

Responses to Electrical Stimulation of the Premotor Area Following Ablation of The Motor Area in Primates

by

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Cerebral spastic palsy is in most instances due to lesion in the motor and premotor areas or the frontal lobes. Out of 353 cases of cerebral palsy, 2 cases showed clinically the signs of low decerebration and 33 cases the signs of high decerebration. In cases of high decerebrate type, voluntary activity was completely abolished and the postural reflexes were steadily demonstrated. When areas 4 and 6 are bilaterally removed, primates, including man, are virtually reduced to the thalamic reflex status, exhibiting all the postural reflexes. However, in cases of cerebral spastic paralysis showing the signs of paraplegia, diplegia and hemiplegia, some part of the precentral area seems to remain intact. In these cases, isolated movements are somewhat vigorously performed at the proximal joints, though movements which are performed at the distal joints are the flexor and extensor synergies and, frequently, the distal joints are rigidly held in the decerebrate attitudes.

FULTON proved in monkey that, if in one hemisphere as little as 15 to 20 per cent of the agranular frontal cortex remained intact, the animal ultimately regained some degree of volitional movement in all four extremities. TAKAHASHI found in monkey with bilateral ablation of area 4 that passive flexion and extension movements of each joint of the affected limbs were followed by flexor and extensor synergies of the adjacent joints. These clinical and experimental findings suggest that, in spastic paralysis, the extrapyramidal motor areas, especially the premotor area, play the role in performance of volitional movement in the affected extremities.

Though many reports have been made concerning the functions of the premotor area, there still remain several problems which should be elucidated. The results of an electrical stimulation of the cerebral cortices in primates were reported by C. VOGT, O. VOGT, PENFIELD and others in detail. ITO and MURAKAMI also performed experimental study in which an electrical stimulation of area 6a was carried out under awake state in monkey with bilateral ablation of area 4. In ITO and MURAKAMI's experiment, three different kinds of movement were evoked from many points diffusely scattered over area 6a: 1) Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs. 2) Contraversion and ipsiversion of the head and eyes. 3) Turning of the head and eyes accompanied with stereotyped flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes. In case accompanied with 3), when the head was passively

immobilized, an electrical stimulation of area 6 a no longer evoked response of the limbs. This fact suggests that when area 4 is bilaterally removed, movements induced from area 6 a are followed by the tonic neck reflexes. It is the purpose of this paper to elucidate the neural mechanism responsible for complicated patterns of voluntary movement, posture and reflex found in case of spastic paralysis. In this experiment, in monkey with bilateral ablation of area 4, responses evoked by an electrical stimulation of area 6 a with implanted electrodes under awake state were observed. Furthermore, the responses obtained were analyzed by bilateral section of the upper three cervical posterior nerve roots and bilateral destruction of the fastigial nucleus.

MATERIALS AND METHODS

A total of 12 monkeys (*macaca cynomologa*) were used in this experiment. After area 4 was bilaterally removed, Delgado's plate electrodes were placed on both areas 6 a. Electrodes consisted of six silver wires which were arranged in parallel with their tips at a distance of 5 mm. from one another and cemented together (Fig. 1). Operation was done under thiopental sodium anesthesia with the aid of a cytoarchitectural map of the precentral area which was made by ITO and MURAKAMI. Responses induced by an electrical stimulation of area 6 a were observed and recorded by movie. And then these animals were divided into two groups. In the first group, the upper three cervical posterior nerve roots through which the afferent fibers for the tonic neck reflexes pass were sectioned. In the second group, bilateral electrolytic destruction of the fastigial nucleus of the cerebellum was carried out through stereotactically oriented electrode. In both groups, responses evoked by electrical stimulation of area 6 a after the second operation were compared with those after the first operation. An electrical stimulation of area 6 a was performed with a 60-cycle alternating current at 1 to 2.5 volts with the animal held in a restraining chair under awake state (Fig. 2). After the animals were sacrificed, the cortical stimulation points were accurately recorded. In the second group, the location and the extent of fastigial lesions were routinely controlled on serial histological sections (Table 1).

