THE ORIGIN OF THE NEURAL ACTIVITY RESPONSIBLE FOR CANINE CHOREA

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INTRODUCTION

A specific type of muscle contraction occurring in dogs has been known for many years. These muscle contractions are generally considered a result of nerve tissue damage from an infection with the virus of distemper. Blaine (1817) wrote, "The distemper is very frequently attended with convulsions: it is also now and then preceded by them. These convulsive affections are of two kinds: one is a simple paralytic affection, which, in addition to the weakness, frequently leaves a spasmodic twitching also in one or more of the limbs for life. The other is a perfect fit...."

Although Blaine mentioned only involvement of the limbs, other areas of the body known to become involved include abdominal, thoracic, and cervical musculature, temporal and masseter muscles, tongue, anal sphincter, and retractor bulbi muscles. Various combinations of muscles involved occur in different patients.

The outstanding feature of this abnormal muscle activity is the repetitive contractions of the same muscle, or the same group of muscles, for indefinite periods of time. This repetitive nature of the muscular activity in the same muscles of an individual patient has no counterpart in man.

Various names such as tic, tremor, twitch, spasms, hyperkinesia, and myoclonus have been given to this condition. However, the term most commonly used is chorea, and because of its wide acceptance and familiarity it will constitute the terminology used in this study.

The location of the inciting factor responsible for initiating

chorea is unknown. The pathologic physiology involved in the maintenance of the repetitive nature of chorea is also unknown. The purpose of this study was to investigate the site of the neural discharge responsible for the muscle contractions of chorea.

REVIEW OF LITERATURE

Whittier (1956), cited eight references written before 1900 pertaining to experimental surgical procedures on dogs with chorea. The following comments concerning these eight references are given as interpretated by Whittier.

Chauvau (1862), in an attempt to perform euthanasia, transected the cervical spinal cord of a dog with chorea and noted continued muscular activity after the transection. Contractions of the thoracic musculature provided sufficient respiration to maintain life. Carville (1869), Gowers (1875), Gowers and Sankey (1877), Quincke (1885), and Horsley (1886), all noted that dividing the spinal cord of a dog with chorea did not stop muscular activity caudal to the transection. LeGros (1870), in addition to reporting persistence of the muscle contractions after spinal cord transection, demonstrated a decrease in forcefulness of the contractions following section of certain dorsal roots, and abolition of the contractions following section of pertinent ventral roots or section of the motor nerves. LeGros also observed that the force of muscular activity was decreased if the spinal cord was stimulated above the level of activity, and increased if stimulated from below. Horsley (1886), reported abolition of the muscular activity following section of pertinent motor nerves. Wood (1893), demonstrated persistence of the muscle contractions after transection of the spinal cord, and noted the force of activity was markedly increased following section, and that the frequency became asynchronous between rostral and caudal segments. Muller (1897), made the observation that if the patients were left to themselves the

twitching was generally less marked, but that under physical excitement became much more aggravated.

There have been four reports since 1900 pertaining to experimental surgical procedures on dogs with chorea. McGovern (1948), reported results of unilateral excision of the premotor cerebral cortex in three dogs. Prior to surgery unilateral electrical stimulation of the excitable motor cortex appeared to potentiate the chorea on both sides of the body. He demonstrated that stimulation of the premotor suppressor band inhibited muscular activity. A summary of McGovern's three cases follows:

1. Excision of the left premotor cortex was performed on a dog with chorea of both rear legs and the left foreleg. Two weeks after the operation the chorea was much worse being pronounced in all four limbs. Two months following the operation the chorea had disappeared in the left front and left rear limbs, but was still present, although reduced, in the right rear limb. Ten weeks after the operation the chorea became more pronounced in the right rear limb and euthanasia was performed.

2. Excision of the right premotor cortex was performed on a dog with chorea of the left front leg, left rear leg, and both temporal muscles. Two weeks following the operation the chorea had increased in force in the left rear limb, and was present in both limbs of the right side. By the end of three weeks there was pronounced activity in all four limbs, and in the mandibular musculature. The activity gradually diminished so that by the end of five weeks after the operation it had completely disappeared from all regions of the body.

3. Excision of the right premotor cortex was performed on a dog with chorea of the neck muscles. There appeared to be some stiffness in the front legs. The rear limbs were normal. Ten days following the operation the chorea was much more severe and had spread to all the forequarter muscles. During the next three weeks the chorea gradually became less pronounced and by eight weeks had disappeared.

Turbes (1954), noted that stimulation of the contralateral motor cortex, cerebral peduncles, and pyramids, resulted in cessation of the muscular activity. Turbes also reported the muscular activity was abolished

by ventral and dorsal rhizotomy, by muscle tenotomy, and by bone fracture with a shortening effect on the musculature.

Whittier (1956), reported persistence of the muscular activity following bilateral ablation of the anterior cerebrum and after sectioning of the corticospinal tracts at the level of the medulla. Whittier also reported a decrease in characteristics of the muscle contractions following transection of dorsal roots, and cessation of activity following transection of ventral roots.

