EXPERIMENTAL SPASMODIC TORTICOLLIS*
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Spasmodic torticollis is an involuntary hyperkinesis involving the muscles of the neck primarily on one side. Characteristically, paroxysms of moderate to severe contractions of the muscles occur which may be painful, and the resulting deformities of rotation of the head and flexion of the neck may be functionally incapacitating. The muscles of the neck mainly involved in this abnormal involuntary movement are the sternocleidomastoid, the trapezius, the splenius, and the scalenes,1,7 though almost all the ipsilateral muscles are involved to some degree.13 The bizarre posturing of the head that results is often striking and disabling, consisting of strong clonic-tonic lateral flexion of the head, rotation of the head with occiput toward the same side combined with torsion of the head toward the side of flexion. It has been shown that there is usually bilateral involvement of the muscles of the neck,13,25 and at times strong elements of retroflexion of the head are also present. This descriptive definition eliminates from this presentation other types of so-called torticollis.6,15,18,20

The term spasmodic has been applied primarily to this affliction to denote the paroxysmal nature of the complex contractions of muscles. It has long been recognized that environmental stimuli, particularly in the psychic and emotional sphere, will precipitate or accentuate these paroxysmal contractions. In a nonstressful, secure environment, the deformity may be barely discernible and yet become strikingly apparent when the individual is in a state of stress. These paroxysms do not seem to be related directly to vestibular posturing mechanisms. Later in the course of the disease, more fixed positions of head and neck may occur because of secondary structural changes in muscles of the neck and cervical spine.

The lesion in the central nervous system of man that causes spasmodic torticollis has never been established and disagreement continues as to whether the basic etiology is actually organic2,9,15,20 or purely psychogenic.1,10,27 Some clinicians feel that the organic substrate for the disease is definite, but that the expression of the syndrome is strongly associated with psychogenic factors.2,9,12,15,20

Human studies have not shown convincing focal pathological lesions as

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the cause of the torticollis, though the neostriatum, basal ganglia, vestibular apparatus, putamen, extrapyramidal and vestibular pathways, and diffuse chronic changes in ganglion cells have all been implicated.

Spasmodic torticollis was fortuitously produced in 7 monkeys in which lesions were produced in the mesencephalic tegmentum during the course of other experiments in our laboratories. Since the lesion in the central nervous system responsible for torticollis appears to be unknown and since a psychogenic etiology has been widely cited in the literature, these monkeys with spasmodic torticollis of proven organic etiology were studied.

METHODS

Experiments were carried out on 7 monkeys (Macaca mulatta). Monkeys #1 through #6 in this series, weighing 2.2–3.7 kg., were operated on under sterile conditions by the stereotactic method to produce electrolytic lesions in the medial reticular formation of the mesencephalon. Fine nichrome electrodes, 0.5 mm. in diameter and insulated with Formvar except for a bare tip, 0.5 mm. long, were introduced into the calvarium through a small trephine opening centered over the sagittal sinus in the frontal region. The electrodes were angled 30 degrees from the vertical zero plane and oriented to traverse down the axis of the brain stem at 2 mm., 2½ mm., or 3 mm. from the midline. The electrode was introduced to the mesencephalic-pontine junction, where an electrolytic lesion was made using the Grass Stimulator, Model 120, with a current of 5 ma., 60 cycles or more, 10–20 volts, for 30 seconds. Five similar lesions were made at 1-mm. intervals as the electrode was withdrawn along the tract of entry. The opposite side was then done in a similar manner since all animals had bilateral lesions. Five of the animals had only one such operative procedure, but monkey #2 had two such operations 3 weeks apart.

All animals were carefully observed immediately following operation for neurological deficits, and upon recovery from anesthesia were observed at least twice daily for several weeks and observations were recorded daily.

In monkey #7, an implanted electrode, 0.35 mm. in diameter, was placed stereotactically into the medial reticular formation at the mesencephalic level 1 mm. lateral to the midline. The electrode was fixed to the skull by means of a plastic cap device under sterile conditions. Immediately upon recovery from the anesthesia, no neurological deficits were present. The next day the rostral tip of the implanted electrode was no longer visible above the scalp and roentgenograms of the skull showed that the electrode tip was now beneath the calvarium (Fig. 1B). Presumably the animal had somehow pushed the electrode farther into his brain. At this time a slightly dilated left pupil was present together with typical spasmodic torticollis (Fig. 1A).

Photographs and a short movie strip were made to document the torticollis and its spasmodic nature.

At the end of the observation period, the brain of each animal was perfused with normal saline followed by 10 per cent formalin and the brain was removed intact. Subsequently, serial sections of the brain were made and stained by the Weil and thionin techniques.

RESULTS

I. Experimental Studies. The spasmodic torticollis produced in the 7 monkeys was striking in its similarity to clinical spasmodic torticollis, and
relatively constant in its characteristics from one animal to another. As is usual, the torticollis was classified “right” or “left” according to the direction of rotation of the occiput. In 6 animals, it was obvious immediately on recovery from anesthesia, but in animal #2, the torticollis did not appear until 7 days after operation, presumably secondary to further brain-stem softening. In the early weeks after operation, the abnormal rotation and tilt of the head were usually hardly discernible when the animal was quiet and calm. If fear or excitement was induced by almost any means, extreme accentuation of the cephalic rotation and torsion to as great as 90 degrees with approximation of ear to shoulder rapidly appeared, achieved by complex clonic and tonic contraction of the muscles of the neck, predominantly the sternocleidomastoid muscle. The maximum position of the torticollis was maintained tonically as long as fear or excitement was at its peak (Fig. 1A). When the animal became accustomed to this environmental threat or change, the intensity of the tonic rotation became less and the torticollis was manifested by a clonic, almost alternating movement of the head. As the threatening situation disappeared, the posture of the torticollis steadily became less marked and 5 to 10 minutes later was no longer obvious if the monkey was again in its normal placid environment. Continued, repetitive threatening situations, however, would cause the torticollis to persist at moderate to severe degrees. Except for animals #3 and #6, who showed moderately severe dysfunction of the brain stem in addition to the torticollis, the animals did not appear to be functionally disabled by the torticollis and were able to feed themselves and maneuver adroitly even when the paroxysms were severe.