RESULTS

Experiment I. Stimulation of area 6 a after bilateral ablation of area 4.

1. Symptoms following bilateral ablation of area 4.

When area 4 was bilaterally removed from an adult monkey, the animal remained

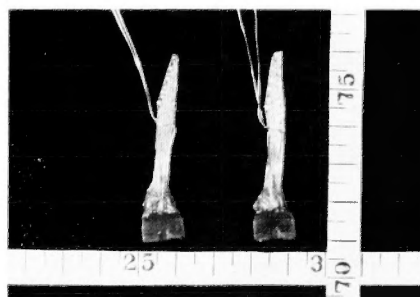


Fig. 1 Plate electrodes.

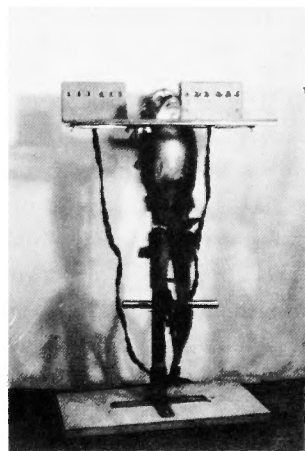


Fig. 2 Restraining chair. Electrodes are connected with respective lamps which are lighted up simultaneously with stimulation of corresponding cortical point.

Table 1. Operative Procedures Performed and Period of Observation of Postoperative Findings.

Monkey Mark	Weight (Kg)	1st Operation	Period of Observation after 1st Operation	2nd Operation	Period of Observation after 2nd Operation
A	1.5	Bilateral Removal of Area 1 and Implantation of Plate Electrodes on Both Areas 6a	8 (Days)	Bilateral Section of Upper Three Cervical Posterior Nerve Roots	60 (Days)
B	1.0	"	8	"	15
C	1.2	"	11	"	120
D	1.2	"	7	Bilateral Destruction of Fastigial Nucleus	15
E	1.0	"	7	"	10
F	1.3	"	7	"	11
G	1.2	"	6	"	12
H	2.2	"	9	"	11
I	1.8	"	8	"	13
J	1.3	"	7	"	18
K	1.2	"	8	"	14
L	1.5	"	9	"	14

in a lateral or crouching position for 1 to 2 days after operation. Thereafter, purposeful movements reappeared at the proximal joints, which allowed the animal to use the extremities in rhythmic progression. However, active movements of the distal joints, especially of the fingers, were profoundly affected and dexterity of finer movements of the fingers was never regained. The tonic neck reflexes were demonstrated in 8 out of the 12 monkeys for 3 to 4 days after operation and disappeared with the restoration of voluntary movement. The righting reflexes were elicitable in 9 animals for 5 to 7 days after operation and disappeared thereafter. The positive supporting reactions of the legs were also demonstrated in 8 animals and remained in the same state up to the time of the second operation. During the course of experiment, passive flexion and extension movements of each joint of the involved limbs were followed by flexor and extensor synergies of the adjacent joints (Table 2).

2. The results of an electrical stimulation of area 6a in monkey with bilateral ablation of area 4.

The results of this experiment were briefly summarized in Tables 3 and 4. Various types of movement were induced from 99 points in and around areas 6a of 24 hemispheres:

a) Turning of the head and eyes was evoked from 91 of the 99 stimulation points. Contraversion of the head was induced from 87 points and ipsiversion of the head from the remaining 4 points.