Breazile (1966), transected the spinal cord between the last thoracic and first lumbar vertebra in six dogs and noted an immediate increase in rate of the movements of the rear limbs in each case. He further reported that transection of the dorsal roots of all nerves caudal to the spinal cord transection did not influence the rate or forcefulness of the muscular activity. Breazile used electromyographic recordings to demonstrate the presence of synchronized muscular activity in both flexors and extensors of the same limb. After transection of the dorsal roots, the electromyographic activity was abolished in those muscles antagonistic to the observed movement of the limb. He concluded the activity of the antagonists was reflexly induced by stretching of these muscles during the spontaneous contraction of the agonists.

MATERIALS AND METHODS

Thirteen dogs with chorea were obtained from Manhattan, Topeka, Salina and Kansas City. The status of each dog regarding breed, age, sex, location of the chorea, and duration of the chorea prior to surgery, is listed in Table 1.

The specific muscles involved were generally not identified, especially where the chorea involved neck, trunk, and abdominal musculature. However, where chorea involved a rear limb, the observed movement of the limb was flexion and the most noticable muscles involved were the semitendinosus and anterior tibial muscles. Where chorea involved a front limb, the observed movements were flexion of the elbow and extension of the carpus. In these cases the most noticable muscles involved were the biceps brachii, brachialis, and the extensor carpi radialis.

The rate and forcefulness of the muscle contractions of the limbs with the dogs at rest, and when aroused, were noted prior to surgery. Dogs were considered resting when lying in the cage with their head down and eye-lids closed. They were considered aroused when they opened their eyes. Walking in front of the cage, or opening the cage door were sufficient stimuli to cause arousal. The forcefulness of the muscle contractions was measured by observation of the degree of gross limb movements and changes were recorded as either increased or decreased.

Intravenous pentabarbital, without pre-medication, was used as the anesthetic. Neither tracheal intubation nor artificial respiration were used. The initial anesthetic dose was approximately 12 mg. per pound.

Table 1. Status of Thirteen Dogs With Chorea.

Dog	Breed	Age	Sex	Location of Chorea	Duration of Chorea
1	Mix	1 year	M	All four limbs	3 months
2	Scotch Terrier	1 year	F	Right rear limb	6 months
3	Mix	8 months	M	Temporal, masseter, both rear limbs	7 days
4	Mix	1 year	M	Both front limbs, neck & trunk	3 months
5	Mix	1 year	F	Both rear limbs	6 months
6	Pointer	3 months	M	Both rear limbs	3 days
7	Labrador	14 months	F	Right front and right rear limbs	10 days
8	Wire Hair	5 months	M	Left front limb	20 days
9	Beagle	1 year	F	Right rear limb	Unknown
10	Labrador	1 year	M	Right rear and left front limbs, Abdominal	14 days
11	Mix	2 months	M	Right rear limb, Temporal	3 days
12	Mix	2 months	F	Left rear limb	6 days
13	Mix	9 months	F	Right rear limb	3 months

Anesthesia was produced by slow administration of the anesthetic in all except four dogs (1, 3, 12, 13). These four dogs were anesthetized by rapid injection of the anesthetic agent.

The hair was clipped, the skin scrubbed with surgical soap and the area draped for each surgical procedure.

A spinal cord transection between the last thoracic and first lumbar vertebra was performed on five dogs (1, 3, 5, 6, 7). Transection of the spinal cord was accomplished by incising the skin and fascia the length of four vertebra close to the dorsal spines of the last two thoracic and first two lumbar vertebra. Muscles were removed from the lateral surface of the vertebral arches by blunt dissection. The spinal canal was opened by removing the caudal articular process of the last thoracic and the cranial articular process of the first lumbar vertebra with rongeurs. The dura was grasped with forceps and the circumference of the dura plus the spinal cord was cut with scissors. Following transection, the cut ends of the spinal cord retracted from each other. Three dogs (3, 5, 6) were not allowed to recover from anesthesia. Dogs 1 and 7 were allowed to recover from anesthesia and were maintained for 19 days and 10 days respectively. Following spinal cord transection and recovery from anesthesia, a rate of front and rear limb movements was first recorded in dog 1 without opening the cage door while he was lying in the cage. He was then lifted to a standing position and a second rate obtained. This procedure was performed daily on dog 1 for 10 days.

A rate of front and rear limb movements was first recorded in dog 7 without opening the cage door while she was lying in the cage. Other stimuli were then applied; pinching the toe or pinching the muscles with

the fingers of one hand and application of pressure to the foot or tail. Contraction rates were recorded during application of the stimuli and immediately following cessation of the stimuli in dog 7.