The torticollis persisted in all animals from the time of onset until death, except in animal #7 in which it disappeared 2 months after operation. This animal had the smallest lesion of the entire group. In all the monkeys, the paroxysmal, spasmodic nature of the torticollis persisted except in monkey #1, who lived for 6 years with his torticollis. In this beast, the striking paroxysmal nature of the abnormal posture of the head gradually became less obvious as the head became mechanically fixed in the torticollis position after about 1 year, apparently because of secondary fixation of structures of the
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Fig. 1B. Monkey #7. Roentgenogram of skull showing implanted mesencephalic electrode.

neck. Even under these circumstances, however, the paroxysmal nature of the spasms of the cervical muscles was obvious on emotional stimulation.

Table 1 demonstrates the neurological deficits observed in these 7 animals. As shown, the spasmodic torticollis was present from the time of operation until death in 5 of the 7. Bilateral 3rd nerve paresis was present in 4; unilateral 3rd nerve paresis in 2; and a unilateral 6th nerve paresis in 1 monkey. Weakness of the extremities of variable degree was present in 3 of the animals on one side, and ataxia or dysnergia was present in 5 of the animals to a variable degree. Bizarre circling activity was present in 5 and significant lethargy was present in 3, with coma in only 1 animal. These deficits were the most common in the group, and it is of importance that the maximum neurological deficits were seen in the animals who had the maximum electrolytic lesions in the mesencephalon (#3 and #6). The neurological deficit which showed least variability from animal to animal was the spasmodic torticollis (Fig. 1A).

Table 2 describes the pathology of lesions associated with torticollis. Thorough study of the cross sections of the brain stem in these animals showed that the lesions were produced in three ways. Direct electrolytic destruction with asymmetrical bilateral lesions occurred in animals #2, #3 and #5 (Fig. 3). Vascular occlusion of the ventral perforating vessels of the mesencephalon because of the extreme ventral position of the electrolytic lesion interrupting the paramedian vascular supply occurred in animals #1, #4 and #6 (Fig. 4). Mechanical manipulation of an implanted brain-stem electrode by animal #7 produced a discrete anatomical dorsal-ventral slicing effect in the paramedian area of the mesencephalon (Fig. 5).
TABLE 1

Neurological deficits produced from the brain-stem lesions

<table>
<thead>
<tr>
<th>Deficits</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>#6</th>
<th>#7</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Spasmodic torticollis</strong></td>
<td>*Left</td>
<td>*Right</td>
<td>*Left</td>
<td>*Left</td>
<td>*Right</td>
<td>*Left</td>
<td>Right</td>
</tr>
<tr>
<td><strong>Cranial nerve palsy</strong></td>
<td>Bilat. III *Right</td>
<td>*Right III partial</td>
<td>Bilat. III *Left</td>
<td>Bilat. III *Left</td>
<td>*Left VI</td>
<td>Left III</td>
<td></td>
</tr>
<tr>
<td><strong>Extremity weakness</strong></td>
<td>0</td>
<td>*Left arm; paraplegia</td>
<td>*Left side</td>
<td>Bilat. leg weakness</td>
<td>0</td>
<td>*Paraplegia</td>
<td>Left side</td>
</tr>
<tr>
<td><strong>Lethargy</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>*Coma</td>
</tr>
<tr>
<td><strong>Ataxia</strong></td>
<td>Fell to right; dysynergia</td>
<td>*+</td>
<td>*+</td>
<td>+</td>
<td>+</td>
<td>dysynergia</td>
<td>0</td>
</tr>
<tr>
<td><strong>Bizarre circling or posturing</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>*+</td>
<td>*+</td>
<td>0</td>
</tr>
</tbody>
</table>

* Persisted, otherwise transient only.