b) Turning of the head evoked from 50 of the 91 stimulation points was followed

Table 2 Symptoms following Bilateral Ablation of Area 4

Monkey Mark	1 Day	3 Days	5 Days	7 Days	10 Days
A	V	(-)	h (+) k (+) s (+)	Rhythmic gait h (+) k (+) s (+)	Synergies of fingers h (+) k (+) a' (+) s' (+) e' (+) 2nd operation was done 9 days after 1st operation
	M	(+)	(-)	(-)	
	R	(+)	(±) Both lower limbs	(-)	(-)
	S	s-w (+) h-t (+)	s-w (+) h-t (+)	s-f (+) h-t (+)	
	SP	(+)	(+)	(+)	(±)
B	V	(-)	Rhythmic gait h (+) k (+) s (+) e (±)	Synergies of h (+) k (+) a (+) w (+)	
	M	(±) Both upper limbs	(-)	(-)	
	R	(+)	(+)	(-)	(-)
	S	s-w (+)	s-w (+)	s-f (+)	s-f (+)
	SP	(+)	(+)	(+)	(+)
C	V	(-)	h (+)	h (+) k (+) s (+)	Rhythmic gait h (+) k (+) a (±) s (+) e (+) w (±) (-)
	M	(±) Both lower limbs	(-)	(-)	(-)
	R	(±) Both lower limbs	(±)	(±)	(±)
	S	s-w (+) h-a (+)	s-w (+) h-a (+)	s-w (+) h-a (+)	s-w (+) h-a (+)
	SP	(+)	(±)	(±)	(±)
D	V	(-)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+) s (±)	Synergies of fingers h (+) k (+) a (±) e (+) w (+) 2nd operation was done 8 days after 1st operation
	M	(+)	(±) Both lower limbs	(-)	(-)
	R	(+)	(+)	(-)	(-)
	S	s-w (+) h-a (+)	s-f (+) h-a (+)	f (+) h-a (+)	f (+) h-a (+)
	SP	(±)	(±)	(±)	(±)
E	V	(-)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+) s (+) e (±)	Synergies of fingers h (+) k (+) a (+) w (±) s (+) e (+)
	M	(+)	(-)	(-)	(-)
	R	(±) Both lower limbs	(-)	(-)	(-)
	S	s-w (+)	s-w (+)	s-f (+)	s-f (+)
	SP	(+)	(±)	(±)	(±)

	V	(-)	(-)	Rhythmic gait h (+) k (+) s (+)	Rhythmic gait h (+) k (+) a (+) s (+) e (+) w (+)	
F	M	(±) Both lower limbs	(±)	(-)	(-)	"
	R	(+)	(+)	(-)	(-)	
	S	s-f (+) h-a (+)	s-f (+) h-a (+)	e-f (+) h-t (+)	e-f (+) h-t (+)	
	SP	(+)	(+)	(±)	(±)	
	V	(-)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+)	2nd operation was done 8 days after 1st operation	
G	M	(-)	(-)	(-)		
	R	(-)	(-)	(-)		
	S	s-w (+)	s-w (+)	s-w (+)		
	SP	(+)	(±)	(±)		
	V	(-)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+) s (+)	Rhythmic gait h (+) k (+) s (+)	2nd operation was done 10 days after 1st operation
H	M	(-)	(-)	(-)	(-)	
	R	(±) Both lower limbs	(-)	(-)	(-)	
	S	h-a (+)	h-a (+)	h-a (+)	h-a (+)	
	SP	(±)	(±)	(±)	(±)	
	V	h (±)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+) s (+)	2nd operation was done 9 days after 1st operation
I	M	(-)	(-)	(-)	(-)	
	R	(±) Both lower limbs	(±)	(-)	(-)	
	S	h-a (+)	h-t (+)	h-t (+)	h-t (+)	
	SP	(+)	(±)	(±)	(±)	
	V	(-)	h (+) k (+)	Rhythmic gait h (+) k (+)	Synergies of fingers h (+) k (+) a (+) s (+)	2nd operation was done 8 days after 1st operation
J	M	(+)	(±) Both lower limbs	(-)	(-)	
	S	s-w (+) h-t (+)	s-w (+) h-t (+)	s-f (+) h-t (+)	s-f (+) h-t (+)	
	SP	(±)	(±)	(±)	(±)	
	V	(-)	(-)	h (+) k (+)	Rhythmic gait h (+) k (+) s (+)	2nd operation was done 9 days after 1st operation
	M	(±) Both lower limbs	(-)	(-)	(-)	
K	R	(-)	(-)	(-)	(-)	

