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NEUROPATHOLOGY OF RHESUS MONKEYS SUBJECTED TO -GX IMPACT ACCELE--ETC(U)
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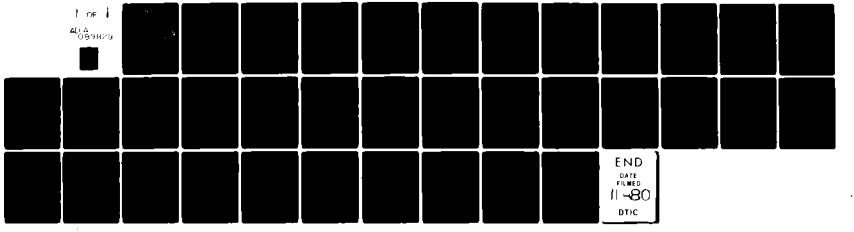

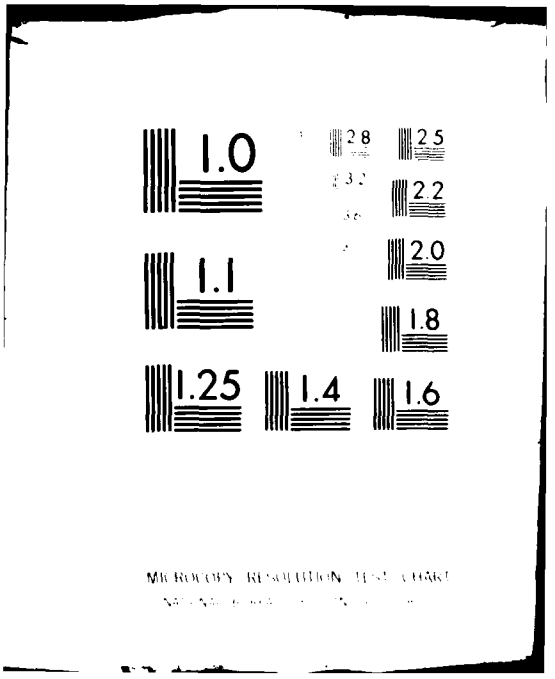
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OFFICE OF NAVAL RESEARCH

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(6) Neuropathology of Rhesus Monkeys Subjected to - G x Impact Acceleration,

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by

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BACKGROUND

In a continuing medical research program designed to define the means for objective evaluation of crash protective and escape systems, there are three major projects:

a. Measurement of the living human kinematic response envelope to impact accelerations in up to 27 different vector directions; up to the limit of voluntary tolerance for peak acceleration, rate of onset of acceleration, and duration at peak acceleration; and with three different sizes of human volunteer subject covering the range of 3rd through 98th percentile of sitting height relative to the U.S. Navy anthropomorphic survey of 1965.

b. Derivation of performance specifications for human analogues from these data and the development of those analogues, including mathematical models and a family of dummies.

c. Definition of that portion of the human kinematic response envelope which is injurious, using primate models, so that a human injury model can be developed.

The research reported here is a portion of project C. As part of this project, primates are fitted with both inertial and physiological instrumentation; to measure the kinematic response and the physiological response to the kinematic response, respectively. The determination of the neuropathological cause of the neurophysiological response completes the evidentiary chain from inertial input to tissue injury.

PREVIOUS WORK

The pathomorphological findings of a large series of animals which were subjected to acceleration levels in the +Gz and the +Gx

vectors by direct impact to the head with intensities which extended from subconcussive to lethal intensities were described previously (1, 2, 3).

Unterharnscheidt and Higgins carried out carefully controlled studies of non-deforming head angular acceleration using squirrel monkeys undergoing flexion of the head and neck through 45° (4, 5, 6).

Acceleration of the head may be translational (linear) or angular in nature. Translational acceleration is produced in a body if the resultant of the applied forces passes through the center of gravity of the body. If the applied force system does not go through the center of gravity, rotational acceleration is produced. For the head, attached as it is to the neck, any prolonged translational acceleration would lead eventually also to angular acceleration.

In addition to these accelerations, which may be thought of as steady-state whole-body effects, the blow also produces waves of compression which propagate through the skull and eventually develop a highly transient but very complicated stress pattern. This process is further complicated by differences in the propagation characteristics of the skull and the brain. If any local stresses exceed the level of tolerance of the tissue presumably lesions will be produced or some form of tissue damage will occur.

Translational acceleration was administered from above (impact direction V according to SPATZ 1950) using the concussion gun described by FOLTZ et al. (7). A single impact of subcommotio strength, at a speed of 7.1 m/sec resulting in a peak of 250 G,

imparted to the freely movable head of a cat, caused neither behavioral nor histologic changes in the CNS; whereas repeated impacts of the same intensity, without causing primary traumatic lesions, did produce secondary traumatic alterations due to circulatory disturbances. Lesions in the cerebellum included scattered loss of Purkinje cells (especially at the summits of the lobuli of the vermis), proliferation of Bergmann's glia, thinning of the granular cell layer with glial reaction, and glial proliferation in the striae medullares and white substance. Alterations in the cerebrum were less severe; they consisted of disseminated ischemic nerve cells and a moderate glial proliferation in the white substance.

