box made of iron and then by hardening the plaster. Subsequently a hole was made for breathing at the site corresponding to the nose. The mask was fixed to the impact slider; the animal's face was pressed air-tight against the mask for solid fixation, the body was suspended in a hammock, a foaming urethane form was fixed beneath the slider against the anterior aspect of the body to serve as a body protector.

The impact apparatus is as illustrated in Fig. 1. The thrust column thursts a sled forward at a preset acceleration and action time. This causes the impact slider to glide forward on the slider guide. The lead block pierces into the stopping device and an impacting blow is afflicted to the animal's head. After impact on the head the sled stops at a distance of approximately 40 feet, the brake getting into motion immediately. The impact time is determined by the speed of the slider and the stopping device piercing into the lead block.

After impact the animals were subjected to the above-mentioned examinations until they succumbed to death or in the case of survivors for about one hour. Pathological examination, microangiogram, determinations of monoamine and lactic acid contents in various portions of the brain were conducted in all cases and the results between fatal and non-fatal cases were compared.

![Fig. 1. The method of experimental head injury by the use of a 12 in. HYGE impact tester.](image-url)
Results

A blunt head injury was successfully provoked by this maneuver in all 14 animals. Six animals survived the procedure, while the other eight died within 20 minutes of impact on their heads.

1. Magnitude of impact and changes in intracranial pressure

The magnitude of impact was found to be equivalent to an acceleration in the horizontal direction of 1200–1500 G with a duration of action of 3–5 m sec. There was no appreciable difference between dying animals and survivors and a product of body weight \( \times \) effective acceleration that exceeded 30 Kg invariably proved fatal.

Changes in intracranial pressure induced were characterized by a positive pressure of 2–4 Kg/cm\(^2\) at the site of impact of blow in the frontal region and triphasic pressure changes (approximately 1 Kg/cm\(^2\) negative → positive → negative) at the occipital pole. Pressure at the posterior fossa changed to negative and then to positive by a total of 0.5 Kg/cm\(^2\) in surviving animals, while in dying animals it changed to positive, then to negative by 0.8 Kg/cm\(^2\), the change occurring in different phases and over a longer period of time as compared with that observed in survivors (Fig. 2).

2. Changes in ECG and respiration

Impact of blow gave rise to apnea or depression of respiration invariably in all instances. Within several seconds or minutes respiration restored a state of normalcy. ECG showed evidence of apnea or depressed respiration together with inversion of QRS, absence of P, positivity of T wave and bradycardia, these latter changes reflecting a functional deficiency of or abnormalities of reflexes in the vagus and sympathetic nerves due to lesions in the central nervous system. In the group of dying animals within 20 minutes of impact, respiratory standstill was prolonged and ECG changes were marked. ECG tracings from four each of surviving and of dying animals are shown in Fig. 3. As can be seen, even atrial fibrillation and flutter manifested in an extreme case (No. 29). The chest generally was free from any injury due to impact and pathological examination revealed no lesions in lungs and the heart attributable to impact of the blow itself.

In keeping with these alterations in ECG, blood pressure fell and cardiac output also diminished. Whereas animals surviving the impact injury recovered from these changes invariably in 10 to 15 minutes, blood pressure was steadily on the decline and the pulse tended to slow down in dying animals.
3. Blood gas analysis and acid-base balance (Fig. 4)

In the surviving group, a slight degree of acidosis, a transient fall of the partial pressure of oxygen in arterial blood and a rise in the partial pressure of carbon dioxide were observed. These changes being of a 15-min. duration. The arterio-venous difference of the partial pressure of oxygen in cerebral blood was still, however, rather increasing when recovery from the above-mentioned changes was attained.

In contrast, all the dying animals exhibited an abrupt decrease of the partial pressure of O2 and elevation of the partial pressure of CO2 in arterial and venous blood consequently with a hardly appreciable arterio-venous difference of the partial pressure of oxygen. The animals fell into a state of severe acidosis. The blood pH was decreasing rapidly 5 minutes after sustaining impact injury finally to reach a level of 6.85 at 15 minutes, when PaO2 of 10 mmHg and PaCO2 of 120 mmHg were recorded.

4. Status of brain damage

Despite the presence of severe hypoxia and metabolic acidosis, intracranial hemorrhage, cerebral contusion and edema were not observed. Also in spite of a negative one atmospheric pressure at the occipital pole, no bruises and hemorrhages due to cavitation were found there (Fig. 5). Incarceration of the brain in the tentorium or the foramen magnum was not present.

Histological examination of brain tissues revealed marked changes in nerve cells of the brain-stem, notably of the medulla oblongata, pons and mid-brain, where edematous swelling or homogenization of nerve cells, a decrease in or disappearance of Nissl's bodies and changes due to hypoxia were predominant (Fig. 6). Axons in the affected area appeared meandering or looked like a screw. Furthermore, the disappearance of oligodendroglia was prominent. The nerve cells of the cerebral hemisphere were free from this change, appearing almost normal. In non-fatal cases, unlike fatal ones, histological findings of nerve cells were approximating to those of healthy animals, with no appreciable changes in nerve cells in all instances, but with the only exception of a slight eosinophilic change. The hypoxic lesions centered around the lower brain-stem are not considered to have resulted from the post-
impact depression of cardiopulmonary function because it is highly improbable that a lower portion of the brain-stem would be selectively affected with hypoxia.

