Many syndromes associated with mass lesions above the tentorium are now ascribed to the effects of transtentorial herniation of the temporal lobe. Among those already explored to some extent experimentally are ipsilateral pupillary dilatation and cardiorespiratory variations. Less attention has been given to the mechanisms underlying impairment of consciousness and loss of upward gaze. This paper reports the first stage of an attempt to elucidate the various effects of tentorial herniation dynamically, by animal experimentation.

The pattern of midbrain deformity consequent on temporal lobe herniation has been of particular concern on account of the association of one of us (WBJ) with Sir Geoffrey Jefferson’s clinic in Manchester where the clinicopathological correlatives of this phenomenon have been studied for some years (Jefferson, Johnson and Yates, Johnson). Fixing in situ with formalin the brains of patients dying of cerebral compression these workers found consistent patterns of distortion related to the site of the hernia, which was in turn a reflection of the situation of the primary compressing lesion. Attention was drawn to the association of loss of upward gaze with compression of the dorsal midbrain, caused by a posterior, as distinct from a lateral, hernia.

There have been relatively few attempts to produce hernias experimentally. The classical work of Reid and Cone consisted in the introduction of fluid into the extradural space in acute experiments, whilst hygroscopic material was relied on for chronic compressions. In monkeys these workers succeeded in producing an ipsilateral dilated pupil, and at autopsy there was invariably a hernia directly distorting the third nerve. Perret injected coloured, melted paraffin into the white matter of the parietal lobes of cats and sacrificed the animals after varying periods of time. Those allowed to survive only half an hour showed little evidence of herniation of brain tissue, but this was increasingly more apparent over the next 24 hours. Similar amounts of herniation were found over the following 4 days, after which the hernias became less apparent. This experimental lesion was a static one,
and not very closely analogous to a developing, pathological mass. Tarlov and Giancotti,\textsuperscript{12} studying the Kocher-Cushing guides to raised intracranial pressure, inflated epidural balloons, both above and below the tentorium, in dogs. Only when the compression was supratentorial, occasioning an uncal cone, did the classical signs appear. Ishii and co-workers\textsuperscript{9} produced hernias incidentally as part of another study, using a technique similar to that employed by us.

\textbf{METHOD}

This has been developed from a technique used in previous studies on cerebral swelling (Stern\textsuperscript{11}).

Most of the experiments were carried out on adult mongrel cats weighing between 2 and 4 kg. The majority were anesthetised with intravenous pentobarbital sodium (30 mg./kg., supplemented by 15 mg./kg. as required). Some animals were curarised using gallamine triethiodide (Flaxedil) in order to allow of aroused electroencephalographic records. Yet others were prepared according to the encephale isolé technique of Bremer,\textsuperscript{1} modified by ligation of the dural sac before transection of the cord to prevent loss of fluid both at this time and during compression. This preparation was needed to study eye movements which are absent during curarisation, whilst under anaesthesia highly abnormal responses are obtained (Hyde and Eliasson\textsuperscript{2}). These two types of unanaesthetised animal were prepared under ether anaesthesia, when a tracheotomy was done and mechanically assisted respiration commenced; procaine hydrochloride was infiltrated into the wounds before the ether was discontinued, and recordings were not made until 2 hours later. Body temperature was maintained throughout the experiment; if this is neglected the rectal temperature can drop to 30°C within an hour or so, and this could conceivably alter the reactions to compression.

Condom balloons were placed in the extradural space through a burr hole which was then closed with a plastic button and sealed with dental cement. Through polyethylene tubes the balloons were inflated with saline, using a micrometer-driven syringe capable of delivering increments of 0.1 cc. slowly. A femoral artery was cannulated with polyethylene tubing filled with 10 per cent solution of sodium heparin, and the cisterna magna was exposed and punctured so as to lose no fluid. Pressures from these two sites were measured using Statham transducers and a Sanborn recorder. In a few cases the supratentorial extradural pressure was measured from a second balloon containing just enough fluid to fill the recording system. Respiration, when separately recorded, was measured by a pneumograph led to the recording equipment.

