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Through the Eyes of Monkeys: Questions About Uncal Herniation

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When neurointensivists go in for brain cutting their deceased patient will often display herniation of the uncus of the temporal lobe. We can see compression of the third nerve that is often pointed out by the scalpel. As expected, the mass bearing down on the brainstem and cerebellum causes cerebellar tonsils to descend. Case closed!

Both clinical and laboratory knowledge contributed to understanding of mass effect. In the laboratory, the vital signs of acute mass effect were well known after Cushing's classic experiments [1]. During Cushing's year in Europe as a young 31-year-old surgeon, he would study the effects of sudden increased intracranial pressure, and although he looked at cortical vessels through a burr hole, he did not study brain tissue shift (he would do that much later). Others studied the mechanics of brain shift and cranial nerve compression in animals and recorded unexpected findings. The clinicopathological correlation in brain herniation turned out far more ambiguous. Most of these experiments began in the early 1900s and similarly, as in Cushing's experiments, involved the introduction of rapidly inflated intracranial balloon catheters. The combination of previously known abnormal vital signs and close clinical observation of change in responsiveness of the exposed animal led to the understanding of how rapid inflation could cause brainstem shift. The phenomenon has been the focus of a long history of curiosity-driven animal experiments, which later had important clinical applications. One could argue that this article should be dedicated to all the monkeys, cats and dogs to which we owe so much.

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Animal Studies on Pupillary Changes

It seems so clear from a neuropathological and biomechanical point of view. The pressurized brain is squeezed medially and inferiorly under the tentorium, into the perimesencephalic cistern. Then it compresses the ipsilateral cerebral peduncle the moment it crosses the incisura. When bilateral (and thus more central), it involves the parahippocampal gyrus, the lingual gyrus, and, posteriorly, the isthmus of the gyrus fonnicatus, and the mass effect is away from the tentorial opening.

The clinical signs have been explained by dysfunction of the peripheral part of the third nerve from its compression against the tentorial edge by the uncus, resulting in a lateralized fixed and dilated pupil. (Sometimes, and usually initially, miosis can be seen from overexcitability of the peripheral oculomotor nerve.) Focal necrosis from infarction of the uncus and parahippocampal gyrus may occur as a result of arterial compression. Temporal or occipital lobe infarction can occur by compression of the calcarine branch of the posterior cerebral artery against the tentorium but does not produce clinically recognizable signs. Much later, compression of the aqueduct of Sylvius may cause obstructive hydrocephalus, adding to the pressurized mass. The displaced midbrain forces the contralateral cerebral peduncle against the tentorium, resulting in injury to the corticospinal and corticobulbar pathways. As the midbrain continues to descend through the incisura, venous congestion and stretched perforating arteries within the midbrain and pons tear, leaving hemorrhages [2].

The knowledge that cranially expanding processes could lead to clinical findings has intrigued surgeons since the early 1900s. Several pathology studies were performed, and various types of herniation were investigated in a detailed manner.

One of the earliest animal studies was performed by Sorgo [3], who injected paraffin into the subdural space

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of cats, which resulted in 8 animals displaying sluggish light reflex of the ipsilateral pupil with no change in the opposite pupil. The ipsilateral pupil subsequently dilated, followed by the opposite pupil. In all cases, Sorgo discovered herniated brain tissue in the cisterna ambience with compression of the aqueduct. His resultant paper suggested that pupillary change correlated with direct involvement of the oculomotor nucleus and that there was not always pressure on the peripheral nerve side. Perret performed similar experiments and also found distortion of the mesencephalon and herniation to the ambient cistern at the same side of the lesion [4]. Thompson and Malina introduced lesions in primates and dogs in which respiratory difficulties were found upon elevation of supratentorial pressure until it approximated systolic blood pressure [5]. Caudal displacement of the brainstem was also found, but no histological studies were made.

Tarlov and Giancotti also inflated balloons within the skulls of dogs and found progressive drowsiness, ipsilateral pupillary constriction rather than dilatation, and decerebrate rigidity with slowing of respiration, bradycardia but inconsistent blood pressure changes. They noted this was rapidly followed by apnea [6]. Plum and Posner suggested that downward movement of the posterior cerebral artery compresses the third nerve [7]. The previously mentioned correlation between fixed dilatation of the pupil and herniation was clearly described by the classic studies by Reid and Cone [8].

Jennett and Stern replicated the experiment, sometimes in cats [9] but mostly in monkeys, and showed that ipsilateral pupillary constriction occurred in most cases, although they also found some mild dilatation on the contralateral side [9]. They studied the pattern of midbrain deformity after previous investigators reported loss of upward gaze with compression of the dorsal midbrain from a posteriorly located uncal herniation, which was distinct from lateral herniation.