Comparison was made of cerebral microangiograms obtained from three groups of animals, i.e. animals not receiving an impact, those surviving the impact and those dying of the impact. In the group of animals dying, branches of perforating arteries which supply the hypothalamus and those supplying the median part of the mid-brain, pons and medulla were poorly visualized. In the periphery of these blood vessels, there was angiographic evidence of cessation of blood flow, narrowing of lumen and small hemorrhages. In the group of animals surviving the impact, blood vessels of the brain-stem were almost free of abnormalities, while at the site of the impact in the frontal region and at the opposite pole, luminal narrowing or enlargement of blood vessels were in evidence (Fig. 7). Densitometric measurements of the degree of retention of contrast medium in the periphery of perforating arteries showed that stasis or congestion of blood occurred only in a lower portion of the brain-stem where luminal narrowing of blood vessels and a stoppage of blood flow were observed on microangiogram, a finding indicating the loss of a self-regulating capacity of cerebral circulation and the existence of microhemorrhages.

A study of the lactic acid content in various parts of the brain revealed that the tissue level of this substance was markedly elevated at the tip of the temporal lobe and also in the portion

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**Fig. 5.** Macroscopic change of the brain in the primary death group. There is a demyelinated area (arrows) and small hemorrhagic lesions, but no contusion even in the impacted frontal pole or occipital pole where pressure gradient is prominent.

**Fig. 6.** Histological changes of the brain in the primary death group. The main pathological findings caused by ischemic damage (C, D, E, F, G) are observed at the level of midbrain, pons, and medulla oblongata.

A: There is no change in the cerebellum.
B: Spongy alteration and disappearance of oligodendroglia are observed in the cerebral subcortical white matter.
C: Edematous swelling of the nerve cells in the brain stem.
D: Glia cells are observed around degenerated nerve cell (satellitosis) in the brain stem.
E, F: Screw like degeneration of the axons in the lower brain stem.
G: Chromatolysis and pyknosis of the nerve cells were observed midline structure of the lower brain stem.
of the brain-stem where circulatory disturbance was clearly observable on microangiogram, rather than at the site of impact.

In an effort to ascertain as to whether hypoxia due to this local disturbance of cerebral circulation itself impaired the function of the brain stem and thereby caused central dysregulation with resultant impairment of cardiopulmonary function or some other chemical agent was also involved in this sequence of phenomena, measurements were made of the monoamine contents in various portions of the brain.

5. Changes in the monoamine contents of various cerebral regions (Fig. 8)

In the surviving group, the site of impact, occipital region, hypothalamus, mid-brain, medulla and cerebellum were all found to contain norepinephrine at a concentration level in great degree the same as normal. In the dying group, the norepinephrine level was noted to have elevated by more than 1.0 µg/g at the site of impact and in the mid-brain, medulla and cerebellum. The increment was especially significant for the medulla.

Serotonin content was found to have increased by 0.2—0.3 µg/g in the hypothalamus and mid-brain but was found to have decreased in the medulla of survivors. In animals dying, in contrast, the tissue level of serotonin had elevated in all parts studied except the occipital region. The increment was as great as approximately 1.0 µg/g for an area extending from the hypothalamus to the medulla, a value which was far in excess of the corresponding

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Fig. 7. Comparing of microangiograms at the brain stem of the normal animal (left side) with those of primary death group (right side).

The medial perforating arteries of the brain stem become narrow with irregular vascular wall. The microhaemorrhages of distal parts of those arteries are observed in primary death group. In these ishemic area, brain damage caused by anoxia is histologically observed as shown in Fig. 6.

Fig. 8. The alteration of serotonin (5HT) and norepinephrine (NE) content in the various parts of the brain following impact.

Barr shows normal monoamine content.

White circles denote the monoamine content of survival group.

Black circles denote the monoamine content of primary death group.
value for the site of impact.

From the above-mentioned results of investigation it becomes evidently clear that a fatal brain injury caused by an impact on the head (consisting mainly of a linear acceleration operated in the antero-posterior direction) occurs when the acceleration is greater than 1500 G., the duration of action is longer than 3 m/sec, the subject monkey weighs more than 8 Kg and also that such a fatal brain injury is not secondary to a sequence of changes. That is increased intracranial pressure, incarceration of the brain, and lesions of the brain stem, is a primary one caused by a peculiar mechanism. In such an instance, impact of the blow, with instantaneous stoppage of blood flow through and luminal narrowing of the perforating arteries of the brain-stem, gives rise to hypoxic acidosis and an elevated tissue level of serotonin in areas supplied by these arteries; these changes in their turn, however, aggravate microhemorrhages and circulatory disturbance, resulting in a functional impairment of the median part of the brain stem. This functional disturbance of the brain stem gives rise to a respiratory stand-still and cardiac dysrhythmias which in turn bring about hypoxia and acidosis of the brain. These latter changes will prove fatal unless they are brought back to the road of recovery quickly within 10 to 15 minutes.