L	S	h - a (+)	h - a (+)	h - t (+)	h - t (+)	2nd operation was done 10 days after 1st operation
	SP	(±)	(±)	(±)	(±)	
	V	(-)	(-)	Rhythmic gait h (+) k (+)	Rhythmic gait h (+) k (+)	
	M	(-)	(-)	(-)	(-)	
	R	(±) Both lower limbs	(-)	(-)	(-)	
	S	h - a (+)	h - a (+)	h - t (+)	h - t (+)	
	SP	(+)	(±)	(±)	(±)	

V : Voluntary movements. M : Tonic neck reflexes. R : Righting reflexes.
 S : Flexor and extensor synergies. SP : Positive supporting reaction.
 s : Shoulder. e : Elbow. w : Wrist. f : Finger. h : Hip.
 a : Ankle. t : Toe.

by stereotyped flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes. Moreover, in stimulation of 35 of the 50 points, the responses evoked in the limbs were the typical flexor and extensor synergies of all four limbs (Fig. 3). Fig. 4 is a summarized diagram showing the location of the 35 stimulation points in 24 hemispheres from which movements of the head and limbs were induced. Furthermore, in stimulation of the remaining 15 points, the responses were evoked in one to three limbs. In these cases, when the head was passively immobilized, an electrical stimulation evoked no response of the limbs. However, if the head was released, turning of the head accompanied with movements of the limbs promptly appeared. (Fig. 5).

c) Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs were evoked from 8 stimulation points. Moreover, similar responses of the limbs accompanied with turning of the head were evoked from 13 points.

Fig. 6 is a summarized diagram showing the location of the 99 stimulation points in 24 hemispheres from which various kinds of movement were induced. As seen in this figure, these stimulation points of six kinds are diffusely scattered in and around area 6 a mingled with one another. From these facts, it is thought that area 6 a is made up of several small circumscribed anatomically and functionally homologous areas, each of which is capable of inducing movements of the head and limbs.

Experiment II. Electrical stimulation of area 6 a in monkey with bilateral ablation of area 4 and bilateral section of the upper three cervical posterior nerve roots.

In 3 monkeys with bilateral ablation of area 4, turning of the head accompanied with flexor and extensor synergies of all four limbs identical in pattern with the tonic neck reflexes was evoked by an electrical stimulation of 11 points. In these monkeys, the same cortical points as those inducing movements mentioned above were again stimulated after bilateral section of the upper three cervical posterior nerve roots.

1. Symptoms following the second operation.

Voluntary activity which had been regained after the first operation, bilateral ablation of area 4, remained unchanged after bilateral section of the upper three cervical posterior

Table 3. Responses of Monkey to Stimulation of Area 6a after Bilateral Ablation of Area 4.