Placing intravenous pentobarbital balloons through a burr hole in the extradural space inflated with saline, they anesthetized mongrel cats and cynomolgus monkeys. They measured pressures at the balloon site and cisterna magnum. They recorded EEG recording cortically and right into the midbrain with depth electrodes. In total, they induced 50 tissue herniations at the site of the compression mass. Unilateral and bilateral frontal balloons caused bilateral dorsal herniation with side-to-side narrowing of the dorsal midbrain at the level of the superior colliculi (Fig. 1). Middle fossa balloons caused lateral hernia "indenting, skewing and shifting" in the midbrain. The herniated tissue was the retrosplenial gyri and posterior

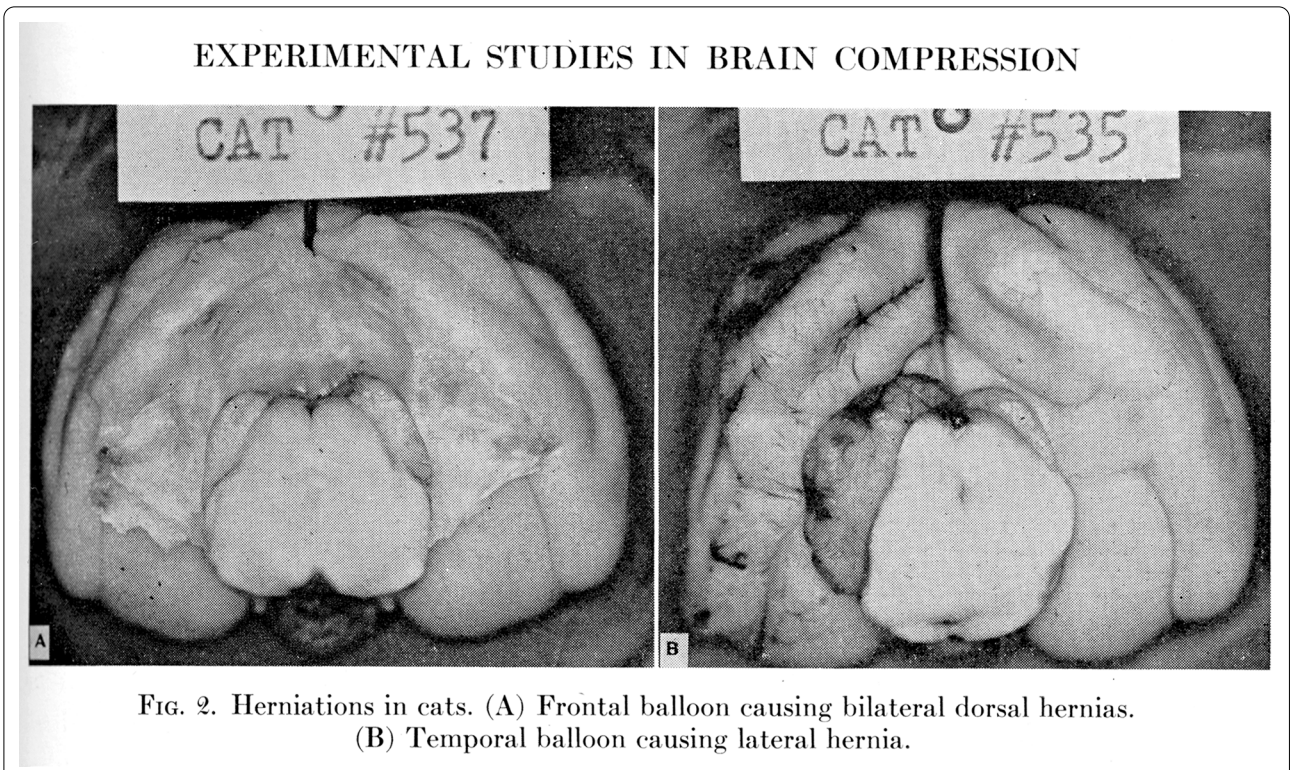

Fig. 1 Unilateral and bilateral frontal balloons caused bilateral dorsal herniation in brains of cats with side-to-side narrowing of the dorsal midbrain at the level of the superior colliculi. From Fig. 2 [9] with permission