Electroencephalographic recordings were made on a 6-channel Offner ink-writing machine. Cortical leads from the intact skull were from screws in the calvarium; for the exposed cortex silver electrodes with ball tips were used. Midbrain depth electrodes were of 40 gauge stainless-steel, enameled wire, stiffened except for the last 2.5 cm. with several layers of Epoxylite. These thread-like wires were introduced stereotactically through hypodermic tubes which were then withdrawn over the electrodes which were stiff enough to allow of this. The flail terminal segment was able to move with the midbrain as it became distorted. Position of the electrodes was confirmed at the end of the experiment by making an electrolytic lesion.

For studying compression in freely moving animals chronic implants of both
balloon and electrodes were made. For cortical recording extradural silver wires were employed; for the midbrain the same method was used as in acute experiments. Individually shielded lead wires were used which satisfactorily eliminated artefacts of movement. In addition to cats, Cynomolgus monkeys* were used for this part of the study, and they required restraint to prevent interference with the plug. Lucite collars designed by Dr. J. Fuster, Department of Psychiatry, University of California, Los Angeles were used; these allow the hands to reach the mouth for feeding, but not the top of the head. In all cases monopolar records, from an occipital midline reference, were made.

RESULTS

Midbrain Distortion. In 50 cats hernias and midbrain distortions were produced which corresponded remarkably with those found in human beings (Fig. 1). The hernias showed the same relationship to the site of the compressing mass as in the clinical material. Unilateral and bilateral frontal balloons alike produced bilateral, dorsally placed hernias which led to side-to-side narrowing of the dorsal midbrain at the level of the superior colliculi (Fig. 2). Middle fossa (temporal) balloons caused a massive lateral hernia, indenting, skewing and shifting the midbrain. The herniated material consisted of the retrosplenial gyri and the posterior hippocampus. No tegmental haemorrhages were found, apart from some of the early attempts with depth electrodes. That most of the animals did not die of compression but were sacrificed may

in part account for this, but there were 9 who did so die—3 each with bifrontal, unifrontal and temporal balloons. These animals shared in the immunity from haemorrhages.

Cisternal Cerebrospinal Fluid Pressure. This rose stepwise with injections of 0.2 cc. every 5 or 10 minutes (Fig. 3). The variations in cisternal cerebrospinal fluid pressure were closely mirrored in the supratentorial compartment. The capacity for compensation varied from one animal to another.

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* Stereotactic placements were based on a map of the Cynomolgus brain being completed by Dr. W. Ross Adey, Department of Anatomy.
but frequently a pressure rise of over 200 mm. water following an injection would by the end of 5 minutes be reduced to 50 mm. above the level before injection. Pupillary dilatation eventually occurred, but at no constant pressure, nor after any predictable number of injections. However, the balloon volume at this point was normally between 1.5 and 2.5 cc. which is approximately 10 per cent of the intracranial volume in the cat. The pupillary dilatation was usually readily reversed by reducing the pressure in the balloon. Before persistent dilatation of the pupil there were sometimes transient periods of dilatation immediately after the previous one or two injections.

**Pupil.** Bifrontal balloons consistently caused simultaneous, bilateral pupillary dilatation. Unilateral balloons, whether frontal or temporal, might lead to one of four patterns of pupillary involvement.

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**Fig. 2.** Herniations in cats. (A) Frontal balloon causing bilateral dorsal hernias. (B) Temporal balloon causing lateral hernia.

**Fig. 3.** Cisternal cerebrospinal fluid pressure during compression.
a) Pure ipsilateral dilatation occurred in 7 cases, although in the two frontal compressions behaving in this manner very symmetrical midbrain distortion was found (Fig. 4).

b) Some mild dilatation on the contralateral side at some stage during the ipsilateral dilatation occurred in 19 cases.

c) The contralateral pupil was the larger at some stage during the compression in 6 cases. This state of affairs persisted in one case, and no explanation for this could be found at autopsy.

d) Bilateral dilatation occurred in 4, for no apparent reason in 2 of these cases. One of the others followed very rapid compression, and the fourth was after tentorial resection.