Spinal cord transection plus dorsal rhizotomies were performed on dogs 2, 10, 11, 12, and 13. The skin and fascia were incised on both sides of the dorsal spines of the vertebra from T10 to the sacrum. The muscles on both sides of the dorsal spines for the entire length of the incisions were removed with scissors. The spinal canal was opened with rongeurs between the last thoracic and first lumbar vertebra as previously described, and the dura and spinal cord transected at this site. Then the dorsal spines, lamina, and articular processes of all vertebra from this opening to the sacrum were removed with rongeurs. Hemorrhage was controlled by applying pressure with strips of cotton. It was necessary to ligate the dorsal branch of the intercostal artery on either side of the fifth lumbar vertebra. The opening was extended until it was nearly level with the ventral surface of the spinal canal thus revealing the dorsal root ganglia. The dorsal and ventral roots of the three sacral and all coccygeal nerves were transected as they crossed the junction between the last lumbar vertebra and the sacrum. The dorsal and ventral roots of the first three lumbar nerves of both sides were transected. The innervation to both rear limbs now consisted of only four intact nerves (L4, L5, L6, L7) on both sides of the spinal cord. The dorsal roots of these remaining nerves were cut in succession, first on one side, then on the other side. On dogs 2 and 10 with dorsal rhizotomies, the dura was opened and the numerous dorsal root filaments were cut adjacent to the spinal cord. On dogs 11, 12, and 13 the dura was not opened, the individually enclosed dorsal and ventral roots were bluntly separated extradurally,

and the dorsal root transected. Following completion of spinal cord transection and dorsal rhizotomy on dog 13, the four ventral roots (L4, L5, L6, L7) of both sides were cut and the spinal cord was removed from the spinal canal. Dogs with combined spinal cord transection and dorsal rhizotomy were not allowed to recover from anesthesia.

Intracranial surgery was performed on dogs 4, 8, and 9. All brain tissue rostral to the pons was removed from the cranial cavity of dogs 8 and 9. To accomplish the cerebral ablations in dogs 8 and 9, a skin and fascia incision was made from between the orbits, along the external sagittal crest to the external occipital protuberance. Temporal muscles of both sides were reflected ventrally as far as possible, and the calvarium removed with rongeurs. The dura over each cerebral hemisphere was incised. The cerebral hemispheres were removed through the dural opening. All remaining brain substance to the rostral border of the pons which included the olfactory tracts, thalamus, hypothalamus, and mid-brain, was removed from the skull with the handle of a scalpel. The internal carotid arteries at the optic chiasm and the basilar artery at the rostral border of the pons were crushed with hemostats. The entire cavity was then packed with cotton and pressure maintained until hemorrhage ceased. Following cerebral ablation in dog 9, the spinal canal was opened between the last thoracic and first lumbar vertebra as previously described, and the spinal cord transected at this site. No additional surgery was performed on dog 8.

Bilateral removal of the anterior and posterior sigmoid gyri was performed on dog 4. A four inch skin and fascia incision was made from between the orbits, extending caudally along the external sagittal crest.

The temporal muscles of both sides were reflected ventrally and the bone over the sigmoid gyri was removed with rongeurs. The dura was incised over each hemisphere and the gyri were removed with the handle of a scalpel. The fascia and skin were sutured with 00 silk. The dog was allowed to survive for 12 days.

The tendon of insertion of three different actively contracting muscles were freed in dogs 4, 10, and 11. The extensor carpi radialis tendon of the left foreleg was freed from its attachment to the metacarpals on dog 4 on the day of euthanasia, 12 days after the bilateral removal of the anterior and posterior sigmoid gyri. The brachialis tendon of the left foreleg was freed from its attachment to the radius and ulna in dog 10, 30 minutes after spinal cord transection and dorsal rhizotomy was performed. The anterior tibial tendon of the right leg of dog 11 was freed from its attachment on the metatarsals 5 minutes after the spinal cord transection, but before dorsal rhizotomy.

Dogs 5, 12, and 13 received 100mg. of 2% procaine intravenously three days before operative procedures were performed.

RESULTS

All dogs had visible limb movements occurring at the rate of 60 to 80 per minute while at rest prior to surgery. All dogs except two (1, 7) had visible limb movements of 100 to 120 per minute when aroused. Dog 1 was handled daily including temperature taking and venapuncture for two months prior to his inclusion in this study. He was an unexcitable dog with a limb movement rate in his cage or on the examination table of 65 to 80 per minute. Dog 7 was the only dog in which counts were made while asleep. The rate of limb movements of this dog changed from 70 per minute when asleep to approximately 160 per minute when aroused. The forcefulness of the muscle contractions increased with arousal in all dogs except dog 1. The rate and forcefulness of the contractions of the temporal muscles noted in dogs 3 and 11 were more erratic than limb movements noted in any of the dogs. Approximately 75% of the temporal muscle contractions were distinct and seemed to involve the whole muscle, while the other contractions were indistinct and seemed to involve only part of the muscle. There was notable lack of definite rhythm to the rate of the temporal muscle contractions. Several contractions in rapid succession would be followed by several contractions with longer intervals between the contractions. The rate of the temporal muscle contractions of dogs 3 and 11 ranged from 40 to 50 per minute and were not synchronized with the limb movements of either dog.