Code Address of Monkeys and Electrodes	Stimulation Voltage (v)	Responses					Remarks
		Head	Upper Limbs		Lower Limbs		
			Right	Left	Right	Left	
Ar 1	1.0	C	F	F			
Ar 3	1.0	C					
Ar 5	1.0	C	F	E	F	E	M
Ar 6	1.0	C					
Al 2	1.0	C	E	F	E	F	M
Al 3	1.0	C	E	E			
Al 4	1.0	C		E		E	
Al 5	1.0	C	E	F	E	F	M
Br 2	1.0	C					
Br 3	1.0		F	F	F	F	
Br 4	1.0	C	F	E	F	E	M
Br 5	1.0	C					
Br 6	1.0	C					
Bl 1	1.0	C	E	F	E	F	M
Bl 2	1.0	C					
Bl 3	1.0	C	E	F	E	F	M
Bl 4	1.0	C					
Bl 5	1.0	C					
Bl 6	1.0	C	E	F		F	m
Cr 2	1.0	C	F	E	F	F	
Cr 3	1.0	C	E	E	E	E	
Cr 4	1.0	C	F	F	E	E	
Cr 5	1.0	C					
Cr 6	1.0	C	F	E	F	E	M
Cl 1	1.0	C	E	F	E	F	M
Cl 2	1.0	C	E	F	E	F	M
Cl 3	1.0	C			E	E	
Cl 4	1.0	C					
Cl 5	1.0	C	E	F	E	F	M
Cl 6	1.0	C	E	F	E	F	M
Dr 1*	1.0	C	F		F		m
Dr 3	1.0	C	E	E			
Dr 5	1.0	C	F	E	F	E	M
DI 3	1.0	C	E	F	E	F	M
DI 5	1.0	C	E	F	E	F	M
DI 6	1.0	C	E		E	F	m
Er 1	1.0	C					
Er 2	1.0	C					
Er 4	1.0	C	F	E	F	E	M
Er 5	1.0	C		E	F		m
Er 6	1.0	C	F	E	F	E	M
El 1	1.0	C					
El 2	1.0	C					
El 4	1.0	C					
El 5	1.0	C					
El 6	1.0	C					
Fr 3	1.0	C					
Fr 5	1.0	C					
Fr 6	1.0	C					
Fl 1	1.0	C				E	E
Fl 2	1.0	C		E	F	E	F
Fl 3	1.0	C		E	F	E	F
Fl 5	1.0	C		E	F	E	F
Fl 6	1.0	C					
Gr 1	2.0	C					
Gr 2	2.0	C					
Gl 1*	1.2	C		E	F	E	F
Gl 3	2.0	C					
Gl 4	2.0	C		E	F	E	F
Gl 6	2.0			F			
Hr 1*	2.0	C					
Hr 2*	2.0	C					
Hr 3	2.0	C		F	E	F	E
Hr 4	2.0	C					
Hr 5	2.0	C					
HI 1*	2.0	I		F	E	E	E
HI 2*	2.0			E	E		
HI 3	2.0	I		F	E	F	E
HI 4	2.0	C		E	F	E	F
HI 5	2.0			E	E		
Ir 1*	1.2	C		E			
Ir 2	1.0	C					
Ir 3	1.2	C		F			m
Ir 4	1.2	C		F	E	F	E
Ir 6	2.0	C					
Il 2*	1.2	C		E	F	E	F
Il 3	1.5	C		E	F	E	F
Il 4	1.2	I		F	E	E	E
Il 5	1.2	I		F	E		
Jr 1	1.2	C		F	E	F	
Jr 2	1.2	C		F	E		m
Jr 3	1.2	C		F	E	F	E
Jr 4	1.2	C					
Jr 5	1.5	C			E		E
Jl 3	2.0	C		E	F	E	F
Jl 5	2.0	C		E	F	E	F
Jl 6	2.0			E	F	E	
Kr 1*	2.0	C					

Kr 3	2.0	C	F	E	F	E	M	Lr 2	1.2	C	F	E	F	E	M
Kr 4	1.2					E		Lr 4	1.0					E	m
Kr 6	2.0		E	E	F	F		Ll 2*	1.0	C	E	F	E	F	M
Kl 1*	1.2	C						Ll 3	2.0	C	F	F	E	E	
Kl 3	1.2		F	F	E	E		Ll 4	1.5	C	E				m
Kl 6	1.2	C	E	F	E	F	M								

Code Address of Monkeys and Electrode : Large letters stand for monkey, small letters for side of hemisphere, and numbers for electrode number.

C : Adversive movement of the head. I : Ipsiversive movement of the head.

F : Extension. F : Flexion. M : Tonic neck reflexes evoked in all four limbs.

m : Tonic neck reflexes evoked in one to three limbs.