![Fig. 4. Pupillary changes during compression of cat. (A) Before compression. (B) With temporal balloon inflated.](image)

**Mechanism of Pupillary Dilatation.** The explanation of the ipsilateral dilated pupil proved a little less obvious, pathologically speaking, than in the monkeys of Reid and Cone. True, a herniation through the tentorial hiatus was always found in our cats. This was so even if the animal was sacrificed immediately the pupil began to dilate; the pathology was the same if survival for a few hours with normal pupils and the balloon deflated was permitted. But this hernia did not, even when massive, ever come into contact with the third nerve, which did not look distorted (Fig. 5). It seemed important in these circumstances to determine directly whether function of the third nerve was impaired during pupillary dilatation.

A concentric bipolar stimulating electrode was placed stereotactically in the trunk of the third nerve emerging from the brain stem. Square waves of 4 volts at a frequency of 10 per second were delivered from a Grass stimulator. Normally the eyeball visibly oscillated at the rate of stimulation. When the pupil dilated with compression this response, which is a measure of conduction in the third nerve, disappeared to return on release of pressure. The possibility that this might be an ischaemic phenomenon was explored by repeating the experiment after death. Anoxia is then complete, the nucleus inactive on this account, but the nerve still able to conduct. A satis-
factory response was obtained which was abolished again by inflating the balloon but reappeared when the pressure was released. This was repeated on three consecutive animals. We concluded that the peripheral nerve was indeed the site of involvement, and that the mechanism was mechanical rather than ischaemic presumably caused by impingement of the nerve on unyielding structures.

Preliminary exploration of the order of involvement of the various functions of the third nerve suggests that the commonly accepted belief that the pupil alone is involved initially may have to be revised. When this study is complete it will be the subject of a separate communication.

Cardiorespiratory Alterations. As the pupils dilated following inflation of a bifrontal balloon there was always some respiratory slowing but the pulse and blood pressure remained steady. Unilateral compressions, frontal or temporal, did not usually bring about any change in vital signs at the stage of pupillary dilatation; occasionally there was a little slowing of breathing (Fig. 6). However, if the tentorium, which is bony in cats, were resected, or a posterior fossa decompression performed, before the balloon was inflated then a different sequence of events was witnessed. Respiratory slowing to the point of apnoea, bradycardia and rising or falling blood pressure either accompanied pupillary dilatation or even anticipated it (Fig. 7). A sufficiently rapidly inflated temporal balloon would also bring about this sequence.

Electroencephalographic Changes. Records were made from the last 12 animals, all temporal compressions. An over-all pattern of abnormality is becoming clear. As the pupil began to dilate either flattening, or less commonly slowing, of the record occurred. Complete flattening eventually developed in most animals, activity reappearing within a few seconds of release of pressure (Fig. 8). This flattening occurred both in anaesthetized animals and in alert preparations being artificially respired throughout. Simultaneous records of pulse and blood pressure showed them to be un-
altered during flattening. There was no question then of this being the effect of terminal anoxia. Moreover the flattening could still be produced by direct compression of the midbrain, when the vault of the skull had been removed and the dura mater opened to obviate the possibility of local cortical ischaemia caused by pressure against the skull. It seemed therefore to be a consequence of events occurring in the compressed midbrain. Conclusions on this aspect of the problem must await the results of further experiments which are being carried out.

Compression of Freely Moving Conscious Animals. To attempt a correlation of levels of consciousness at different degrees of compression, chronically implanted animals were compressed whilst able to move within the range of a metre length of electroencephalographic cable attached to the head. Cats became slow and sleepy after the first few injections, going on then to obvious hypokinesia. An upright sitting posture with head bowed would be held for minutes, or a paw just withdrawn from water would be held poised in mid air. The electroencephalogram remained normal at this time, but
further increments now gave a stereotyped reaction. There was sudden opisthotonus lasting a few seconds, but the sitting or standing stance was maintained through this and there was no concomitant change in the electroencephalogram. Later there was another component to this reaction, tonic extension of the forepaws. Eventually the ipsilateral pupil dilated, the electroencephalogram slowed and the animal was quite unable to support itself. Contralateral rigidity, sustained opisthotonus, rhythmically switching tail and rapid respiration completed the syndrome. If the balloon was not released the second pupil dilated and the animal succumbed. If released, rigidity rapidly subsided and within 5 minutes the head could be supported and the electroencephalogram was returning to normal.