Where more than one limb was involved on the same dog, casual observation of the gross limb movements suggested that the movements of the different limbs were synchronized. However, if the movements were observed

for a period of time, eventually a contraction would occur in one limb without a simultaneously occurring contraction in the other limb. By placing a hand on each of two involved limbs of the same dog, small muscle contractions not producing a gross movement of the limb could be palpated. The small contractions did not occur simultaneously in the two limbs, and were sufficiently erratic in rate as to negate attempts to count their rate.

Pentabarbital when administered slowly produced a decrease in the forcefulness of the contractions. Slow induction of anesthesia to deep surgical levels resulted in a decrease of the rate to approximately 50 per minute. When the anesthetic was continued to produce euthanasia, a point was reached immediately prior to death where the contractions could be seen but no longer caused a movement of the limb. Pentabarbital administered rapidly resulted in cessation of the movements of the rear limbs in dogs 1, 3, 12, and 13 during induction of anesthesia prior to surgery. Dogs 12 and 13 had chorea in only one rear limb and in both instances the movements ceased following rapid induction. Dog 3 had chorea of both rear limbs and the temporal and masseter muscles. The movements stopped in the rear limbs but continued in the temporal and masseter muscles following rapid induction of anesthesia. Dog 1 had chorea of both front and both rear limbs and the activity stopped in the rear limbs but continued in the front limbs following rapid induction of anesthesia. In each instance where cessation of rear limb movement followed rapid induction of anesthesia, activity returned in the rear limbs within ten minutes, even though the level of consciousness remained unaltered at a surgical level. Surgical procedures performed on each dog are listed in Table 2.

Table 2. Surgical Procedures Performed on Thirteen Dogs With Chorea.

Dog	Cord Transection	Dorsal Rhizotomy	Cerebral Ablation	Tenotomy
1	Yes	No	No	No
2	Yes	Yes	No	No
3	Yes	No	No	No
4	No	No	Bilateral Ant. & Post. Sigmoid gyri	Ext. Carpi Radialis
5	Yes	No	No	No
6	Yes	No	No	No
7	Yes	No	No	No
8	No	No	All rostral to pons	No
9	Yes	No	All rostral to pons	No
10	Yes	Yes	No	Brachialis
11	Yes	Yes	No	Ant. tibial
12	Yes	Yes	No	No
13	Yes	Yes	No	No

RESULTS OF SPINAL CORD TRANSECTION

Muscle contractions of the rear limbs continued without interruption following spinal cord transection in dogs 1, 3, 5, 6, and 7. There was an immediate increase in the rate and forcefulness of the movements of the rear limb or limbs of dogs 3, 5, and 6. This was observed to the greatest degree in dog 3 where the rate of rear limb movements increased from 80 to approximately 160 per minute. The rate increased in dogs 5 and 6 from approximately 60 before the transection to 100 per minute after the transection. No change in rate of the contractions of the temporal and masseter muscles occurred in dog 3, nor of the front limb movements of dog 6. During attempts to count the femoral pulse of dog 5, the rear limb movements were noted to increase each time the quadriceps muscles were squeezed over the femoral artery. Dogs 1 and 7 were allowed to survive following spinal cord transection. Both had chorea of front and rear limbs. Neither dog exhibited an increase in rear limb movements following spinal cord transection. Rates of front and rear limb movements of dog 1 following spinal cord transection are noted in Table 3.

Dog 7, also allowed to survive spinal cord transection, had a limb movement of 70 to 80 per minute while at rest, and a rate approximately 160 per minute when aroused prior to induction of anesthesia. Chorea was present in the right front and right rear limbs. Just prior to spinal cord transection, the dog received additional anesthetic and a rate of 42 for both limbs was recorded which did not change after spinal cord transection. Ten minutes after transection a rate of 44 per minute for both legs was present, and thirty minutes after the transection the front limb rate was 54 while the rear limb rate was 40 per minute. Some recovery from anesthesia could be seen at this time. Twenty hours after the tran-

Table 3. Rates Per Minute of Front and Rear Limb Movements of Dog 1, for 10 Days Following Spinal Cord Transection.

DAY	ATTITUDE	FRONT LIMB RATE	REAR LIMB RATE
1	Lying in cage	103	76
	Held in standing position	121	77
2	Lying in cage	105	75
	Held in standing position	103	77
3	Lying in cage	117	76
	Held in standing position	123	77
4	Lying in cage	107	79
	Held in standing position	108	84
5	Lying in cage	101	75
	Held in standing position	115	88
6	Lying in cage	64	65
	Held in standing position	163	80
7	Lying in cage	75	78
	Held in standing position	103	85
8	Lying in cage	76	76
	Held in standing position	87	88
9	Lying in cage	83	75
	Held in standing position	84	75
10	Lying in cage	81	83
	Held in standing position	85	86

section, following complete recovery from anesthesia, the resting and undisturbed rate of the front limb was 90 while the rate of the rear limb was 44 per minute. Rates associated with various forms of stimulation after spinal cord transection are noted in Table 4.