Discussion

The present experiment was conducted in an attempt to elucidate the mechanism whereby impact on the head causes injuries to the brain and also to establish a system of evaluating the severity of brain injury on a single scale. Since the biomechanics of impact injury to the brain is quite intricate, linear acceleration coupled with changes in intracranial pressure, and shear strain also come into play. Since the pathogenic mechanisms of brain injury still remains obscure, it seems necessary that experimental studies on this subject be carried with an impact by a simple acceleration to affect the impacted skull and the brain. The mask-on-face method utilizing a 12 in HYGE impact tester, following the results of the present experiment, was found to have the advantage of permitting a relatively simple acceleration in the antero-posterior direction only to operate upon the skull and, moreover, of yielding as high an acceleration as 1200-1500 G. When viewed in terms of brain damage, the experimental procedure did not produce any changes that may lead to the occurrence of incarceration of the brain, e.g. skull fracture and intracranial bleeding. The only lesions observed being impaired microcirculation and microhemorrhage of a lower portion of the brain-stem due to primary brain injury per se. In addition, the severity of lesions of the lower brain-stem was shown to vary in accordance with the severity of head trauma. All these findings may be said to indicate the possibility of obtaining an injury severity index denoting the correlationhip between the magnitude of impact and the severity of brain injury.

The results of the present experiment also suggest that death of the injured monkeys occurred as a result of the following sequence of changes: ischemia of the brain stem to central dysregulation, to cardiac dysrhythmia and respiratory disturbance, to circulatory disturbance of the brain and to aggravation of primary brain stem injury. Here arises the question of whether actual autopsy cases of fatal brain injury have provided any clinical evidence agreeing with this.

The lesion of the brain stem between the inferior margin of the thalamus and the first segment of cervical spinal cord are known results of head injury in man and experimental animals. It is thought that in both man and animals, such lesions are the basis of coma and lesions of the rostral brain stem are more significant in producing coma, whereas those lower down impair respiration and circulation, though coma in animals results from relatively lower or more caudal lesion than in man.

These facts support the concept that primary fatal brain stem injury may occur by impact on the head and, in fact, by the mechanism as demonstrated by the results of the present experiment. As to whether the lesion under investigation is localized or not, was recognized in an experiment that 18% of fatal cases of blunt head injury were due to primary impact injury of the brain-stem. Since, however, other cerebral tissues were also found affected, it seems more logical to regard the lesion of the brain stem as representing one of generalized changes but not resulting from direct shearing
According to this theory, involvement of vascular factor cannot be denied. Crompton surmises that the lesion of the brain stem probably results from shearing strains at the cranio-cervical junction due to fixation by the edge of the tentorium and there will be shearing of small blood vessels to produce these characteristic unilateral tegmental infarcts and hemorrhage.

The present experiment showed no evidence of tissue damage caused by shearing strain. However, it became obvious from a study of changes in intracranial pressure that death occurred more frequently in that group of animals in which the negative-positive pressure curve of infratentorial pressure and that of pressure at the occipital fossa were reversed in phase. From these facts it is unquestioned that a force operated on these areas of the brain. The finding that lesions were more common in the median part of the brain stem perfused by perforating arteries suggests that circulatory and vascular factors play a significant role.

The demonstration of the brain stem as the site of primary impact injury has rendered it possible to unify scales for the study of relationship between the force of impact on the head and brain injury. The present study also demonstrated adequacy for this purpose of examining the anatomical and functional status of the cardiopulmonary system as an expression of central dysregulation caused by primary injury.

The new concept of primary lower brain stem damage as an essential pathogenetic factor for fatal brain injury in head trauma has thus been made clear. Using this damage as index, the study has paved the way to obtainment of an injury severity index, based on a single scale, denoting the relationship between the magnitude of impact and the severity of brain injury.

**Conclusion**

In an attempt to investigate the relationship between the severity of brain injury due to impact on the head and the magnitude of impact and thereby to establish an injury severity index based on a single scale, the experiment was conducted using a dynamically simplified impact so as to eliminate factors that may give rise to secondary fatal lesions such as open brain injury, intracranial hemorrhage and cerebral edema.

In this experiment, a 12 in. HYGE impact tester was employed, by means of which an impact of 1200–1500 G, 3–4 m/sec in duration, was given to the face of rhesus monkeys through a mask in the horizontal, antero-posterior direction. When a product of body weight × effective acceleration exceeded 30 Kg, the impact caused primary injury in the brain-stem, which consisted of luminal narrowing of blood vessels, stoppage of blood flow and small hemorrhages, leading to death of the animals.

The mechanism whereby the impact causes death was demonstrated to involve the following sequence of pathological changes: primary injury, to central dysregulation to respiratory and circulatory disturbance and to circulatory disturbance of the brain.

These findings strongly indicate the possibility of establishing an injury severity index, based on a single scale, denoting the relationship between the magnitude of impact and the severity of brain injury.

**References**

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