TABLE 2

Descriptive pathology of brain-stem lesions

<table>
<thead>
<tr>
<th>Animal</th>
<th>Torticollis</th>
<th>Destroyed Area Responsible for Torticollis</th>
<th>Method of Production of Lesion</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1 (T9)</td>
<td>Left Immediate Severe Persisted</td>
<td>Right paramedian vascular softening at superior mesencephalon level, involving medial longitudinal fasciculus, III nerve nucleus, medial red nucleus, decussation of brachium conjunctivum, elements of medial reticular formation</td>
<td>Vascular occlusion ventral perforating vessels at mesencephalon level on right by electrolytic lesion midline extreme ventral position</td>
<td>6 years (sacrificed)</td>
</tr>
<tr>
<td>#2 (T12)</td>
<td>Right 7-day delay Mild</td>
<td>Left direct paramedian destruction of decussation brachium conjunctivum, major portion of red nucleus, medial reticular formation at mesencephalon superior colliculus level</td>
<td>Direct electrolytic destruction (asymmetric bilateral lesions) with medial lesion on left</td>
<td>8 days (sacrificed)</td>
</tr>
<tr>
<td>#3 (T13)</td>
<td>Left Immediate Severe Persisted</td>
<td>Extreme softening of entire central mesencephalic tegmentum, worse on right; not involving upper pons levels</td>
<td>Presumed massive electrolytic destruction secondary to faulty electrode insulation; minor asymmetry electrode positions</td>
<td>15 days (died)</td>
</tr>
<tr>
<td>#4 (T15)</td>
<td>Left Immediate Severe Persisted</td>
<td>Almost identical to #1, Right paramedian softening mesencephalon (nearly midline)</td>
<td>Ventral vascular occlusion on right (similar to #1)</td>
<td>6 months (sacrificed)</td>
</tr>
<tr>
<td>#5 (T17)</td>
<td>Right Immediate Severe Persisted</td>
<td>Left massive destruction medial mesencephallic tegmentum including essentially same structures as in #2</td>
<td>Same as #2</td>
<td>9 months (drug trial)</td>
</tr>
<tr>
<td>#6 (T18)</td>
<td>Right Immediate Severe Persisted</td>
<td>Right paramedian superior mesencephalic tegmental vascular softening involving right medial longitudinal fasciculus, III nerve nucleus, superior decussation brachium conjunctivum (extensive softening up into subthalamic area)</td>
<td>Ventral vascular occlusion of superior mesencephalon vessels by ventral electrolysis in tegmentum (similar to #1 and #4)</td>
<td>17 days (died)</td>
</tr>
<tr>
<td>#7 (E11)</td>
<td>Right Immediate Severe 2 months duration</td>
<td>Left paramedian superior mesencephalic through inferior mesencephalic tegmental slice-like (doroventral) lesion cutting decussation brachium conjunctivum (as in #1), medial longitudinal fasciculus, possibly medial reticular formation—but not red nucleus</td>
<td>Manipulation of in-lying brain-stem electrode by animal—a discrete physical slicing dorsoventrally (1.5 mm.)</td>
<td>3 months (sacrificed)</td>
</tr>
</tbody>
</table>
Fig. 2. Diagram of sagittal section of brain stem of monkey. Shaded area designates lesion that was present in all animals, presumably responsible for the torticollis. A, B, C indicate approximate levels of cross sections in subsequent Figs. 3, 4 and 5.

Fig. 3. (A) Photomicrographs of cross sections of brain stem (Weil stain) at levels A, B and C (Fig. 2) in monkey #2. Round hole marks left side. Electrolytic lesions (monkeys #2, #3, #5).

(B) Line drawings of lesion of torticollis (heavy, diagonal lines); same monkey; same levels. Lesions with horizontal lines were not common to other animals with torticollis.
Fig. 4. (A) Photomicrographs of cross sections of brain stem (Weil stain) at levels A, B and C (Fig. 2) in monkey #1. Round hole marks left side. Vascular lesion (monkeys #1, #4, #6).
(B) Line drawings of lesion of torticollis (heavy, diagonal lines); same monkey; same levels.

Fig. 5. (A) Photomicrographs of cross sections of brain stem (Weil stain) at levels A, B and C (Fig. 2) in monkey #7. Round hole marks right side. Mechanical lesion.
(B) Line drawings of lesion of torticollis. Same monkey; same levels.
The pathologic lesions were strictly limited to the mesencephalic level of the brain stem in animals #1, #2, #4, #5 and #7. Animal #3 had extreme softening of the entire central mesencephalic tegmentum which extended up into subthalamic areas. Animal #6 also had extensive softening into the subthalamic area. The path of the electrode was visible on microscopic examination in the paramedian position as it passed through areas above the mesencephalon in all instances, but was not associated with any significant destruction except possibly in animal #7 where the slicing effect had caused a slightly larger tract in the subthalamic area than in the other animals.

Fig. 2 is a sagittal drawing of the monkey brain stem with the shaded area representing the only lesion common to all 7 animals.

Fig. 3 shows the photomicrographs and diagrams of lesions in the cross section of the brain stem of monkey #2 at levels A, B and C (Fig. 2). These lesions are very similar to those in monkeys #3 and #5. In these animals, there was asymmetry of the electrolytic lesions with direct paramedian destruction of the decussation of the brachium conjunctivum, a major portion of the red nucleus, medial reticular formation at the mesencephalon level, and the medial longitudinal fasciculus. These lesions were on the side opposite to the torticollis. The destructive lesions on the same side of the torticollis were more laterally placed and did not involve areas common to the other animals in the series. None of the lesions at level C were common to the other animals with torticollis (Figs. 4 and 5).

Fig. 4 shows the photomicrographs and diagrams of lesions in the cross section of the brain stem of monkey #1 at levels A, B and C (Fig. 2). They are representative of the vascular occlusive lesions in animals #4 and #6. All these lesions were on the side opposite to the torticollis. In the mesencephalic tegmentum, paramedian vascular softening involved the medial longitudinal fasciculus, 3rd nerve nucleus and rootlets, medial red nucleus, decussation of brachium conjunctivum, and elements of the medial reticular formation.