Table 4 Responses of Monkey to Stimulation of Area 6a after Bilateral Ablation of Area 4.

Responses	Number of Stimulation Point
1. Contraversion of the head and eyes	28
2. Contraversion (or ipsiversion) of the head and eyes accompanied with flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes.	
a) Responses of all four limbs.	35
b) Responses of one to three limbs.	15
3. Various combinations of flexor and extensor synergies of bilateral or contralateral limbs.	8
1. Various combinations of flexor and extensor synergies of bilateral or contralateral limbs accompanied with turning of the head.	13
Total	99

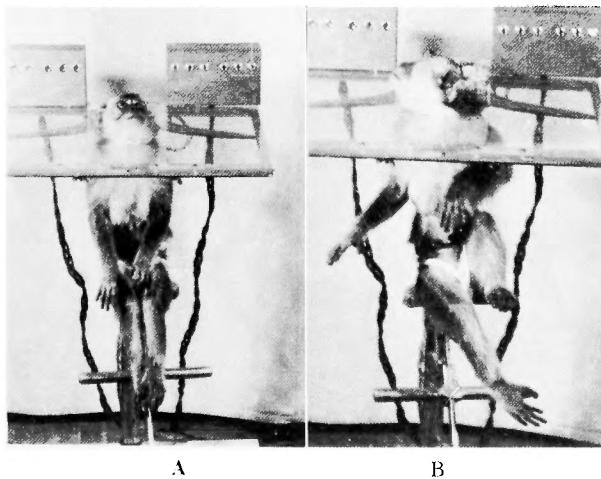


Fig. 3 Monkey K. A. A, Posture before stimulation. B, Turning of head and flexor and extensor synergies of four limbs identical in pattern with the tonic neck reflexes which are induced by stimulation of point K16 in area 6a.