Impacts of concussive (commotio) strength, i.e., producing the clinical symptoms of cerebral concussion in cats, (i.e. unresponsiveness), have a velocity of 8.3-9.4 M/sec, resulting in peak accelerations of 280-400 G. After one such impact, the histologic alterations prove to be traceless with the methods of investigation presently available. We found, in particular, no evidence for glial cell proliferation. However, after repeated impacts of equal intensity and intervals of one to two days, the cerebral cortex showed, in addition to scattered ischemic nerve cells, extensive focal and pseudolaminary necroses of the parenchyma and loss of nerve cells in various parts of the Ammon's horn formation. Tissue alterations in the cerebellum, although less intense, corresponded in quality to those caused by successive impacts of subcommotio strength.

It follows that blunt impacts of intensities that do not cause noticeable tissue alterations when applied singly, may elicit

secondary alterations due to circulatory disturbances when applied successively in repeated experiments. A sustained permanent brain injury can, therefore, result from secondary lesions alone, with no primary traumatic alterations present at all. The time interval between impacts has a distinctive influence on the nature of the morphologic alterations.

Considerable primary traumatic lesions are produced by impacts with a velocity of 10.5 m/sec or more, which produce peak accelerations of 400 G or more. In all instances there were subarachnoid and subdural hemorrhages, so-called cortical contusions at the pole and the counterpole, single intracerebral hemorrhages, and traumatic necroses. Speeds of the impacting instruments of 17.2 and 18.3 m/sec are fatal to a cat. Accelerations produced by these impacts were not measured because fractures occurred (1, 2, 3, 8, 9). See Table in reference (10).

Rotational Acceleration. Unterharnscheidt and Higgins carried out carefully controlled studies using 24 squirrel monkeys (saimiri sciureus) undergoing flexion of the head and neck through 45° (4, 5, 6). The equipment used in these studies was designed by Higgins and Schmall (11). The monkeys were subjected to rotational accelerations ranging from 101,000 to 386,000 rad/sec^2. The result was a continuum of clinical effects from no observable signs through concussion to death. See Table reference (5).

The lowest rotational accelerations employed (101,000 - 150,000 rad/sec^2) caused apparently no primary or secondary alterations in the cerebrum. However, the next higher accelerations, up to 197,000 rad/sec^2, produced in 10 of 13 animals subarachnoid hemorrhages,

combined in one instance with primary traumatic hemorrhages in the oculomotor nerve, and tears and avulsions (mainly of veins and capillaries) in superficial cortical layers in 8 animals. Accelerations of more than 200,000 rad/sec^2 caused severe primary traumatic hemorrhages in the cortex and white substance. Rotational accelerations of more than 300,000 rad/sec^2 were not survived. The monkeys subjected to these extremely high accelerations were the only animals to show additional hemorrhages in more central regions of the brain, i.e., very close to the central pivot.

Nearly all the animals tested showed small rhectic hemorrhages in various segments of the spinal cord. Capillary and venous hemorrhages were more frequently found disseminated in the gray substance and were caused by longitudinal and transverse stretching of ascending and descending vessel branches. They were seen in all segments of the cord. These lesions were not fatal and produced no clinical signs in the animals. In two instances, a subdural hemorrhage was found in the cauda equina.

It must be pointed out that the primary traumatic lesions found in the cortex were venorhectic, and occasionally arterio- or capillary rhectic, hemorrhages of the more superficial cortical layers, as evidenced by torn vessel walls. Also, these hemorrhages were always associated with vessel systems running at right angles to the cortical surface. See Table in reference (10).

In summary, not only does a qualitative difference exist between the primary traumatic cortical hemorrhages produced by rotational acceleration and the so-called cortical contusions found

in translational injuries, but there are also different patterns of distribution for the primary traumatic lesions encountered in both types of acceleration, inasmuch as these lesions are arranged in a cylindrically symmetric pattern after translational acceleration, as compared to a radially symmetric pattern located close to the midline after rotational acceleration.

Except for the question of location, these considerations seem to be valid also for the interpretation of findings in the spinal cord, although correlations are not as patently manifest here as they are in the brain. Nevertheless, the relation between severity of primary traumatic lesions and magnitude of acceleration is evident throughout the entire CNS.

The present study reports on a carefully controlled series of experiments with whole body -Gx impact acceleration exposures of Rhesus monkeys with completely restrained torso but unrestrained head and neck. That is, the animal is accelerated backwards with the unrestrained head and neck undergoing flexion. Thus, impact acceleration is transmitted from the sled to the torso, and then indirectly via the vertebral column to the head.

EXPERIMENTAL EQUIPMENT

A 225,000 Pound Thrust Horizontal Accelerator with sled, control console and enclosed environmentally controlled 700-foot track at NBDL in New Orleans was used. This can impart 200 G to the lightweight primate sled.

The inertial Data Acquisition System samples 24 channels of inertial data at 2000 samples/sec/channel, digitizes it, and stores the digitized data in magnetic discs in real time.

The Physiological Data Acquisition System is designed to acquire EEG, ECG, somatosensory evoked potential and respiration, for 16 channels via FM/FM telemetry with a maximum band width of DC - 100 Hz.

The Photographic Data Acquisition System includes sled and laboratory mounted cameras, lights and control console, as well as phototarget design which is necessary for obtaining precise 3-dimensional photographic data of primate kinematic response, especially displacement. A complete description is published elsewhere (12).