RESULTS OF SPINAL CORD TRANSECTION PLUS DORSAL RHIZOTOMY

The forcefulness of the rear limb movements diminished in dogs 2, 10, 11, 12, and 13 following transection of the dorsal roots. The first dorsal rhizotomy was performed on dog 2. This dog had chorea of the right rear limb only which did not change in rate after the spinal cord transection. Additional anesthesia had been administered just prior to the spinal cord transection. In dog 2 the dura was opened and the dorsal root filaments cut adjacent to the cord. The chorea stopped after all dorsal roots were cut on dog 2, and was not present 20 minutes later at the time of euthanasia.

Dorsal rhizotomy via the open dura was performed in dog 10. This dog had chorea of the right rear and left front limbs and abdominal musculature. When anesthetized, but before surgery, both limbs appeared synchronized at a rate of 48 per minute. Immediately following spinal cord transection the front limb rate was 48 while the rear limb rate was 100 per minute. After all dorsal roots were cut there were faint muscle contractions remaining in the right rear limb.

The dura was not opened in the dorsal rhizotomy preparations in dogs 11, 12, and 13. Dog 11 had chorea including the temporal muscles and the right rear limb before anesthesia and spinal cord transection, but in both rear limbs and temporal muscles following spinal cord transection. After all dorsal roots were cut on dog 11, faint muscle contractions occurring at a rate of approximately 160 per minute were noted.

Table 4. Rates Per Minute of Front and Rear Limb Movements of Dog 7, 20 Hours Following Spinal Cord Transection.

METHOD OF STIMULATION	RIGHT FRONT LIMB RATE	RIGHT REAR LIMB RATE
None, lying in cage	90	44
Opened cage door, placed hand on head	200	40
Pinching toe of right rear foot	150	80
Pinching flexors of right knee	150	100
Pinching right quadriceps	150	96
Pressure on left rear foot	150	100
Release of pressure from left rear foot	150	36
Pressure on left rear foot	150	96
Release of pressure from left rear foot	150	40
Pressure on left rear foot	150	120
Pinching flexors of left knee	150	92
Stopped pinching flexors of left knee	150	40
Pressure on tail	150	72
Release of pressure on tail	150	40
None, lying in cage	110	36

The faint contractions were present at the time of euthanasia 10 minutes later.

Dog 12 had chorea of the left rear limb only. After four dorsal roots (L4, L5, L6, L7) on the right side were cut the forcefulness of the movements of the left limb was much reduced and occurred at a rate of approximately 160 per minute. Additional anesthetic was administered and the rate reduced to approximately 76 per minute. After the dorsal roots of L4, and L5 on the left were cut the movements appeared to stop. However, close examination revealed a faint movement in the left semitendinosus muscle occurring at a rate of approximately 124 per minute. The muscle contractions continued after the two remaining dorsal roots (L6, L7) on the left were cut.

Dog 13 had chorea of the right rear limb. This dog was recovering from anesthesia before spinal cord transection was accomplished. The rate of the rear limb movements was approximately 150 per minute before and following spinal cord transection. When additional anesthetic was administered the rate decreased to about 80 per minute. After all dorsal roots were cut the movements ceased except for faint contractions of the semitendinosus muscle on the right limb. The four remaining ventral roots (L4, L5, L6, L7) of both sides were then cut and the cord removed from the spinal canal. The muscle contractions continued and were present 10 minutes later at the time of euthanasia.

RESULTS OF CEREBRAL ABLATIONS

Following the removal of all brain rostral to the pons of dog 9, the movements of the right rear limb continued unchanged. The spinal cord was then transected and again the rear limb movements remained unaltered. Following either the brain ablation or the spinal cord transection, the

movements of the right rear limb could be increased from 48 to about 100 per minute by squeezing the muscles of the involved limb.

Removal of all brain rostral to the pons of dog 8, resulted in the movements of the left front limb continuing unchanged. The limb movements were present four hours later at the time of euthanasia.

Dog 4 was allowed to survive 12 days following bilateral ablation of the anterior and posterior sigmoid gyri. The dog had chorea of both front limbs, the neck, and trunk before surgery. He could rise, support weight and walk only with assistance. The pre-surgical movements were erratic in forcefulness and irregular in rhythm. Following surgery chorea appeared in both rear limbs and the movements in all previously involved muscles became more forceful and more regular in rhythm. There was no appreciable change in the rates after surgery from the pre-surgical rates in either the resting or aroused state. During the 12 days the dog could not rise, but could support weight if his feet were placed properly.

RESULTS OF TENOTOMY

Affected muscles in three of the subjects were freed from their insertion to bone. These were the brachialis muscle in dog 10, the anterior tibial muscle in dog 11, and the extensor carpi radialis muscle in dog 4. All muscles continued to contract even though their insertion was free.

RESULTS OF INTRAVENOUS PROCAINE

Dogs 5, 12, and 13 were given 100mg. of 2% procaine intravenously. All muscle contractions stopped abruptly following the administration. The dogs appeared normal and could walk without signs of chorea. Ten to 30 minutes after receiving procaine the chorea returned in the same muscles previously involved.