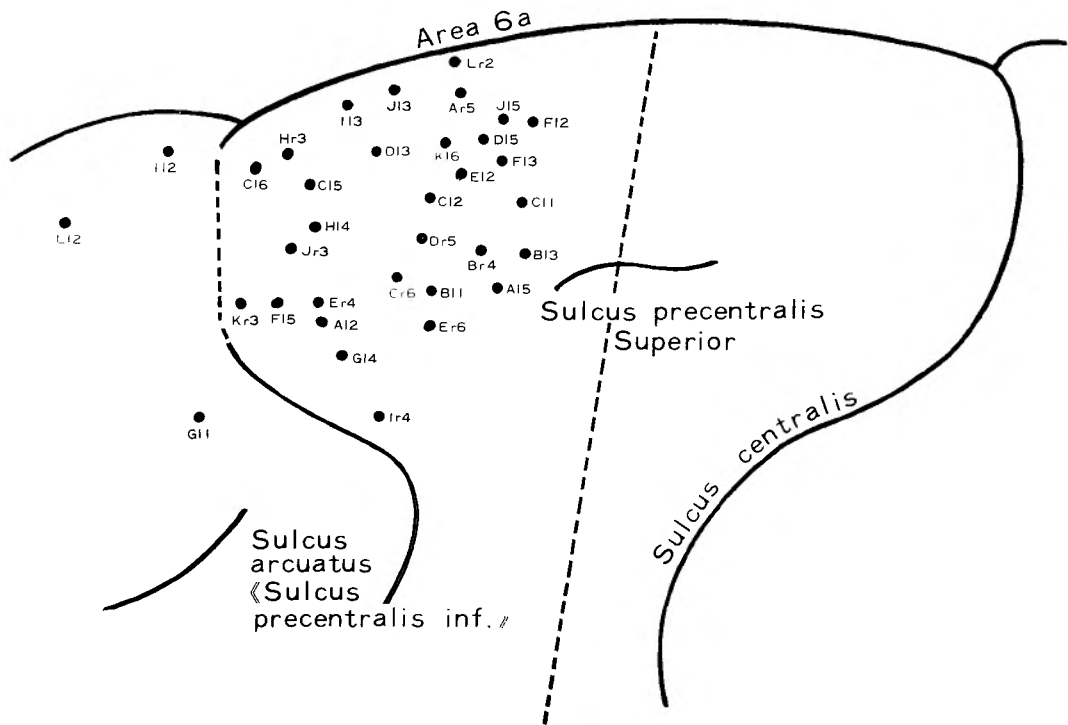


Fig. 4 Summarized diagram showing the location of 35 stimulation points in 24 hemispheres from which turning of the head accompanied with synergic movements of the limbs identical in pattern with the tonic neck reflexes was evoked.

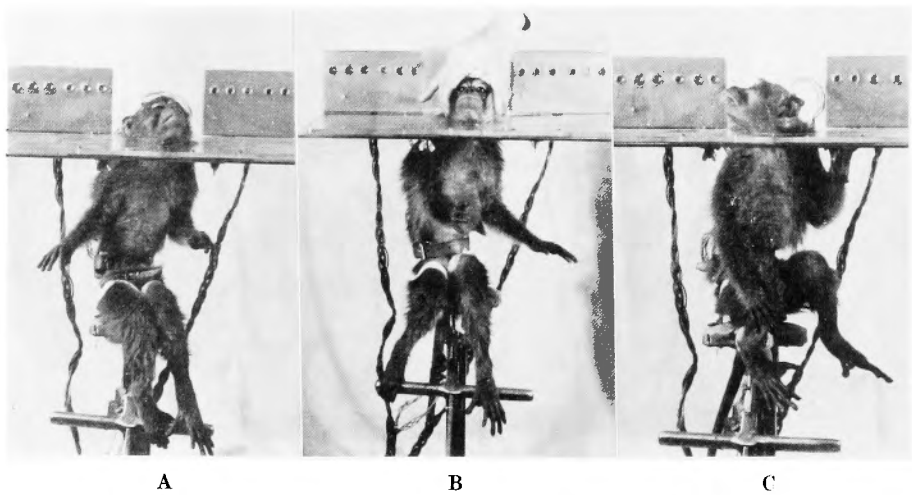


Fig. 5 Monkey A. A, Posture before stimulation in monkey with bilateral ablation of area 1. B, When the head is immobilized, an electrical stimulation of point A15 evokes no response of the limbs. C, When the head is released, turning of the head and flexor and extensor synergies of all four limbs identical in pattern with the tonic neck reflexes are promptly induced.