The Transducer Monitoring System was developed for primates which permits precise determination of acceleration, velocity and displacement at the mounting site. Transformation of the data to coordinate systems fixed in the anatomy is accomplished using the results of x-ray anthropometry which measures the precise three dimensional spatial position of the instrumentation coordinate system relative to the head/anatomical coordinate system. A complete description is published elsewhere (13). The head acceleration was measured by a rigidly mounted array of six linear accelerometers locked to an implanted pedestal bolted to the calvarium capable of measuring angular and linear acceleration and velocity in three dimensions. A complete description is published elsewhere (14, 15, 16).

Sled acceleration was also measured.

Two different types of restraint systems were used, namely a rigid moulded one and a harness vest. There seems to be no difference in the lesions produced, since the head and neck kinematic response is not markedly altered.

EXPERIMENTAL PROCEDURES

Eleven Rhesus monkeys were subjected to sled accelerations ranging from 10.3 to 158.2G in the -X vector. Animals No. 3912, 4099, 3146 and 3935 were run repeatedly until acutely fatal injury occurred. Subsequently, the other animals were run only once in order to avoid possible cumulative effects of multiple runs. The results of the injurious run or the solitary run for the animals run once are listed in table 1.

The 5 surviving animals were sacrificed after different survival times. One of these animals was so severely injured (the sled acceleration was 122.9G) that it had to be sacrificed in a moribund state 90 hours after the run. It was determined that this was a threshold case of medullo-cervical injury without subluxation.

Before, during and after the acceleration, epidural EEG, somatosensory evoked potential, and ECG were recorded. Non-fatal runs were followed periodically with these neurophysiological recordings. These data will be reported separately.

Pre and post run x-rays of the entire spine were performed.

Maintenance and utilization of the primates was under the direct control of a specialist in laboratory animal medicine, who will report the clinical findings separately.

AUTOPSY PROCEDURES

The autopsy report must determine not only the cause of death, but also a concise description of the distribution and quality of the tissue alterations in brain and spinal cord which can be considered the morphological end states of the applied

mechanical inputs. This requires comprehensive and detailed neuropathological procedures which are not ordinarily undertaken.

Techniques for removal of brain and spinal cord in necropsies vary to some degree. Therefore, in order to describe, evaluate, quantify and compare the morphological end states, a standardization of the techniques used is a necessity.

This should include, but not be limited to, a detailed gross and microscopic examination of all injured organs, exclusive of the central nervous system, which will be handled separately as described below. It should also include a description of the status of both common and internal carotid arteries and both vertebral arteries. In case of an evident injury to these vessels, the entire specimen should be taken out and examined.

In these experiments, the area between lower medulla and upper cervical spinal cord, that is, the atlanto-occipital junction, is the zone of the most extensive stress. The brain and spinal cord down to the cauda equina must be removed in toto, leaving the unopened spinal dura mater on the specimen, using a posterior incision and laminectomy. This is quite important because the level of the cranio-cervical junction is destroyed by using ordinary autopsy procedures.

The following standardized autopsy method is used: The skin and galea of the skull are removed with the underlying muscles and the skull opened in a horizontal plane. The pedestal is removed with a rongeur.

The number and location of the epidural electrodes used for recording the EEG and the macroscopical location of intracerebral

electrodes are described.

At this point, the removal of the brain is interrupted and preparation begun for removal of the entire spinal cord from the dorsal aspect.

A deep incision is made along the spinous processi and the paravertebral muscles are removed. The entire bony spine is exposed laterally to the lateral processi. Using a rongeur, the spinous processi, the dorsal half of the spinal arcs and the lateral processi of the sacral, lumbar, thoraxic and cervical segments are removed. Only segments C_1 and C_2 as a whole are left untouched to be removed later from the entire cervical spine for examination of the ligaments, bones, discs, and vessels.

The dorsal and ventral roots of each segment are now carefully cut and the spinal cord with the cauda equina removed in toto. The preparation and removal begins at the cauda equina and proceeds to the cervical area. The last region of C_1 and C_2 are established by careful dissection of the posterior and ventral roots in the intact spinal canal. The procedure is sensitive, since the C_1 - C_2 block must be left intact for further study of expected traumatic lesions of the bony and ligamentous structures in the upper third of the cervical area.

After dissecting the uppermost dorsal and ventral spinal roots, the spinal cord with surrounding spinal dura mater is pulled from the spinal canal. It now becomes evident whether or not the upper cervical spinal cord suffered a complete traumatic separation from the lower medulla oblongata.

The brain and spinal cord are fixed in a 10% solution of

formalin for 10 days; the formalin being changed on the second day.

After complete fixation, the exposure and removal of the brain are continued. The base of the skull is gradually removed with a rongeur until the entire brain is exposed. After the cranial nerves have been dissected, the entire brain with the surrounding dura mater is removed.

The remaining parts of the base of the skull and anterior and lateral parts of the neck are then removed in toto. Both cranial ends of the internal carotid arteries are identified and then the area from proximal to distal exposed, downward to the carotid bifurcation.

Brain and spinal cord are photographed in color as well as black and white at the end of the procedure.

HISTOLOGICAL TECHNIQUES

A Spielmayer assortment of tissue blocks for histologic examination is prepared. The following areas of brain and spinal cord are cut from each monkey for embedding in paraplast and celloidin: the frontal, parietal, and occipital lobes, the temporal lobe with hippocampus formation; the entire hemisphere with basal ganglia, the mid-brain, pons, medulla oblongata, pituitary, the vermis cerebelli and cerebellar hemispheres, and each segment of the cervical, the thoracic, lumbar, and sacral spinal cord (using horizontal sections) and cauda equina. Longitudinal sections of the entire lower medulla and cervical region are cut from a number of animals which show no traumatic transection between lower medulla and upper cervical spinal cord.