Fig. 5 shows the photomicrographs and drawings of lesions in the cross section of brain stem of monkey #7 at levels A, B and C (Fig. 2). These lesions were produced by mechanical slicing effect of the implanted electrode. The lesion involves the left paramedian superior mesencephalic through inferior mesencephalic tegmental region with a slice-like (dorsal-ventral) lesion cutting the decussation of the brachium conjunctivum, involving the medial longitudinal fasciculus, and medial reticular formation as well. It does not appear to include significant portions of the red nucleus, being medial to it. Fig. 1B is the roentgenogram of the skull of this animal with the implanted electrode in place, the rostral end actually being beneath the calvarium at this time.

Monkeys #3 and #6 were so severely incapacitated by the lesions produced in the mesencephalic tegmentum that they deteriorated and died at 15 days and 17 days respectively. Animals #2, #4 and #7 were purposely sacrificed after variable periods. Animal #1 was sacrificed 6 years after the production of his torticollis and is the only one in which chronic changes of
torticollis were apparent. The sternocleidomastoid muscles were excised and studied microscopically, but the only change was that of gross difference in the size of the two muscles, without significant evidence of fibrosis. The muscle involved in the torticollis was larger than the opposite one.

Since lesions in nearby portions of the mesencephalic tegmentum of monkeys have been shown to produce a clinical syndrome similar to Parkinsonism which can be modified by anticholinergic drugs, it seemed worth while to test the effect of anticholinergic drugs on spasmodic torticollis, which is also a hyperkinetic syndrome. Attempts to modify the torticollis in this series of animals by administration of atropine, scopolamine, Diparcol and Pagitane were not successful since the observations were fragmentary and it was not certain that adequate levels of the drug were achieved.

II. Clinical Studies. A limited series of observations were made on patients with spasmodic torticollis receiving anticholinergic therapy. Adequate data could be obtained in only 5 cases. Of these, sustained objective improvement was obtained in 2 patients, though minor and transient improvement was obtained in the remainder. Brief clinical summaries of these 2 patients are presented.

Case 1: D.C.M., a 48-year-old lumber worker. Onset of spasms of the right neck with rotation of the head (occiput, right) 4 months before admission, with subsequent steady worsening. Spasmodic contractions were much worse when under emotional tension. Severity of torticollis prevented work. Past history was negative.

Typical right spasmodic torticollis was present; right pupil was slightly dilated. Neuropsychiatric work-up, Amytal interviews, and physiotherapy were not helpful. Electroencephalogram was normal. A combination of scopolamine, 0.3 mg. q.i.d., with Benadryl, 50 mg. t.i.d., gave excellent relief of spasms. Scopolamine and Artane in various combinations were less helpful. Anticholinergic drug CT-357, 5 mg. t.i.d., gave dramatic improvement. He returned to work and was still doing well 1 year later on this drug.

Diagnosis: Right spasmodic torticollis (presumably secondary to left mesencephalic lesion—cause unknown).

Case 2: S.O., a 46-year-old pipe-fitter. Onset of spasms of left neck, and rotation of head 3 years before admission; gradual progression and spasmodic paroxysms, worse on emotional stress. During the last 6 months rapid increase in severity prevented working. Section of cervical muscles 2 months before admission was ineffective. He had had severe “chickenpox encephalitis” 6 years previously.

On examination he exhibited left spasmodic torticollis with some retroflexion, and mild left cerebellar deficits. Electroencephalogram was normal.

Pagitane, 2.5 mg. q.i.d., gave improvement which allowed return to work in 2 weeks. Six months later, P-189 (anticholinergic drug), 5 mg. q.i.d., was added because of some regression. Further improvement followed. At 1 year, Pagitane was increased to 6 times a day and then 9 a day in order to maintain functional improvement. At 1½ years, no further neurological deficits were present and the Pagitane was reduced to 4 per day with striking increase in the torticollis. Return to the previous dosage resulted in improvement. This cycle was repeated twice with the same results. At 2½ years, the maintenance drug dosage was Pagitane, 2.5 mg. q.i.d., and P-189, 9 tablets (5 mg.) per day.
Diagnosis: Left spasmodic torticollis, secondary to "chickenpox encephalitis" (right mesencephalic lesion).

Comment. In these 2 instances of spasmodic torticollis in humans, therapy resulted not only in objective reduction of torticollis when the patients were under emotional stress but the functional disability was reduced to a point where they were able to return to their previous occupations. It may be of some importance that the dyskinesia in both these instances was confined to a simple nonprogressing spasmodic torticollis. In the other 3 cases, only minor degrees of improvement were obtained with anticholinergic therapy, and the spasmodic abnormal movements gradually spread to involve axial muscles other than those in the cervical region. In 2, the final diagnosis is now dystonia musculorum deformans.

DISCUSSION

Production of true spasmodic torticollis in the experimental animal has not been reported and the lesion essential to its production has not been known. v. Economo and Karplus reported in 1909 that unilateral tegmental lesions that involved the red nucleus were associated with disturbances of static posture of the head in cats. More recently, Kemberling et al. produced a sustained "torticollis-like" posture in cats by extensive combined lesions of the vestibular nuclei and the adjacent reticular substance. However, in neither instance was spasmodic torticollis produced but rather a tonic abnormal posture consisting of rotation and flexion of the head. Carrea and Mettler investigated extensively the function of the brachium conjunctivum in the monkey and observed that unilateral lesions of the brachium conjunctivum associated with damage to the medial longitudinal fasciculus in the mesencephalic tegmentum were associated with "flexion of the head to the side opposite." In their protocols they described that "the head was rotated toward the left and flexed toward the right side" following lesions in the left mesencephalon. Though no mention was made of any spasmodic component of this abnormal posture of the head it would appear that they may have been observing a torticollis similar to that reported here. Although they implicated the medial longitudinal fasciculus in the genesis of this posture, subsequent studies by Carpenter showed that lesions confined to the region of the red nucleus may "provoke rotation and tilt of the head to the side opposite to the lesion." Carpenter related this finding to "torticollis in clinical neurology." He made no comment regarding its spasmodic nature, but rather emphasized the tonic postural deviation.

