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4. Supported by National Institutes of Mental Health grant MH-08579-02. We thank Dr. Arnold Leiman for assistance in the initial training of the animal from which these data were obtained; Hansook Ahn and Robert Nagel for assistance with data processing; and the staff of the NYU Computing Center, University Heights, for their cooperation.

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Cerebral Concussion in the Monkey: An Experimental Model

Abstract. *A statistically significant experimental model has been developed for reproducing head injury by impact in the monkey. Results with 80 monkeys subjected to occipital impact under specified conditions (duration of phenomena, 1 to 10 milliseconds) enable the construction of curves relating the production of experimental cerebral concussion in 10, 50, and 90 percent of the monkeys to the average impulse of the blow in pounds·seconds, as well as to the average linear acceleration of the head. These curves are proposed as a baseline from which blows to various parts of the head, as well as nonimpacting impulsive loads, can be studied under various conditions of protection and according to various time regimes.*

Despite many attempts to describe the mechanical and physiological responses of the central nervous system to head impact (*1–4*), little is known about the relation of impact to response; still less about the response itself. The impact-response relation is fundamental to design of rational head protection—only one of the practical needs for such knowledge. However, there is a more basic aspect to the understanding of brain response to impact. The sudden abolition of consciousness after a blow on the head—cerebral concussion—includes, as may be expected, a multitude of events occurring simultaneously or in sequence. There is reason to suspect that study of some of these events—their functional disorganization and reorganization during and after impact—could lead to better understanding of the functions of the nervous system.

We now report a technique whereby the injurious aspect of head impact can be quantitatively determined and related to the occurrence of concussion. We used 80-odd rhesus monkeys (*Macaca mulatta*) in these experiments. The value of using primates in such work has been discussed (*5, 6*); it is argued that the anatomical similarities between monkey and man are more likely to permit valid extrapolation of data than information obtained from quadrupeds.

Adult rhesus monkeys, anesthetized with Nembutal and seated in a specially designed chair, received blows to the occipital region of the head. The blows were delivered by a piston actuated by compressed air; it weighed 3.8 lb (1.4 kg) and had a 1 in.^{2} (6.45-cm^2) hard-rubber cap at the impacting end. By control of the air pressure behind the piston, impacts could be varied from a gentle tap to a fatal, crushing blow. The posture of the monkey was such that the head could move freely forward after impact, although the body was restrained by waist, lap, arm, and leg belts.

The impact and response of the head were measured directly. The applied force as a function of time was sensed by a bonded strain-wire dynamometer fitted in series between piston and impacting rubber tip; piston velocity was recorded as the voltage generated as a magnet, encased in the piston body, passed through a surrounding coil.

Responses of the head were measured by means of photography and accelerometers. Displacement of the head with time was determined from high-speed motion pictures taken at 4000 frames per second, in which a selected point on the skin, at an estimated projection of the center of gravity of the monkey's head, was compared with a stationary background grid. Linear acceleration–time history of the head was sensed by piezoelectric crystal accelerometers weighing 1 g and fixed rigidly to the skull.

Changes in intracranial fluid pressures with time were sensed at various sites by low-impedance semiconductor strain-gage pressure transducers; they were placed in holes bored in the skull and attached so that the 5 mm-diameter sensitive surface was flush with the inner wall of the cranial vault; they were secured to the bone with self-tapping screws, and a layer of dental cement assured water-tight closure of the skull. The outputs of the various

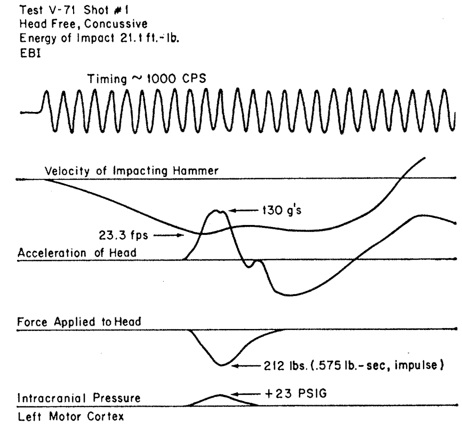

Fig. 1. Oscillographic record of physical measurements during impact; traces for velocity, acceleration, force, and intracranial pressure with a 1000-cy/sec time trace are displayed.

gages and transducers were fed into amplifiers and recorded by a tape recorder that could be played back into a direct-writing string oscillograph. Timing impulses were provided by a tuning-fork oscillator (1000 cy/sec).

The level of anesthesia in each monkey was carefully controlled so that aversive response to noxious stimuli, especially ear pinch, was consistently present; abolition by impact of such response was the criterion of concussion, and the duration of abolition was the duration of cerebral concussion. This criterion proved significantly more reliable than suspension of the corneal and palpebral reflexes or changes in other physiological indices such as the electroencephalogram, electrocardiogram, arterial blood pressure, respiration, and cerebrospinal fluid pressure, which were also recorded before, during, and after impact.

Impact force and velocity of the piston, the displacement-time history of the head relative to a fixed grid, the linear acceleration of the head, and intracranial pressures were measured during most of the tests on the 80 monkeys. Data from experiments in which skull fracture was produced and from tests in which multiple blows were given are not included in this study. A typical record (Fig. 1) shows that the applied force–time curve is roughly triangular; total duration is about 6 msec and it reaches a peak in about 2 msec. As would be expected, the acceleration and intracranial-pressure pulses follow about the same pattern. In all records, the duration of the force was between 1 and 10 msec, averaging 4 msec.