DISCUSSION

The rate of the visible muscle contractions of the limbs of a resting or undisturbed dog with chorea is characteristic in this disease. A resting contraction rate of 60 to 80 per minute increased in all dogs, except dog 1, when they were aroused with visual or auditory stimuli. It was not necessary to touch the dogs in order to produce the increase in rate. The forcefulness of muscle contractions also increased with the increase in the rate in all subjects except dog 1. Although forcefulness was measured by observation only, the muscle contractions varied from barely perceptible limb movements at rest, to contractions that caused marked flexion of a limb when aroused. These observations confirm the report of Muller (1897), that the twitching action is aggravated by excitement. Observation of changes in rate and forcefulness of muscle contractions, where the arousal stimuli were visual or auditory without touching the dog, suggests the brain is capable of altering the movements of the limbs.

Persistence of the movements in all dogs while under surgical anesthesia with pentabarbital is a remarkable feature of canine chorea. When the anesthetic was administered slowly the initial change was a decrease in forcefulness followed by a decrease in rate. In extremely deep anesthesia, when euthanasia was desired, the muscle contractions did not have sufficient force to move the limb, but the rate approximated the unanesthetized resting or asleep rate. It is difficult to account for the cessation of the movements in the rear limbs following rapid administration of pentabarbital, especially since the activity in other muscles continued (dogs 1 and 3). It is postulated the triggering mechanism for the activity in

the rear limbs is more sensitive than in other muscles, thus accounting for the belief that chorea is more often observed in a rear limb than elsewhere.

The observation that rear limb movements continued following spinal cord transection in all eleven dogs, confirms the finding of previous writers. These observations prove unequivocally that neural activity does not originate in the brain then traverse the spinal cord to cause the rear limb movements in chorea. Whether the rate and forcefulness of the muscle contractions of the rear limbs increases, or does not change immediately after transection, appears to depend on the level of anesthesia. That facilatory, excitatory, and inhibitory influences from the brain converge on the lower motor neuron is well known and it has been suggested that the brain is capable of altering the movements of the limbs. However, the results obtained following spinal cord transection establish that concurrent excitatory impulses from the brain do not cause the rear limb movements of chorea. If it is postulated that as anesthesia lightens, the brain is able to exert more inhibitatory influence on the lower motor neurons, then the rate of the rear limb movements should decrease as anesthesia lightens. If it is postulated that as anesthesia lightens the brain is able to exert more excitatory influence on the lower motor neurons, then spinal cord transection should eliminate this excitatory influence resulting in a decrease of activity. Since this was not the situation, it might be assumed that spinal cord transection causes local stimulation of the neural mechanism responsible for the limb movements. Thus it would appear that pentabarbital in addition to reducing cerebral excitatory activity also alters the threshold of the chorea mechanism by changing local sensitivity.

Studies of dog 1 were made one and one-half years before it was learned the rate of rear limb movements could be increased by peripheral stimulation of the rear limbs. There was no appreciable change in rate from the resting to the aroused state in dog 1. It is suggested the reason for no appreciable change in rate was due to lack of anticipation of either a pleasant or unpleasant experience when this dog was approached. He had been handled daily for two months before being included in this study. Following spinal cord transection and recovery from anesthesia, the rate of front limb movements was greater than the rate of rear limb movements for seven days. On days 8, 9, and 10 the front and rear limb rates were similar whether 'lying in cage' or 'held in standing position'. This no response to arousal was similar to the pre-surgical response to arousal, and it is suggested the reason was also similar. Dog 7, allowed to survive spinal cord transection, had chorea of the right front and right rear limbs. The pre-anesthetic rate of both limbs was 70 to 80 at rest, and approximately 160 per minute when aroused. Following spinal cord transection it was evident that stimulation of either rear limb or the tail resulted in an immediate marked increase in the right rear limb movements, and cessation of the stimuli resulted in an immediate decrease in the movements. During this period of applying various stimuli, the front limb rate remained near the pre-surgical aroused rate of approximately 160 per minute. This asynchrony between front and rear limbs remained for the 10 days the dog was allowed to survive. The observation that peripheral stimulation of a rear limb or tail following spinal cord transection resulted in an increased rate and forcefulness of rear limb movements, has not been previously reported. The results reveal that various forms of peripheral stimuli, such as pressure on the tail, pinching

a toe, or squeezing the muscles of a rear limb, have a decided affect on rate and forcefulness of the muscle contractions. This suggests the neural cells responsible for the abnormal activity are hypersensitive to afferent impulses. This hypersensitivity, or perhaps decreased threshold, is not the result of removing cerebral influence over the rear limbs since chorea movements can not be produced by the same peripheral stimuli on cases without chorea but with a spinal cord transection from other causes.