In contrast, a spasmodic rather than tonic torticollis was obtained in the monkeys reported in this series. The lesion common to all 7 animals (Fig. 2) involved a portion of the decussation of the brachium conjunctivum, the medial longitudinal fasciculus, and portions of the medial reticular formation. It did not necessarily involve the red nucleus nor elements of the 3rd nerve. This critical lesion thus involves the central core of the mesencephalic tegmentum at the level of the decussation of the brachium conjunctivum.
Although many of the lesions resulted in widespread damage to mesencephalic structures, spasmodic torticollis was still obtained with a very focal, restricted lesion fortuitously placed in this critical region (Fig. 5). Ross-Duggan\textsuperscript{22} also has observed a spasmodic torticollis in monkeys following lesions involving the medial portion of the 3rd nerve nucleus and the medial longitudinal fasciculus at the mesencephalic-diencephalic junction. Although the anatomical details are not available, it appears that the same critical region of the brain-stem core was involved.

The direction of clinical torticollis is defined by the direction of rotation of the occiput. In all of our animals, the direction of torticollis was to the side opposite the lesion. It is of interest that the static torsion of the head described by Carrea and Mettler,\textsuperscript{4,5} as well as Carpenter,\textsuperscript{3} was also to the side opposite the lesion.

If there is a similarity between the torsion of the head described by others\textsuperscript{3,4,5} and the spasmodic torticollis seen in our animals, certain inferences regarding the anatomical substrates involved can be drawn. Although the medial longitudinal fasciculus was involved in all our monkeys, Carpenter\textsuperscript{3} has shown that lesions of this structure are not essential to the production of torticollis. Since lesions confined to the brachium conjunctivum before it becomes imbedded in the reticular formation do not result in torticollis,\textsuperscript{8} it may be that destruction of the brachium conjunctivum at its decussation is not essential. Furthermore, both our data as well as previous studies indicate that lesions of the red nucleus do not produce torticollis. Thus, the only remaining structure damaged by this critical lesion of the mesencephalic tegmentum is the medial reticular formation. However, this region is morphologically and functionally exceedingly complex and assignment of a specific syndrome such as torticollis to specific circuits in the brain stem is not warranted on the basis of the currently available data.

It has long been known that electrical activation of the mesencephalic tegmentum will elicit tonic postural responses,\textsuperscript{16,26} some of which strongly resemble the posture of torticollis. Neural circuits thus are present in the reticular formation which mediate these postural mechanisms. Furthermore, the current studies indicate that critical lesions in the medial reticular formation at the level of the decussation of brachium conjunctivum result in a spasmodic torticollis. It can be postulated that such lesions interrupt certain pathways passing to neurones whose activity is manifest by postural movements of the head and neck. Hyperactivity of these cells then ensues. Although the mechanism of this hyperactivity is unknown, it may either be caused by denervation hypersensitivity to acetylcholine or, more probably, by the removal of inhibitory input. Obviously these hyperactive cells must have an input to drive them and thereby evoke the spasmodic torticollis. Presumably the spasmodic or paroxysmal nature of this torticollis is caused by variations of this input. Since recent evidence would indicate that certain circuits within the reticular formation are also involved in the response to emotional stress,\textsuperscript{26} these circuits may also contribute to the input to the cells
mediating posturing of the head and neck. This would account for the accentuation of spasmodic torticollis by emotional stimuli as observed in both man and monkey.

There is a growing body of evidence that normal transmission in the reticular formation is unusually dependent on acetylcholine. Thus it is unnecessary to assume that the phenomena of denervation hypersensitivity play a major role in the genesis of spasmodic torticollis. On either basis, it might be anticipated that anticholinergic drugs would reduce the hyperactivity of these cells thereby modifying the torticollis. Such appears to be the case in certain clinical instances. As in other hyperkinetic disorders such as Parkinsonism, these effects may be evanescent or transient. Likewise, good results depend on proper choice of drug in adequate doses. Although a large series of patients has not been treated with anticholinergic drugs, our current experience indicates that significant alleviation of torticollis should not be anticipated in all cases. On the basis of the mechanisms postulated, improvement of the torticollis might also be achieved by modification of environmental or emotional stress. This can be accomplished by psychotherapy\textsuperscript{1,10,12,25} or pharmacological means,\textsuperscript{19} including tranquilizing drugs.

Multiple surgical procedures attacking the dystonic muscles,\textsuperscript{21,23,24} their motor innervation,\textsuperscript{23} or the sensory inflow to cervical cord,\textsuperscript{21} have not been uniformly successful in alleviating torticollis. Since the mechanisms underlying torticollis involve reticulospinal circuits, such procedures are attacking only the peripheral manifestations of a centrally engendered process. Other hyperkinetic disorders may be benefited by the use of stereotactically placed subcortical lesions and therefore it is possible that spasmodic torticollis may be benefited in the future by related surgical procedures directed at its central rather than peripheral mechanisms.

CONCLUSIONS

1. Experimental spasmodic torticollis has been induced in 7 monkeys by lesions in the mesencephalic tegmentum. The etiologic lesion, common to all 7 animals, destroyed portions of the medial reticular formation and brachium conjunctivum as well as the medial longitudinal fasciculus.