More subtle behavioural changes can be appreciated with monkeys. Normally aggressive, they became tame allowing not only stroking but provocation without reaction. This was probably part of a hypokinetic syndrome, during which food would be refused even though put to the mouth yet the animals were apparently normally alert, especially as judged from their reaction to visual and auditory stimuli. The electroencephalogram was normal at this time. With continued compression drowsiness, loss of upward movement of the eyes and ptosis and spasticity developed with a dilated pupil on the side of the compression (Fig. 9). Following release of compression the slow, high amplitude waves on the electroencephalogram which developed in only the last few minutes of compression (applied slowly over a period of 3 or 4 hours) became even wilder and continued in this way for several hours. During the whole of this time the animal was hypokinetic and frequently
sleeping yet always easy to arouse and active in searching with the eyes. Normal electroencephalogram and behaviour did not return for some 10 hours.

**DISCUSSION**

With normal bony relationships supratentorial compression in cats affects first the pupil, then the respiration, next blood pressure and lastly cardiac rate. This is somewhat at variance with the reported experience of Tarlov and Giancotti with dogs. The pupils in their animals dilated only after slowing of both respirations and pulse, and alteration of blood pressure was the least common abnormality. The increased susceptibility to cardiorespiratory alterations when the bony support of the tentorium or occiput is removed is in accord with Thompson’s concept of “dynamic axial distortion of the brain stem” as the mechanism for these changes rather than pressure per se. This may constitute a hazard of splitting the tentorium, should supratentorial pressure rise again after this is done.

That behavioural changes should anticipate all measurable physiological alterations is no surprise. But the nature of the akinesia observed in monkeys is interesting, and may be related to akinetic mutism. It closely resembles a chronic behavioural change produced in monkeys by coagulation of the subthalamus bilaterally (Lindsley and Adey). One of us (WBJ) has observed these animals and the resemblance to the compressed monkeys is striking.

The rapidity with which cardiorespiratory, pupil and electroencephalographic changes usually return to normal on releasing the pressure, although the hernia clearly persists, calls into question the rationale for splitting the tentorium in patients with persisting symptoms after the removal of mass.

![Fig. 9. Left temporal compression in an alert monkey, showing electroencephalographic cable and plastic collar. (A) Ptosis, more marked on left. (B) Dilated left pupil.](image-url)
lesions. These experiments suggest that the persistence of a hernia, without the *vis a tergo* of a mass lesion may not be of much consequence. However, Ishii and his collaborators have shown that cerebral oedema follows the release of just such pressure as we have employed. It may be that this would provide the force to enable the hernia to affect the brain stem once again. On the other hand the time relations may be vital, a brain stem that has been compressed for weeks or months behaving differently from one more acutely involved as in the experiments hitherto carried out.

The capriciousness with which, in clinical experience, consciousness is impaired or the electroencephalogram rendered abnormal by expanding lesions may be accounted for by the degree to which herniation at the tentorium has occurred, with compression of the midbrain. In particular both the fluctuating stupor and flattening of the electroencephalogram associated with subdural haematoma (not necessarily both together) may be related to this phenomenon. Certainly these features have not been satisfactorily explained so far, whilst pathologically subdural haematoma is constantly associated with the most dramatic distortion of the midbrain.

**SUMMARY**

Experimental compression of the brain in cats has produced tentorial herniations and deformities of the midbrain comparable to those found in patients dying of cerebral compression.

The effect of the site of compression on the pattern of herniation and midbrain deformity, and on pupillary and cardiorespiratory function has been studied.