All three dogs (1, 7, 10) with chorea of a front and rear limb or limbs, exhibited marked asynchrony between the front and rear limb movements following transection of the spinal cord. This observation confirms that of Wood (1893) who noted that asynchronous rates between rostral and caudal segments followed transection of the spinal cord. Neither dog 1 or 7 revealed significant change in rate of the rear limb movements following spinal cord transection when changed from a resting to an aroused state. This evidence supports the previous suggestion that a cerebral influence is capable of altering the limb movements, and further suggests that the cerebral influence is mediated through the spinal cord and not by some blood borne substance. It also suggests the origin of the abnormal neural activity is located caudal to the spinal cord transection rather than anterior to the transection such as ballistocardiographic effect might produce. In addition, the asynchrony between front and rear limb movements following spinal cord transection would suggest a multicentric origin for the site of abnormal neural activity. The fact there are so many combinations of different muscles involved in different patients with chorea also suggests a multicentric origin, rather than a single site of explosive neural activity which then spreads to other areas.

Although the type of ablations of brain substance described in dogs

8 and 9 in this study have not been previously reported, the results confirm previous suggestions that the neural activity does not originate in the brain. It certainly does not originate from the basal nuclei or the red nucleus of the mid-brain since these parts were removed. The probability of the encephalitic lesions, commonly reported with chorea, leading to loss of an inhibitory influence on the rear limbs is untenable. Cases of spinal cord transection from automobile accidents, herniated intervertebral discs, or experimental surgery, without the development of chorea are commonly observed, refuting loss of cerebral inhibition as the only etiology of chorea.

It remains to be determined why the chorea of two dogs ceased five to eight weeks after McGovern (1948) performed unilateral excision of the premotor cortex, but was still present in the third dog 11 weeks after the same surgery. That cerebral activity is capable of altering the rate and forcefulness of the muscle contractions is well established. The increase in rate seen when the dogs changed from a resting to an aroused state would indicate an excitatory cerebral influence. In addition, McGovern (1948) produced increased muscular activity by stimulation of the excitable motor cortex. The decrease in rate seen by LeGros (1870) when the spinal cord was stimulated above the level of activity, the decrease seen by McGovern (1948) with stimulation of the premotor suppressor band, and the cessation seen by Turbes (1954) with stimulation of cortex, peduncles, and pyramids, would indicate an inhibitory cerebral influence. Thus it appears that the effects of both excitatory and inhibitory cerebral influences on the rear limb movements may be demonstrated. It is possible that surgery such as McGovern performed could eliminate considerable excitatory influence, leaving inhibition intact, thus decreasing the muscular activity. However, the

five to eight weeks delay before cessation of chorea in two of McGovern's three dogs needs explanation. This finding suggests that some disorder of the brain is responsible for initiating the limb movements, but removal of this initiating factor does not eliminate the limb movements until a certain time has elapsed. Perhaps the initiating cerebral influence could be that of lowering the threshold of the neurons at the local or segmental level involved in chorea, thus making these segmental neurons hypersensitive to stimuli. After removal of the cerebral influence, such as spinal cord transection, or ablation of brain substance, a certain time is necessary for repair and return of normal threshold levels of the segmental neurons.

The muscle contractions diminished to barely perceptible movements after bilateral dorsal rhizotomy in five dogs. These faint muscle contractions did not cause movement of the limbs. On the third dorsal rhizotomy (11) it was noted that the post surgical muscle contractions were different from the short, sharp contractions of chorea. This was also observed on dogs 12 and 13 following dorsal rhizotomies. These same faint muscle contractions also remained following removal of the cord from the spinal canal of dog 13. It may be that these muscle contractions are not the contractions of chorea, but the fasciculations of denervated muscle such as are seen at necropsy when a piece of muscle is removed from a fresh cadaver. Since dorsal rhizotomy would prevent afferent impulses from reaching the spinal cord, and as there was a marked decrease, if not a cessation of the movements after the dorsal rhizotomies, it is suggested that the peripheral afferent supply has a decided influence on the muscular activity. One should not construe, however, that the origin of abnormal activity must be initiated in peripheral nerve. It is more likely that the

hypersensitive cells are in the spinal cord since a cerebral influence on the rear limb movements has also been established. LeGros (1870), and Whittier (1956), reported a decrease in muscular activity after section of dorsal roots. Turbes (1954), reported cessation of the activity after dorsal rhizotomy, while Breazile (1966), reported no change after dorsal rhizotomy. The observation by Breazile that dorsal rhizotomy did not alter muscular activity is the only real discrepancy reported for any surgical procedure by any writer, and it is difficult to suggest a reason. Perhaps his subjects were at a light plane of anesthesia and touching the spinal cord in the process of cutting the dorsal root filaments caused stimulation such as may be produced by transection of the spinal cord. Or perhaps Breazile observed the type of muscle contractions such as were noted in dog 13 of this study after the spinal cord was removed from the spinal canal.