The following staining techniques are used:

Hematoxylin - Eosin, Klüver-Barrera, Masson, Masson-Lillie, Palmgren, and Oil-red.

The entire cervical spine is thoroughly examined, especially the alterations in the bony structure, muscles, ligaments, and discs, which are described in detail.

In this report, only preliminary histopathological finding can be described. Evaluated were only those histological specimens which were embedded in paraplast. The specimen embedded in celloidin were not available for this evaluation due to the longer embedding periods. Therefore, only preliminary conclusions relating to neurohistopathology can be drawn in this report.

RESULTS

Morphological Findings

#3948 *Macroscopic Findings:*

Brain and spinal cord are unremarkable. There is no traumatic transection.

Microscopical Findings:

Unspecific granulomatous tissue alterations occur in areas C4/C5 (anterolateral spinal tracts and base of lower medulla). The CNS is otherwise unremarkable.

In conclusion, this animal was involved in only one run. The peak sled acceleration attained was 83.6 G. The animal was sacrificed on the ninth day. Radiological findings are normal. Brain and spinal column are unremarkable, especially as there is no traumatic transection.

#3943 Macroscopic Findings:

Brain and spinal cord are unremarkable. There is no

traumatic transection.

Microscopical Findings:

The dura reveals granulomatous tissue. The CNS is otherwise unremarkable.

In conclusion, this animal was involved in only one run, with a peak sled acceleration of 83.8 G. The animal was sacrificed on the fifteenth day. Radiological findings are normal. The brain and spinal cord show no traumatic lesions, especially no traumatic transection.

#3933 Macroscopical Findings:

Brain and spinal cord are unremarkable. There is no traumatic transection.

Microscopic Findings:

The CNS is otherwise unremarkable.

In conclusion, this animal was involved in only one run, with a peak sled acceleration of 108.5 G. The animal was sacrificed on the 20th day. Radiological findings are normal. The brain and spinal column show no traumatic lesions, especially no traumatic transection.

#3921 Macroscopic Findings:

There is a complete traumatic transection between the lower medulla and upper cervical spinal cord. The torn-off surfaces are uneven and corrugated and brownish discoloration is noted in central areas. The cerebral hemispheres reveal small patchy subarachnoid hemorrhages, primarily near the midline. One of the draining cerebral veins, probably belonging to the left anterior group of the

bridging veins, is enlarged and congested. Otherwise, both cerebral hemispheres are unremarkable.

The inspection of the base of the brain reveals a massive space occupying subdural hematoma covering lateral and ventral parts of the mid-brain and lateral and dorsal parts of the middle region of the medulla oblongata. The basilar artery can be identified. Both vertebral arteries are missing, torn off during the traumatic separation between lower medulla and upper cervical spinal cord. The cisterna cerebello-medullaris is filled with clotted blood.

The cranial nerves at the base of the brain are surrounded and walled in by the hemorrhage. The subarachnoid and subdural hemorrhage extends laterally to the inferior surfaces of both cerebellar hemispheres.

The spinal cord measures 39 cm. There is a massive subdural hemorrhage covering both ventral and dorsal aspects of the entire cervical spinal cord and the thoracic spinal cord, extending into lateral parts of the lumbar and sacral regions. This hemorrhage can also be identified in some area of the cauda equina.

Microscopical Findings:

There is a complete traumatic transection and recent subdural spinal hemorrhages are found. The thoracic spinal cord reveals small circumscribed petechial hemorrhage in base of anterior horn. Primary traumatic hemorrhages can be seen in the lower medulla.

Fresh hemorrhage in aqueduct. Fresh subdural hemorrhages

at base of brainstem.

In conclusion, this animal was involved in nine runs over a period of 206 days. Seven of the runs were performed in the first eight days, the remaining two on the 206th day. The peak sled accelerations were 10.3 G, 38.3 G, 38.5 G, 38.2 G, 39.4 G, 39.6 G, 36.9 G, and (in the last and acutely fatal run) 108.6 G. In the second run, the G-level could not be recorded due to an instrumentational failure. The highest sled acceleration of the multiple runs was 39.6 G.

The last run of 108.6 G was acutely fatal. The radiological examination reveals atlanto-occipital subluxation. There is a complete traumatic transection between the lower medulla and the upper cervical spinal cord. Both vertebral arteries are ruptured and torn from the specimen. Due to the ruptured vertebral arteries, a massive subarachnoid and subdural hemorrhage can be seen at the base of the brain. There is also a subdural hemorrhage covering the spinal cord, extending into the cauda equina.

Microscopically, multiple fresh hemorrhages can be seen in the direct neighborhood of the traumatically transected area of the lower medulla and the upper cervical spinal cord. The primary traumatic lesions not related to the direct area of transection are minute, and are found only at the base of the brain stem and in the thoracic spinal cord.

#3924 Macroscopical Findings:

Brain and spinal cord are unremarkable. There is no traumatic transection.

Microscopical Findings:

Occipital lobes: Cyst due to taenia. The CNS is otherwise unremarkable.

In conclusion, this animal was involved in a single run with a peak sled acceleration of 110.4 G. The animal was sacrificed on the 21st day. The radiological examination reveals normal findings, and there are no traumatic pathomorphological findings visible.