The data describing input and re-

Table 1. Striking impulse and resultant head acceleration at which concussion occurred [1 lb (0.45 kg)].

Monkeys concussed (%)	Acceleration (g)	Impulse (lb/sec)
10	10–14	0.045– .075
50	100–103	.415– .437
90	865–869	2.994–3.026

sponse phenomena were correlated with the occurrence or nonoccurrence of concussion by use of Spearman's rank-correlation method, a nonparametric type of statistical-analysis tool. The results indicated that the experimental values for magnitude of impact force, tangential velocity of the head, and changes in intracranial pressure could not be significantly correlated with the production of concussion by an occipital blow to the freely moveable head of the monkey under such conditions. On the other hand, the peak velocity of the impacting piston and its kinetic energy correlated ($P \leq .001$), while the total impulse of the blow and the peak value of the linear acceleration of the head correlated significantly ($P \leq .01$). We should emphasize that these correlations hold true for impact phenomena that occur within the duration limits of 1 and 10 msec; impacts and head loading for other time regimes have not been explored.

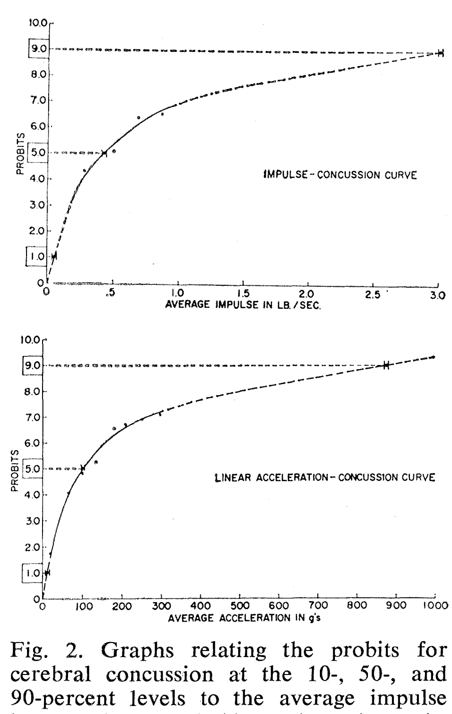

Fig. 2. Graphs relating the probits for cerebral concussion at the 10-, 50-, and 90-percent levels to the average impulse in pounds second (lb. sec) and to the average acceleration in multiples of gravity (g). Note the wide range of values between the 10- and 90-percent levels. The two short vertical lines beside the heavy dot at each of the three levels indicate one standard deviation about a mean.

Of all the statistically significant physical indices of concussion, the magnitude of impulse was the most satisfactory; it could be easily measured with a single force transducer and derived independently of consideration of mass and of other dimensions of either the object struck or the striking object. Among the head-response indices, only the linear acceleration showed significant correlation with concussion.

In order to determine the relation between the striking impulse, responsive head acceleration, and probability of occurrence of concussion, a probit transformation was conducted. This method, commonly used in toxicology to calculate the LD_{50} of drugs, enabled the construction of two graphs relating impulse and acceleration, respectively, to concussion occurring in 10, 50, and 90 percent of monkeys under our conditions (Fig. 2). Our current experiments are being conducted at the 50-percent level in order to obtain maximum information and confirmation of this model.

That the range of impulse applied, as related to concussive probability (Fig. 2), is wide suggests that, whatever the mechanics of concussion may be, the physiological response is not an all-or-none type of phenomenon strictly localized in one area of the brain. This range in values for striking impulse and resulting head acceleration at which concussion occurred (occipital blows, head freely moveable, animal seated) appears in Table 1. The values in Table 1 indicate a range of one standard deviation about a mean value and are rounded off to the nearest unit for acceleration. Again we stress that these values are true only when the duration of the impact phenomena is between 1 and 10 msec.

The graphs in Fig. 2 are used as "dosage curves" would be; they enable us to employ in several ways, with some degree of confidence, an experimental analogue of cerebral concussion in the monkey. For example, we are systematically studying two major fields: (i) the effects of blows to different parts of the head and of blows to each region under different conditions of fixation and protection of head and neck; initial results indicate that reduction of movement between the head and neck (but *not* head fixation) significantly protects against concussion and raises the tolerance of the animal to head impact; (ii) general physiological, electrophysiological, biochemical, and morphological (including ultrastructural) effects to determine functional and pathological changes during and after concussion.

This experimental model may be of use to other workers wishing to study this problem, but hitherto inhibited by lack of a reproducible system for testing hypotheses (*1*). Perhaps the greatest remaining difficulty with such a model is evaluation of the state of consciousness of animals subjected to trauma under anesthesia. Reproducible control of degrees of anesthesia is not possible; thus, determination of the relative significances of anesthesia and concussion in a reduced state of consciousness is very difficult. We would welcome suggestions regarding this aspect.

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Myeloma Cells and Immunoglobulin Formation

The report of Fahey *et al.* (*1*) that human lymphoid cells derived from "Burkitt's tumors" synthesize immunoglobulins in vitro is important for many reasons. The culture of these cells in various media and in large quantities will permit critical studies of the synthesis of these proteins. Further, it may be possible to provoke production of specific antibodies.

The relationship of the anatomy and physiology of these cells to immuno-