2. The torticollis occurred toward the side opposite the lesion. As in man, the torticollis was a hyperkinetic phenomenon accentuated by emotional stress.

3. The physiological mechanisms underlying spasmodic torticollis are discussed.

4. The effectiveness of anticholinergic therapy in certain cases of human spasmodic torticollis is described and possible mechanisms of therapy are presented.

REFERENCES


EXPERIMENTAL SPASMODIC TORICOLLIS

22. Ross-Duggan, J. K. Personal communication.

DISCUSSION*

Dr. Arthur A. Ward, Jr. Obviously my remarks are directed at the interesting presentation given you by Dr. Russell Meyers and his colleagues. The role of ultrasound in subcortical surgery, I think, is something that introduces a fascination not only with respect to the technique itself, but also with respect to the instrumentation. This is very impressive instrumentation, as you saw from the slides, and it is even more impressive when seen in the flesh.

I have one question for Dr. Meyers to which he has given a lot of thought, namely the matter of stereotactic accuracy. All of us have been impressed with the amount of biological variation of the human brain, either with respect to skull or with respect to structures that we can visualize by any radiographic means. For these reasons, as Dr. Meyers himself has

* Discussion pertains to the two preceding papers (by Meyers et al. and by Foltz et al.)
pointed out on past occasions, it becomes rather difficult to be absolutely sure that specific minute lesions of the ansa lenticularis have in fact actually been accomplished until we have serial sections beneath the microscope to verify this. I’d like to ask him, if I might, what anatomical controls he has with the particular apparatus that he has devised.

With respect to ultrasound itself, there are obviously many ways in which subcortical lesions may be produced. We can stick eggbeaters in the brain and make lesions that way. We can produce holes by injecting various chemical compounds that kill brain. We can kill nerve cells or fibers by electric currents, and it is true we can also kill them by ultrasound. The ultrasound technique also possesses some disadvantages, however. It requires a very complex apparatus with very careful monitoring of the acoustic output. With electric currents it is very simple to tell whether your apparatus is functioning. However, with respect to ultrasound, this becomes a good deal more complex. Adequate probes to monitor ultrasound are not easy to construct or calibrate, and I think perhaps Dr. Meyers might tell us a little about the effort involved in calibrating his four focussed transducers before he does one of these procedures.

The second disadvantage, in addition to gross complexity, is the matter of dosage. This is very difficult to determine and, as far as I am aware, factors of dosage with respect to the human brain remain to be determined.

The third is a technical matter which is apparent from his slides, namely the size of the craniotomy. In order to get contact with the dura mater for all these four beams, a rather large craniotomy is required which in turn might possibly raise some questions with regard to morbidity. Exposing a fairly sizable proportion of the dura mater over one hemisphere is not a minor procedure, either in terms of potential morbidity of the brain, or in terms of morbidity to the surgeon, since I would imagine a rather long period of time is required in order to accomplish some of these procedures.

In payment for these potential disadvantages, however, there are obviously certain things that ultrasound will do that other techniques will not. One of these is that, as Dr. Meyers pointed out, it is potentially possible to produce a reversible lesion. None of the other techniques currently utilized will do this. The second is that the lesion can be produced without damage to the blood vessels. This obviously would be a tremendous boon to the accuracy and safety of this procedure in the future.

I think Dr. Meyers will agree that, at the present time at least, this technique is a very useful one from a research standpoint. I do not believe, and he can correct me if this is not the case, that he is advocating that this is something that all of us should be utilizing since the difficulties involved are rather overwhelming. In a certain sense it is sending a boy to do a man’s job.

Dr. H. T. Ballentine: Thanks to Dr. Ward, my remarks on these subjects will be a little bit more brief than I had intended them to be. I have greatly enjoyed both of these contributions and wish particularly to thank Dr. Foltz for the privilege of reviewing his paper several days ago.

Drs. Ward and Foltz have also accorded me the opportunity of presenting some of our own material in discussing both of these papers, and I am going to show a movie, because I have a question that bears upon it. [Motion picture]

In the course of evaluating the accuracy with which focused ultrasound could produce discrete lesions in the midbrain of a cat, we observed this postoperative result. I don’t know whether you can see the torsion of the head, which we naively called a torticollis, but you can see that it is not a fixed position, and that righting reflexes tend to overcome the position of the head, and the animal also has difficulty in turning over on his left side, although he turns to his right very well. As soon as he becomes erect, as you can see, he assumes the same twisted position of his head.

Is this what Dr. Foltz means by spasmotic torticollis?

[Slide] Eight separate lesions were placed in the region of the red nucleus, as you can see from this crude diagram. The object of this particular study was to see how accurately we could destroy the red nucleus with a beam of focused ultrasound.
[Slide] Here you see the maximum longitudinal extent of the lesion and it is stained with Trypan blue. We always inject Trypan blue just when we finish irradiating these animals in order to have the lesions, some of them very small, picked up easily at the time that we cut the brain.

[Slide] And this lesion, stained according to Spielmeyer's technique, shows the maximum volume of the lesion.

My point is this, that any one of the discrete lesions that we made in attempt to destroy the red nucleus might have produced the torticollis in the cat that you have seen. I'm not convinced that Dr. Foltz has defined the exact area that is responsible for torticollis any more than we have. I do feel that he has the target bracketed.