#3935 Macroscopical Findings:

There is no traumatic transection. There are no remarkable findings on either cerebral hemisphere. The cerebral arteries at the base of the brain are intact, but enlarged and congested. Ventral and lateral aspects of the medulla oblongata indicate moderate subarachnoid hemorrhage, more pronounced on the right than on the left side. The nervous tissue in the lower medulla and C_1 is compressed in an antero-posteriorly direction. The firmness of the tissue seems to be decreased. There are no subdural or subarachnoid hemorrhages noted in other parts of the spinal cord.

Microscopical Findings:

Lower medulla and C_1 bilateral central traumatic hemorrhagic necroses extending into the base of both anterior horns and adjacent lateral spinal tracts.

From C_1 extending to C_4, small recent rhectic hemorrhages mainly in gray substance. In C_1 loss of neurons in base of anterior horn with beginning glial proliferation.

Thoracic area: single small rhectic hemorrhages, single neuronophagy.

Th_1 -Th 4: minute rhectic hemorrhages in gray substance.

Lower medulla: Central hemorrhagic necrosis.

In conclusion, this animal was involved in two runs carried out on the same day. The peak sled acceleration of the first run was 105.5 G, that of the second 122.9 G. Immediately after the second run, the animal showed severe clinical symptoms; it was not able to sit or stand. The animal became moribund and had to be sacrificed after 90 hours. The radiological findings are normal. There is no traumatic transection, but the firmness of the tissue between the lower medulla and the upper cervical spinal column seems to have decreased. The macroscopic and microscopic examinations reveal bilateral central traumatic hemorrhagic necroses. The primary and secondary traumatic lesions extend proximally into the medulla oblongata and distally into the fourth segment of the thoracic spinal cord. Due to the survival time of 90 hours, a loss of neurons in the area of C_1 can be detected, along with the beginnings of glial proliferation, consisting of astro- and microglial elements.

#4101 Macroscopical Findings:

Incomplete traumatic transection. Over the right frontal lobe extending into the precentral cortex, a circumscribed subdural hemorrhage can be seen.

Scattered subdural hemorrhages in the cervical and upper half of the thoracic region. There are small patchy subdural hemorrhages in the cauda equina. The tissue at the junction between lower medulla and upper cervical spinal cord is flattened in the antero-posterior diameter. The consistency of the nervous tissue in this area is decreased.

Microscopical Findings:

In area between lower medulla oblongata and C_1, there is a flattening of tissue in antero-posterior direction. The cervical spinal cord from C_1 to C_7 is unremarkable.

Th_1 shows a mesodermal-glial scar formation lateral of a posterior horn extending into the anterior column. There is a diffuse reaction of microglial and astroglial elements in adjacent gray substance. Loss of some neurons with glial restitution can be seen. Th_5 granlomatous tissue in one posterior horn.

Lower medulla: small recent rhectic hemorrhages. Cerebral cortex: leptomeningeal infilatrates.

In conclusion, this animal was subjected to nine runs, covering a period of 26 days. The peak sled accelerations were 34.8 G, 33.3 G, 32.5 G, 32.5 G, 74.8 G, 74.7 G, 75.6 G, 75.3 G, and (in the last and acutely fatal run) 126.3 G. The last three runs were conducted on the last day. Radiologically, an atlanto-occipital subluxation can be detected. There is an incomplete traumatic transection. Additional traumatic alterations consist of a circumscribed subdural hemorrhage over the right frontal lobe and scattered subdural hemorrhages in the cervical, upper parts of the thoracic region, and in the cauda equina. As a result of the mechanical force, the area between the lower medulla and upper cervical spinal cord is flattened, and single primary traumatic hemorrhages can be seen in the area.

#4099 Macroscopical Findings:

Complete traumatic transection between lower medulla and

upper cervical spinal cord. Both vertebral arteries are ruptured at the level of the foramen occipitale magnum, but their proximal parts remain with the specimen. There is a massive subdural hemorrhage covering both cerebral hemispheres and extending dorsally to the parieto-occipital sulci. There exists a sharp demarcation between the subdural hemorrhages covering both parietal lobes and both occipital lobes. The subdural hemorrhage is more marked on the right side than on the left side; the hemorrhage is thicker over the sulci, and minimal or non-existent over the gyri. Basal and lateral parts of the entire medulla oblongata are covered by a layer of blood which is subdurally and subarachnoidally located. Both vertebral arteries and the basilar artery can be identified. Pons and mid-brain are unremarkable.

The lower medulla is completely separated from the upper cervical spinal cord about 14 mm distal to the confluence of both vertebral arteries which form the basilar artery. The cisterna cerebello-medullaris is filled with clotted blood. The surface of the lower medulla at the level of the traumatic transection form the upper cervical spinal cord is uneven and corrugated and brownish in color. The surface, in general, is concave.

In the cervical area, the spinal cord reveals scattered minute subdural hemorrhages on both dorsal and lateral aspects. There are additional scattered subdural hemorrhages located at the thoracic and lumbar regions.

Microscopical Findings:

C_1 multiple recent rhectic hemorrhages in gray and white substance.

Lower medulla oblongata: multiple recent rhectic hemorrhages.

Pons: multiple small recent rhectic hemorrhages near the aqueduct.