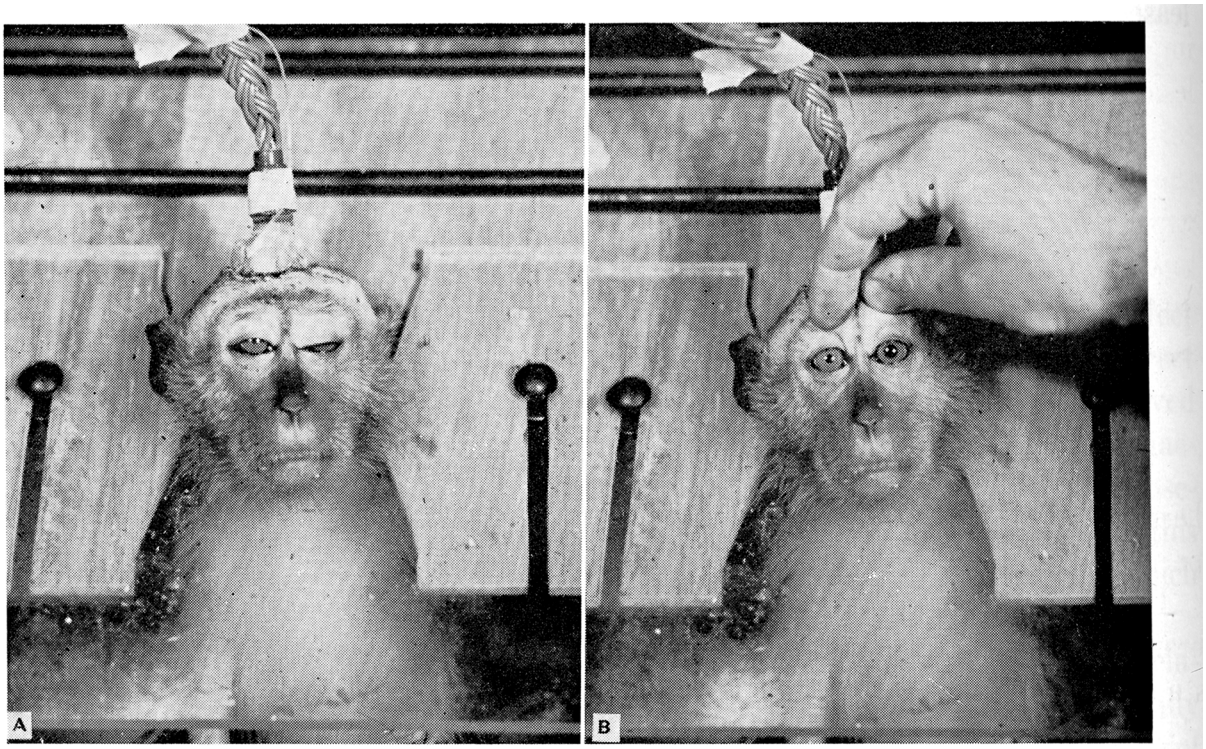

FIG. 9. Left temporal compression in an alert monkey, showing electroencephalographic cable and plastic collar. (A) Ptosis, more marked on left. (B) Dilated left pupil.

Fig. 2 Ptosis and pupillary changes during compression in monkey with temporal balloon inflated. From Fig. 9 [9] with permission

hippocampus. Pressures in the cisternal compartment mirrored the supratentorial compartment. Pupillary dilatation started at 10% increase of the intracranial volume. Jennett and Stern recognized four patterns of pupil change: (a) ipsilateral only but with symmetrical midbrain distortion, (b) larger contralateral pupil, (c) occasional contralateral dilatation, and (d) bilateral dilation with rapid compression. Jennet noted large herniation with pupillary dilation that stopped short of third-nerve compression or even distortion. Their stimulation studies, however, confirmed that the peripheral part of the oculomotor nerve was defective. Contralateral rigidity, tonic extension, and opisthotonus were seen. Unilateral compressions did not cause vitally significant changes except slowing of breathing, but some did occur with rapid balloon inflation. Additionally, the EEG expectedly flattened with pupil dilatation and could improve with release of pressure. Surprisingly, midbrain compression also produced flattening, even when the vault was open, reducing the possibility of cortical ischemia due to pressure against the skull. They noted the following sequence: "With normal bony relationships, supratentorial compression in cats affects first the pupil, then the respiration, next blood pressure, and lastly, cardiac rate." With continued compression drowsiness, loss of upward movement of the eyes, ptosis, and spasticity developed with a dilated pupil on the side of the compression. The monkey experiment was described as follows:

> *Normally aggressive, they became tame allowing not only stroking but provocation without reaction... 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. 2).*

They argued against splitting the tentorium during surgery because although the hernia clearly persists, the rapidity with which cardiorespiratory, pupillary, and electroencephalographic changes usually resolve on releasing the pressure calls into question the rationale for splitting the tentorium in patients with persisting symptoms after the removal of mass lesions.

These experiments show that the mechanism of pupil enlargement has not been definitively explained, and more than one mechanism may be operative. How the opposite pupil enlarges with transtentorial herniation

remains an anatomical mystery with bilateral central (at the nucleus level), third-nerve damage being a more likely mechanism. How the dilated pupil recovers so quickly after mannitol despite being wedged in tissue has always befuddled clinicians. Additionally supportive for brainstem ischemia was a common finding in 13 patients with brief bilateral pupil dilatation with neck flexion held for at least 10 s but only in patients with a depressed consciousness who had not progressed to decerebrate rigidity [10]. More doubts about the biomechanics of the syndrome came with Finney and Walker [11], Fisher [12] and Ropper [13].

Conclusion

The term *uncal herniation* remains a radiologic and pathologic observation, and its true clinical correlate remains unresolved. The term *uncal herniation* for a presumed syndrome of worsening stupor, a widening pupil, and new reflective motor responses will be hard to dismiss—for many practitioners, the concept works very well in practice. The literature and hospital medical notes do not let us forget it. But what is it really? Fisher's preferred term was '*midbraining*' [12] and that may be exactly what it is.

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