Since his neurophysiologic acumen and that of the Ward-Foltz group is well known and highly respected, and since I happen to know they have the necessary ultrasonic equipment, and since I would disagree with him that it is a very complicated procedure as it is set up in his laboratory, I would urge him to get on the ultrasound band wagon and explore this central area with very discrete lesions at 2.7 megacycles and see if he cannot really pinpoint that area that is responsible for torticollis.

DR. HENRY T. WYCH: In 1950, Spiegel, Kimberly and Baird produced lesions in cats in the rhombencephalon showing that when the lesion encroached from the vestibular nuclei on the dorsal lateral part of the reticular formation, persistent changes in posture of the head (similar to spasmodic torticollis) appeared. Lesions of the vestibular nuclei alone produced much slighter postural changes of the head than when both types of lesions were combined.

I would like to show you two slides. Slide 1 shows the tonic posture of the cat's head after a lesion in the dorsal lateral portion of the reticular formation and the vestibular nuclei. Slide 2 shows the histologic lesion encroaching on the dorsal lateral part of the reticular formation.

Recently Dr. Spiegel and I have made a lesion in the medial reticular formation of man in a case of Parkinson's disease with oculogyric crises. The tremor was completely abolished in the contralateral upper limb and markedly reduced in the lower limb. However, this small lesion, which is just dorsal to the red nucleus (about 4 mm. lateral from midline involving the medial reticular formation), did not produce any change of posture of this patient's head.

I would also like to mention that in 1950 Dr. Spiegel and I produced lesions in the substantia nigra. This was in a case of hemiballismus. The ballistic movements were alleviated. The patient died about 4 weeks after surgery from a bronchial pneumonia. Anatomic sections, reproduced in 1952 in Vol. I of our monograph, showed that the lesion was correctly placed in the substantia nigra.

DR. CLAUDE M. BERTRAND: I certainly agree with Dr. Meyers on the need to make precise and minimal lesions within the structures at the base of the brain.

I would like to mention again a simple method of destruction that was used in some 60 cases during the past 5 years.

A fine, blunt-wire leukotome is used in conjunction with a guide.

[Slide] After roentgen rays have been centered in a position 10 mm. below and behind the foramen of Monro, and 15 mm. from the midline, individual variations and possible errors are corrected for by recording and stimulation with a triple lead needle electrode.

[Slide] Then the leukotome is placed in the desired position and section is done by closing and opening every 45 degrees so as to avoid possible traction on blood vessels. Motor power and vision are checked constantly while the lesion is being made.

There have been no instances of hemianopia or hemiplegia in the last 40 cases, which were done in this fashion. This method is accurate, it is safe, it is precise, and it is simple and adaptable on a standard craniograph. Ultrasounds create a lesion which may be very accurately localized, but stimulation and recording and visibility by roentgen rays are so far not its prerogatives.

A point of interest to neurosurgeons is the fact that prothrombin time falls to values as
low as 25 per cent of normal in the 48 hours after lesions have been made. Vitamin K should be given systematically to these patients.

I would like to stress again the importance of not rushing into the substantia nigra and into the thalamus, since all the basal structures seem to be vital to personality. Let us tread very carefully and with trepidation in that region.

Dr. Foltz has brought out the fact that one could produce spasmotic torticollis. In our cats, with lesions in the medial tegmentum, we got mostly tremor and rigidity, but our lesions are more medial although we did get a 3rd nerve palsy in our cases, too.

Dr. Wallace B. Hamby: It seems fitting in a discussion of this sort that we have a representative of Dr. Cooper's clinic here in Dr. Bravo, who would like to make a few remarks on this subject.

Dr. Gonzalo Bravo: I would like to thank Dr. Meyers for his invitation to comment on his paper following my visit to the service in Iowa City. I saw 7 of his 12 patients operated upon there and witnessed one or two stages of 4 ultrasound operations. My comment is to be based on those cases and to take into consideration our experience in Dr. Cooper's service during the 2½ years in which 500 patients with Parkinson's disease have been operated on.

I agree with every word Dr. Ward said about ultrasound and, at the same time, I would like to emphasize that I see ultrasound as a powerful research tool. From a clinical point of view, however, the following facts should be considered: (1) Ultrasound surgery requires 12 hours of surgery on a patient, in two stages. I have seen Parkinsonian patients go to pieces without surgery with such minimal traumas as a strange atmosphere in the hospital or just a pneumoencephalogram. (2) Four superficial burr holes and one through burr hole have to be placed, a needle has to be introduced and a Thorotrast ventriculogram has to be performed. A large 4×5° bone flap has to be turned down, the flap has to be absolutely dried by electrocoagulation, the dura mater has to be exposed for hours under water. (3) Aiming at the target area is based on stereotactic calculations which carry a wide margin of error. (4) I believe that among the 12 patients operated upon by Dr. Meyers there have been some serious complications, including two hemiplegias with aphasia. It is possible that these complications were temporary, and so might be the favorable results, considering the short postoperative follow-up time.

At the present time I think there are other ways to treat the Parkinsonian patient surgically. Ultrasound surgery is to be considered as a research tool but in our minds it is not the elective way to treat the symptoms of Parkinson's disease.

Dr. W. J. Fry: I wish to emphasize first that the lesion produced by a single exposure to ultrasound is, in general, small compared to the structure to be affected. Hence, to implicate a particular structure an array of shots is required. The lesion is thus shaped and oriented by observing the changes produced in the patient's subjective and objective manifestations after each individual exposure.