In conclusion, this animal was involved in two runs on a single day. The peak sled acceleration in the first run was 106.9 G, in the second and acutely fatal run 128.1 G. The radiological findings consist of a C_1 - C_2 subluxation. Morphologically, a complete traumatic transection exists. Both vertebral arteries are ruptured at the level of the foramen occipitale magnum, but their proximal parts remain with the specimen. Additional primary traumatic lesions consist of a massive subdural hemorrhage over both cerebral hemispheres, more marked on the right side than on the left. As a result of the ruptured vertebral arteries, a massive basal subarachnoid and subdural hemorrhage can be seen. The spinal cord reveals scattered subdural hemorrhages in the cervical and thoracic regions. In the direct neighborhood of the traumatically transected area, multiple rhectic hemorrhages can be seen in the gray and white substances. In this animal, additional primary traumatic hemorrhages exist at a distance from the transected area at the base and near the aqueduct of the pons.

#3951 Macroscopical Findings:

Incomplete traumatic transection between lower medulla and upper cervical spinal cord. The spinal cord tissue in this area is compressed in the antero-posterior direction. The consistency of the tissue in this area is decreased.

There is a moderate subdural hemorrhage extending from the cervical spinal cord to the upper third of the thoracic spinal cord.

After removal of the dura mater, a mild to moderate subdural hemorrhage can be seen over both parietal areas.

Microscopical Findings:

C_1: multiple recent rhectic hemorrhages mainly in the gray substance.

C_3: single small recent rhectic hemorrhage in the central part of the gray substance.

Thoracic spinal cord: single minute recent rhectic hemorrhage in central part of the gray substance

Lower and middle medulla oblongata: multiple small recent hemorrhages.

Pons: Single small recent rhectic hemorrhage.

Base of mid-brain, small recent rhectic hemorrhages due to avulsion of vessels.

Parietal lobe: Recent subdural and subarachnoid hemorrhages.

Temporal lobe: Small recent rhectic hemorrhages in the subiculum.

#3946 Macroscopical Findings:

Complete traumatic transection between lower medulla and upper cervical spinal cord. Scattered subarachnoid hemorrhages over the right frontal lobe. The base of the brain reveals a traumatic separation of both vertebral arteries at the level of the lower medulla at the foramen occipitale magnum. Both vertebral arteries and the basilar artery remain in situ.

Lateral parts of the medulla oblongata, pons and mid-brain show a moderate subarachnoid and subdural hemorrhage which extends in the mid-brain region into their central parts and forward to the stalk of the pituitary and to both internal carotid arteries. The cisterna cerebello-medullaris is filled with clotted blood. The hemorrhages extend in this area to dorsal parts of the medulla oblongata and cover anterior parts of both cerebellar hemispheres and parts of the vermis cerebelli.

The lower medulla is in its antero-posterior diameter severely compressed and flattened. The torn-off surface shows, macroscopically, no hemorrhages. The entire spinal cord reveals a massive subdural hemorrhage over ventral and dorsal aspects, more severe over dorsal parts. This subdural hemorrhage extends into the entire thoracic spinal cord, more severe on dorsal parts. Patchy subdural hemorrhages, especially in the posterior subdural space in the lumbar area, can be seen.

Microscopical Findings:

Flattening of spinal cord in the C_1 segment in antero-posterior diameter. Multiple recent hemorrhages in gray and white substance. These hemorrhages extend downwards into segement C_7; then decrease in number and size the farther they are located from the site of the transection.

Th_1: single recent rhectic hemorrhage in one anterior horn.

Lower medulla: multiple small recent rhectic hemorrhages.

Recent hemorrhage at the floor of the IV ventricle and in the aqueduct of Sylvii.

In conclusion, this animal was involved in a single run with a peak sled acceleration of 131.4 G, which was acutely fatal. Radiologically, an atlanto-occipital subluxation is visible. There exists a complete traumatic transection between the lower medulla and the upper cervical spinal cord. Both vertebral arteries are tuptured at the level of the lower medulla at the foramen occipitale magnum. This leads to a massive basal subarachnoid and subdural hemorrhage which extends forward to the stalk of the pituitary and to both internal carotid arteries. Additionally, there is a massive spinal subdural hemorrhage extending into the thoracic region; the lumbar region shows only patchy subdural hemorrhages.

Microscopically, multiple recent hemorrhages are found in the gray and white substances, extending from C_1 to segement Th_1. Identical recent hemorrhages are seen in the lower medulla, at the floor of the fourth ventricle, and in the aqueduct of Sylvii. These primary traumatic hemorrhages decrease in number and size the farther they are located from the site of the traumatic transection.

#3146 Macroscopical Findings:

Complete traumatic transection between lower medulla and upper cervical spinal cord. The leptomeninges over both cerebral hemispheres are unremarkable.

The left occipital pole reveals a subarachnoid hemorrhage measuring about 15 X 8 mm at its greatest diameter.