Direct confirmation of impaired function of the third nerve during pupillary dilatation has been obtained.

Flattening of the cortical and midbrain reticular electroencephalogram from pressure on the midbrain has been demonstrated.

Conscious cats and monkeys have been compressed and behavioural and electroencephalographic changes have been observed.

Advice on methods of electrical recording has been freely given by the Departments of Anatomy and Physiology, University of California Medical Center, Los Angeles. In particular we are indebted to Dr. Jane Hyde and her staff, not only for advice, but for providing facilities for electroencephalography.

**REFERENCES**


DISCUSSION

Dr. Raymond K. Thompson: I should like to congratulate Drs. Stern and Jennett on this well-planned investigation. The development of a technique that will permit the study of the intact, awake animal is surely a step forward. It will allow further studies of consciousness which are so badly needed.

In our studies presented to this Society last year we attempted to demonstrate experimentally that the changes in vital signs formerly attributed to intracranial pressure per se were in reality caused by acute axial distortion of the brain stem. We felt this distortion produced changes in neuronal discharge and conduction in the brain stem. Drs. Jennett and Stern's data show that this altered neuronal activity does occur.

Their work emphasizes that acute mechanical distortion of the neuraxis resulting in altered electrical conductivity needs further investigation. I would predict that some of the obscure and variable clinical signs and symptoms may be explained on this basis.

Dr. Henry T. Wycis: Regarding dilatation of the pupil, I should like to ask Dr. Jennett whether or not the recording from the third cranial nerve was made within or outside the brain stem.

I raise this question because in our studies on the human reticular formation, prior to making lesions in these patients (under local anesthesia) we stimulated this region 4–5 mm. lateral from the midline and 2–4 mm. below the posterior commissure. Stimulation in this area produced dilatation of the pupil and sympathetic effects such as rise in blood pressure, increased sweating and a desire to void. However, if the electrode is too far lateral and comes close to the fibers forming the third nerve, then a unilateral constriction occurs. The question arises whether or not dilatation of the pupil can be explained by compressing factors occurring within or outside the brain stem.

Dr. Howard Freedman: I just want to ask one question. Has it been demonstrated that the pressure under the vault of the skull and the pressure in the cisterna magna is the same in the early course of elevating the balloon volume? Was this studied throughout and was there a difference in the pressure supratentorially and infratentorially in the later stages of elevating pressure over the cerebral hemisphere?

Dr. Orlando J. Andy: This certainly was a very nice piece of work. I would like to make one statement with respect to another factor we have to consider. That is the effect of the balloon on the structures that it is directly compressing.

I think some of the observations enumerated can be accounted for by the direct effects of compression on the structures of the temporal lobe. It would be of interest to remove the tentorium in some of these animals and then repeat the experiments.
Dr. W. Eugene Stern: I would like to acknowledge the fact that Dr. Jennett deserves the credit in this study. He carried the ball and, I think, has done a very nice job.

Dr. Thompson, our thanks for your comments. We consider your observations as presented to this Society last year rather fundamental.

Dr. Wycis, the electrodes in the third nerve were placed approximately 1 mm. outside the stem. When the stimulation was applied to the third nerve, oscillation of the globe occurred, and when the balloon was inflated this oscillatory response was eliminated but returned when the balloon was deflated.

I might state that in none of the brain stems have we demonstrated any gross structural changes, although histologic studies have not been done. There were no visible haemorrhages.

Dr. Freedman, the pressures above and below the tentorium remain parallel, even in the later stages; so insofar as this evidence contributes there was no suggestion of blockage at the incisura of the tentorium.

Dr. Andy, the tentorium was removed in certain of these animals and the changes that were observed differed from those that were noted with the tentorium intact: namely, severe respiratory changes were seen prior to pupillary dilatation, suggesting perhaps that with the tent gone there was a more ready transmission of the distorting effect to the lower brain stem. Once again, as Dr. Jennett suggested, this raises the question of the rationale of exciting the tentorium.