Removing the tendons of the anterior tibial, brachialis, and extensor carpi radialis muscles from their insertions on bone, did not alter the activity in those muscles. This observation differs from that of Turbes (1954), who reported abolition of the activity following tenotomy. If Breazile (1966), is correct that muscular activity of antagonists is reflexly induced, it is possible Turbes removed the tendons of antagonists such as the quadriceps, rather than the agonists which were removed in this study. If such were the case, tenotomy of an antagonist would stop the stretch stimuli in that muscle which was produced by contraction of the agonist, and the muscle contractions would cease in the antagonist. Since tenotomy did not alter the contractions in this study, one can conclude that chorea is not reflexly induced by stretch of those muscles named here.

It must be resolved why procaine administered intravenously stops

chorea yet allows the dog to walk normally and appear mentally alert. Since alterations in cerebral and peripheral stimuli influence rear limb movements, it is possible procaine decreases a hypersensitivity, or raises the threshold, of the lower motor neurons.

SUMMARY AND CONCLUSION

The results of this study allow the conclusion that a muscle contraction in the rear limb of a dog with chorea is not the result of a simultaneous cerebral discharge. However, it was well established that cerebral activity is capable of altering the rate and forcefulness of the rear limb movements by an influence mediated through the spinal cord. The cerebral influence on the rear limb movements was removed upon transection of the spinal cord. The asynchrony between front and rear limb movements following transection of the spinal cord suggests that the brain does not secrete a substance which travels by a route other than the spinal cord to cause rear limb movements.

In addition to the cerebral influence, the chorea mechanism is also altered by peripheral stimuli such as bending the tail or pinching a foot. This peripheral influence on the rear limb movements was removed by transecting the dorsal roots of pertinent nerves.

The results of this investigation suggests that hypersensitive cells located in the spinal cord, caudal to the third lumbar segment and rostral to the sacral segments are involved in chorea of the rear limbs. Transection of the spinal cord plus dorsal rhizotomy removes most, if not all, the afferent supply to the hypersensitive cells. Why these cells are hypersensitive, and which cells are hypersensitive was not established. It is possible the virus has a direct irritant effect on pools of motor neurons or interneurons.

The specific location of the inciting factor responsible for initiating chorea remains unknown. In addition, the physiologic etiology responsible for the repetitive nature of the discharges remains unknown. Although

two dogs (1, 7) in this investigation continued to reveal muscle contractions of the rear limbs for 19 days and 10 days respectively following spinal cord transection, it would be enlightening to allow similar subjects to survive at least three months following spinal cord transection. This longer survival time might strengthen or refute the proposal that some disorder of the brain is responsible for altering the sensitivity of the segmental motor neurons, and more time is necessary for repair and cessation of the chorea.

If chorea of the rear limbs could be produced by injection of the virus following spinal cord transection, the brain could be eliminated as the site responsible for initiating chorea.

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THE ORIGIN OF THE NEURAL ACTIVITY RESPONSIBLE FOR CANINE CHOREA

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Canine chorea is manifested by repetitive muscle contractions of the same muscle, or the same groups of muscles, for indefinite periods of time. The muscles involved may vary in different patients.

In an effort to determine the origin of the abnormal neural activity responsible for canine chorea, 11 spinal cord transections, three cerebral ablations, and five bilateral dorsal rhizotomies from L1 to L7 were performed on 13 dogs affected with chorea. The tendon of an affected muscle was freed from its insertion to bone in three dogs. Procaine was administered intravenously to three dogs. Two dogs with chorea of a front and rear limb were allowed to survive for 10 days and 19 days following spinal cord transection.

The conclusion that neural activity originating in the brain and traversing the spinal cord to cause a rear limb movement is not the mechanism of chorea was based on results of the spinal cord transections and cerebral ablations. Contractions of the muscles of the rear limbs continued without interruption following transection of the spinal cord and following cerebral ablation. Muscle contractions were reduced to barely perceptible movements, or were abolished, by dorsal rhizotomy. Removing the tendon of insertion of affected muscles did not alter the muscle contractions. Intravenously administered procaine caused the contractions to cease for periods varying from 10 to 30 minutes during which time locomotion appeared normal. Surgical levels of pentabarbital anesthesia did not abolish the muscle contractions. Asynchrony of the movements between front and rear limbs which was not present prior to spinal cord transection was apparent in the two dogs allowed to survive spinal cord transection. The observation suggests that a circulating factor is not involved in the muscle contractions of chorea.

The rate of muscle contraction increased when the dogs were changed from a resting to an aroused state thus suggesting that cerebral influence is capable of altering the muscular activity of chorea. The rate of the muscle contractions of the rear limb did not change following spinal cord transection when the dogs were changed from a resting to an aroused state thus suggesting that the cerebral influence is mediated through the spinal cord. Peripheral stimuli such as bending the tail or pinching a rear foot resulted in an increase in the rate of the muscle contractions in the rear limbs following spinal cord transection. This suggests that peripheral stimuli are capable of altering the muscle activity of chorea.

Conclusions based on this study are that cells located in the spinal cord become hypersensitive to cerebral and peripheral stimuli and are responsible for the contraction of affected muscles of the limbs of dogs with chorea. Further research is needed to determine why these cells are hypersensitive and to elucidate the physiology involved in the repetitive nature of the chorea mechanism.