The base of the brain shows a massive space occupying subdural hematoma, covering anterior parts and lateral areas of ventral parts of the medulla oblongata, the entire pons and the mid-brain. It extends frontally into the area of the

infundibulum, walling in the two internal carotid arteries and covering the optic chiasm, and basolaterally into the Sylvian fissure. Proximal to anterior parts of the subdural hematoma are smaller areas of subarachnoid hemorrhage mainly over the gyri, especially the rectal and orbital gyri.
All cranial nerves at the base of the brain, up to the 8th nerve, are surrounded and walled in by the hematoma.
The medulla oblongata which was mechanically torn off at the upper cervical spinal cord, shows at the level of the pyramidal decussation a dark brown discoloration and indentation. The vertebral arteries on both sides are completely missing, nor can the cranial nerves from IX - XII be identified.
Microscopical Findings:
The C_1 segment shows a massive recent subdural and subarachnoid hemorrhage.
Massive multiple recent hemorrhages can be seen in the gray substance, fewer in the white substance, located especially around the ventral fissure. There exists a diffuse astroglial and microglial proliferation in the anterior columns.
C_2 reveals massive recent subdural and subarachnoid hemorrhages. There is also massive recent hemorrhage in the dorsal columns, posterior of the gray substance and the central canal.
The segment from C_3 - C_7 reveal a recent subdural hemorrhage, otherwise unremarkable spinal cord.
Thoracic, lumbar and sacral region recent subdural and subarachnoid hemorrhage in the areas macroscopically described.
The lower medulla shows multiple recent hemorrhages. There is

loss of neurons with mesodermal - glial reaction, furthermore diffuse glial reaction in the white substance.

The pons reveals single recent hemorrhages.

Mid-brain: The basilar artery can be identified, otherwise unremarkable findings.

In conclusion, this animal was involved in ten runs, covering a period of 112 days. One run was performed on the first day, two on the 98th day, two on the 103rd day, two on the 105th day, two on the 110th day, and the last and acutely fatal run on the 112th day. The peak sled accelerations were 24.0 G, 22.7 G, 25.9 G, 50.7 G, 51.3 G, 28.7 G, 108.8 G, 56.5 G, 107.5 G, and the last acutely fatal run of 158.2 G. The radiological examination reveals an atlanto-occipital subluxation. There is a complete traumatic transection between the lower medulla and the upper cervical spinal cord. Both vertebral arteries are torn off and completely missing. Due to the ruptured vertebral arteries, a massive subarachnoid and subdural hemorrhage can be seen at the base of the brain. The entire spinal cord revealed a massive subdural hemorrhage, extending into the cauda equina. Microscopically, multiple fresh hemorrhages in the upper medulla extend into the area of the pons. The microscopic examination reveals astro- and microglial proliferation in ventral parts of the medulla oblongata at the level where, microscopically, the indentation and brownish discoloration was described. These lesions are the result of one of the earlier high-level G runs. It is improbable that the run with a peak sled acceleration of 107.5 G, two days earlier, produced these lesions, because an interval of two days must be considered too short for the development of this glial reaction. It is probable that the run with

a peak sled acceleration of 108.8 G, which took place seven days earlier, led to these local alterations. The survival time of seven days from this run can be considered long enough for the development of glial proliferation as described above.

SUMMARY

The results of these experiments can be expressed in terms of damage to:

A. Central Nervous System, B. Vascular System, C. Skeletal System.

A. Central Nervous System:

Peak Sled accelerations ranging from 10.0 -Gx to 108.5 -Gx did not produce clinical or pathomorphological findings, especially they did not produce traumatic transections of the CNS at the atlanto-occipital junction between lower medulla and upper cervical spinal cord. This group consisted of 3 monkeys.

The lowest level at which a complete traumatic transection occurred was 108.6 G. Another experiment occurred at 110.4 G showed no traumatic transection. A third animal, subjected to a peak sled acceleration of 122.9 G showed severe clinical findings. The monkey was unable to sit or stand, it was moribund and had to be sacrificed after 90 hours. Accelerations in the -X vector between about 110 G and 120 G represent the threshold zone in which injuries may or may not occur. This group consisted of 3 monkeys.

Peak Sled accelerations of more than 120 G in the -X vector produced regularly incomplete or complete traumatic transections between lower medulla and upper cervical spinal cord. All 5 experiments were acutely fatal.

The histological examination of the acutely fatal monkeys reveal multiple hemorrhages in the direct neighborhood of the transected area. These hemorrhages can be termed primary traumatic or rhectic. They occur at the moment of impact due to the mechanical forces. These hemorrhages are usually more frequent in the gray

substance, but they occur in the white substance, too. These multiple petechial hemorrhages can be so massive that they can form a larger hemorrhage due to confluence of the multiple smaller ones. In general, those hemorrhages can be seen in the direct vicinity of the transected area. But in some animals, they extend proximally into the upper medulla, the pons and mid-brain, distally into lower cervical and upper thoracic segments. They decrease in size and number the more distant they are from the transected zone. These primary traumatic hemorrhages are mainly located near the ventral and to a lesser degree near the dorsal surface of medulla, pons and mid-brain. There seems to be an avulsion of vessels at or near the ventral surface of the described anatomical structures due to overstretching. In one case, we could observe these hemorrhages at the base of the temporal lobe in the hippocampus formation. There exists a direct relationship between the severity of the applied forces and the severity and distribution of the pathomorphological findings. The higher the mechanical input expressed as peak sled acceleration, the more severe are the hemorrhages and the larger is the involved area.

B. Vascular System. At 110 G, complete traumatic transections occurred between lower medulla and upper cervical spinal cord. At 120 G, these transections occurred regularly. In each of these instances, both vertebral arteries were ruptured and subsequent subarachnoid and subdural hemorrhages could be found at the base of the brain, and around the spinal cord, extending into different levels, in some cases into the cauda equina.

There were two subtypes of rupture of the vertebral arteries:

(a) The more frequent injury, was that in which both vertebral arteries, and in a few instances, the basilar artery, were completely avulsed.