The question regarding the precision with which the focus of the ultrasound is positioned requires two comments. The first concerns the accuracy of geometric placement of the focus and the second, the accuracy of positioning of the focus with respect to a given structure. Geometric placement was checked by interposing excised brains of animals and humans between the transducer and an acoustic probe at the focus so as to measure the shift of the focus produced by such tissue. At the frequency used in our work, measurements indicate that a geometric accuracy of the order of 0.2 to 0.4 mm. can be realized at the greatest depths of the human brain. On the other hand, determination of accuracy of placement of lesions with respect to the structure to be affected is a problem common to all procedures, regardless of the method of making the lesions. In this connection, histological findings constitute the only dependable data. Since there has been no mortality and hence no histologic material in our series thus far, we can tentatively employ as an index of positioning accuracy the change in the signs and/or symptoms (e.g., tremor, rigidity and aching of muscles) following the first exposure to ultrasound. Thus, in all 5 "substantia nigra" cases in which the focus of the
ultrasound for the first exposure was similarly positioned, a marked reduction in the tremor of the patients' contralateral upper extremities was produced. The consistency of this result, taken in conjunction with other findings regarding somatotopographic representation in this region, indicates that the positioning accuracy of the focus with respect to the target site is probably within 1 mm.

Dr. Ward's comments prompt some remarks on accuracy of calibration. It is certain that to realize predictable selective differentiation among tissue components (neural parenchyma, glia, blood vessels) careful control of dosage is required. Such control is readily possible with appropriate instrumentation. With stable and accurately calibrated acoustic probes, one can routinely predetermine ultrasonic dosages to values that result in selective action. As stated above, no histologic sections on the irradiated human brain are at hand but we have found that the tissues of the central nervous system of rat, cat and monkey require essentially equal dosages of ultrasound to produce the same type of selective action. Empirically, therefore, we started the human work by employing the same dosages that produce selective changes in the animals.

The size of the bone flap removed for the ultrasonic procedures reported here is about the average flap reflected for removal of a brain tumor.

Dr. Bertrand suggests that needles and cannulae possess an advantage over ultrasound in so far as "placement accuracy" is concerned, stating that by means of roentgen-ray methods the tips can be readily seen. I would like to emphasize that such visualization is exactly equivalent to seeing the tip of the pointer used in the ultrasonic method. As our slides demonstrated, the pointer tip used for positioning is seen on the roentgenograms together with the brain landmarks. Positioning accuracy is certainly no worse here than that of a needle inserted into the brain and viewed by roentgen-ray methods.

It seems appropriate to remark that needle and cannula procedures suffer from the considerable limitation that a lesion is produced by enlargement from a fixed center, namely, the position of the tip of the needle or cannula. By such procedures, shaped and oriented lesions could only be produced by penetrating the tissue a number of times. Clearly, the amount of damage that would be imposed upon intervening tissues precludes the use of such techniques. This limitation does not inhere in the ultrasonic method, since the focus of the beam can be freely moved to any desired number of positions and the preselected sites can be irradiated without damage to intervening tissue.

Concerning Dr. Bravo's comments on the patients he examined at Iowa, we wish to emphasize first that, since the primary objective of our present program is the investigation of mechanisms, we have planned and have accomplished a number (three) of distinctly different irradiation procedures on several groups of patients. The application of one of these resulted in undesirable complications in 2 of 3 cases. One of these, to which Dr. Bravo referred, will probably manifest a permanent hemiparesis, but we are not yet certain of the degree thereof because the patient continues to improve slowly. The other patient is markedly hemiparetic and apathetic and appears likely to remain so.

With regard to reoperation, we took the view in the first 3 cases (in which we were gaining experience) that it was preferable to subject the patient to a second procedure rather than to irradiate "too much" structure at the first. For example, in Case 1 the procedure was terminated when complete relief of rigidity in the contralateral limbs was obtained but tremor was unaffected by irradiating in the "ansal" region. The patient was re-admitted 5 months later for a second procedure and was irradiated in the "nigral" region to completely eliminate the tremor in the same limbs. In Case 4, as Dr. Meyers indicated, we eliminated tremor from the contralateral limbs by irradiating a portion of the substantia nigra complex immediately after eliminating rigidity by irradiating the "ansal" region.

DR. ELDON L. FOLTZ: In answer to the comments raised, it is pertinent to point out that the most striking clinical characteristic of the torticollis we have described in the monkeys is its spasmodic nature. Under a normal placid environment, the torticollis may be scarcely obvious and the animal may appear normal, yet whenever activation of the reticular forma-
tion by any of a number of causes occurs, the torticollis immediately becomes evident. This characteristic is present only when the responsible lesion is a very small one as we have demonstrated.

If, on the other hand, the lesion is a larger one in this same critical region, then a more or less tonic torticollis may be produced, as demonstrated by Dr. Ballantine in his movie. In these cases, additional neurological deficits are likewise present. We might say that such a torticollis is then only a part of the neurological deficits instead of the only neurological deficit present as is the case when the lesion is minimal.

The spasmodic nature of the "pure" torticollis is apparently directly related to activation of the reticular formation. Such increased neuronal activity then brings out the defect, as is true in most hyperkinesias. The reticular formation may be activated by postural mechanisms, by incoming or ascending sensory impulses, or by emotional stress, etc.

We have shown that the "pure" spasmodic torticollis is produced by a small discrete lesion in the upper midbrain which primarily involves medial reticular formation. Our experience and the evidence from the other investigators that we have cited indicate that damage of the medial reticular formation is the cause of this torticollis.