(b) The less frequent injury, was that in which a separation of the vertebral arteries occurred immediately above the foramen magnum, so that their proximal parts remained intact in the specimen in situ. In this second type, there was a C_1 - C_2 subluxation instead of an atlanto-occipital separation. Since the cardiac actions in these traumatically transected animals continued for about 20 minutes, relatively large hemorrhages developed which in some instances became space-occupying lesions, and were, therefore, termed hematomas.

Despite peak sled accelerations up to 162.8 G, rupture of a carotid artery was not observed.

Another remarkable finding is the occurrence of subdural hemorrhages over both cerebral hemispheres due to ruptured bridging veins. Since EEG and ECG were recorded in the cases with these developing and expanding hemorrhages, interesting insights into the neurophysiological aspects can be expected from further data analysis.

C. Skeletal System. Two types of lesions of the cervical spine occurred: (1) atlanto-occipital subluxations with massive dislocation of the segments, and (2) one case of a C_1 - C_2 subluxation. Comparisons of the pre- and post-run skeletal x-rays showed no fracture. This is of considerable interest because the lethal injuries were all soft tissue injuries. This indicates that the use of x-rays, in the absence of autopsies to determine injuries in cadaveric research of this type, should be interpreted with great caution.

The specific injury pattern in -X acceleration transmitted

indirectly to the head via the vertebral column consists of tissue damage at the zone of maximal stress at the atlanto-occipital junction with ruptures of both vertebral arteries and concommitant basal and spinal subarachnoid and subdural hemorrhages, and in some instances of subdural hemorrhages over both cerebral hemispheres due to ruptured bridging veins most likely as the result of rotational acceleration.

These findings can be confirmed using the data of 11 additional animals which were subjected to accelerations in the same vector direction. For details, see table 1. The histological evaluation of these monkeys is underway and will be discussed in a later report.

As we have shown before, each vector direction of the impact acceleration produces a different and predictable type of injury in regard to quality and distribution. This was demonstrated in the experiments where the linear and rotational acceleration was translated directly to the head.

In the first series of experiments linear impact forces were directly applied to the calvarium of the animal approximately through the center of gravity of the head resulting primarily in translational motion and deformation of the calvarium.

The second mechanism (HAD II) applied angular impact forces directly to the calvarium by a device molded to the calvarium which forces the head through 45° of forward flexion.

The third mechanism applied impact forces indirectly to the head and neck by acceleration of the entire animal using a pelvic-torso restraint in which the head and neck were unrestraint. Low level - no injury experiments to high level - acutely fatal injury

experiments were accomplished by each mechanism.

As we have demonstrated before a neurophysiological and neuropathological continuum from no lesions to severe and lethal ones can be demonstrated, described and quantified. The system we are dealing with can be described by input-output relationships. Each effective mechanical input to the head and neck corresponds to a predictable and typical morphological end state.

SLED PARAMETERS					PEAK HEAD PARAMETERS			RESTRAINT TYPE	RESULTS		
Animal No.	Run No.	Peak Sled Accel. G	Dur. sec.	Rate of Onset G/Sec.	Ang. Accel. Rad/Sec.^{2}	Linear Accel. M/Sec.	Ang. Vel. Result. Rad/Sec.		Disposition	Radiological Findings	Neuropathological Findings
3948	LX1892	83.6	.0171	7,333.1	22,000	1,640	137	Rigid	Sacrificed 9th Day	Normal	No traumatic transection
3943	LX1891	83.8	.0158	6,325.8	29,800	1,955	150	Rigid	Sacrificed 15th Day	Normal	"
3933	LX1894	108.5	.0146	9,291.1	31,700	2,540	138	Rigid	Sacrificed 20th Day	Normal	"
3921	LX1365	108.6	.0096	13,398.2	58,100	9,250	350	Rigid	Acutely Fatal	Atlanto-occipital subluxation	Complete traumatic transection
3924	LX1893	110.4	.0142	9,292.4	31,000	2,400	142	Rigid	Sacrificed 21st Day	Normal	No traumatic transection
3935	LX1363	122.9	.0166	20,761.9	22,800	1,945	106	Rigid	Moribund, sacrificed after 90 hours	Normal	No traumatic transection; but progressive hemorrhagic necrosis
4101	LX1905	126.3	.0136	13,796.9	16,700	2,820	52	Harness Vest	Acutely Fatal	Atlanto-occipital subluxation	Incomplete traumatic transection
4099	LX1360	128.1	.0136	21,421.4	56,400	5,210	248	Rigid	Acutely Fatal	C_1-C_2 subluxation	Complete traumatic transection

SLED PARAMETERS				PEAK HEAD PARAMETERS				RES-TRAINT TYPE			
Animal No.	Run No.	Peak Sled Accel. G.	Dur. sec.	Rate of Onset G/Sec.	Ang. Accel. Rad/Sec ^{2}	Linear Accel. M/Sec.	Ang. Vel Result. Rad/Sec.		Disposition	Radiological Findings	Neuropathological Findings
3951	LX1895	130.6	.0129	12,682.0	49,200	2,850	220	Rigid	Acutely Fatal	Basal skull fracture	Incomplete traumatic transection
3946	LX1896	131.4	.0135	14,961.5	26,500	2,485	105	Rigid	Acutely Fatal	Atlanto-occipital subluxation	Complete traumatic transection
3146	LX0661	158.2	.0087	14,991.2	*	*	*	Rigid	Acutely Fatal	Atlanto-occipital subluxation	Complete traumatic transection

* Instrumentation Failure

TABLE 1. Summary of the Injury Effects

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