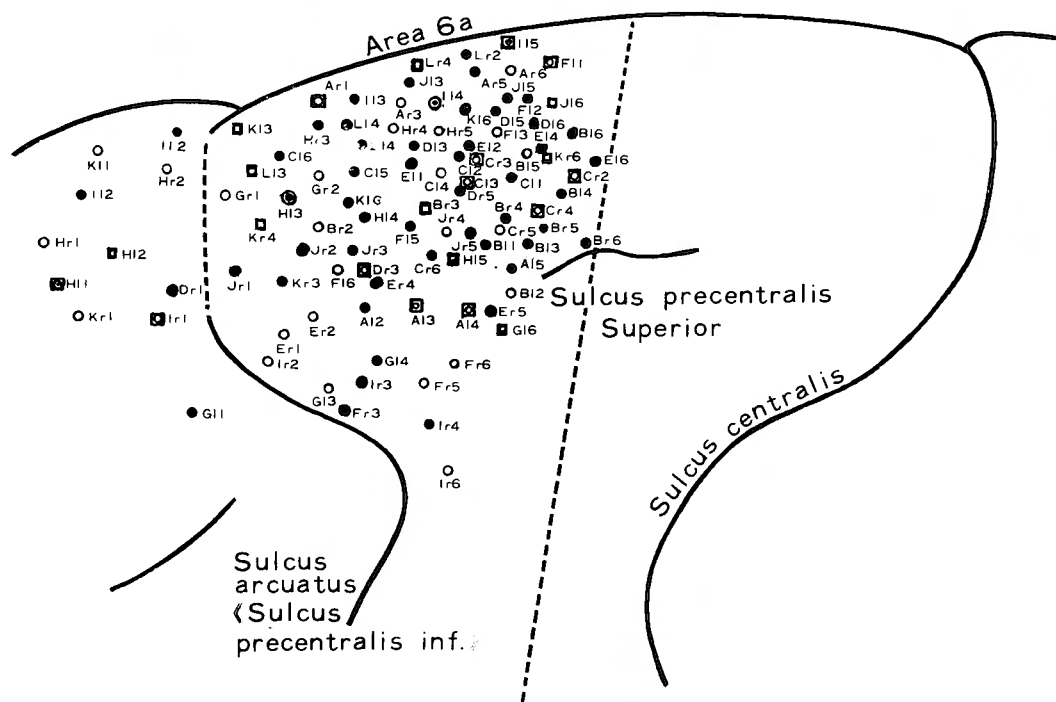


Fig. 6 Summarized diagram showing the location of 99 stimulation points in 21 hemispheres from which various kinds of movement were induced. These points of six kinds are diffusely scattered in and around area 6a mingled with one another.

- Contraversion of the head and eyes.
- Contraversion of the head accompanied with flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes.
- Ipsiversion of the head accompanied with flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes.
- Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs.
- Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs accompanied with contraversion of the head.
- ⊠ Various combinations of flexor and extensor synergies of the flexor and extensor synergies of the bilateral limbs accompanied with ipsiversion of the head.

nerve roots. The animals were able to run or climb, feed with their hands and carried out other fairly well executed movements of moderate complexity.

2. Results of an electrical stimulation of area 6a.

The results of an electrical stimulation of area 6a after the second operation were summarized in Table 5. In stimulation of 10 of the 11 points, turning of the head was no longer followed by response of the limbs (Fig. 7) and, in stimulation of the remaining one point, it was followed by slight extension of one upper limb.

Experiment III. Electrical stimulation of area 6a in monkey with bilateral ablation of area 4 and bilateral destruction of the cerebellar fastigial nucleus.

In 9 monkeys with bilateral ablation of area 4, turning of the head accompanied with flexor and extensor synergies identical in pattern with the tonic neck reflexes was evoked by an electrical stimulation of 24 points. In these monkeys, the same cortical points as those inducing movements mentioned above were again stimulated after bilateral destruction of the fastigial nucleus.

Table 5. Results of Stimulation of Area 6a in Monkey with Bilateral Ablation of Area 1 and Bilateral Section of the Upper Three Cervical Posterior Nerve Roots.

Code Address of Monkeys and Electrodes	Responses of Monkey to Stimu- lation of Area 6a after Bilateral Removal of Area 4			Responses of Monkey to Stimulation of Area 6a after Section of Bilateral Upper Three Posterior Cervical Nerve Roots					
	Stimula- tion Voltage (V)	Responses		Stimula- tion Voltage (V)	Responses				
		Head	Four Limbs		Head	Upper limbs		Lower Limbs	
						Right	Left	Right	Left
Ar 5	1.0	C	M	2.0	C				
Al 2	1.0	C	M	2.0	C				
Al 5	1.0	C	M	2.0	C				
Br 4	1.0	C	M	1.0	C				
Bl 1	1.0	C	M	1.0	C	E			
Bl 3	1.0	C	M	1.0	C				
Cr 6	1.0	C	M	1.0	C				
Cl 1	1.0	C	M	1.0	C				
Cl 2	1.0	C	M	1.0	C				
Cl 5	1.0	C	M	1.0	C				
Cl 6	1.0	C	M	1.0	C				

Code Address of Monkeys and Electrodes : Large letters stand for monkey, small letters for side of hemisphere, and numbers for electrode number. C : Adversive movement of the head. M : Tonic neck reflexes.

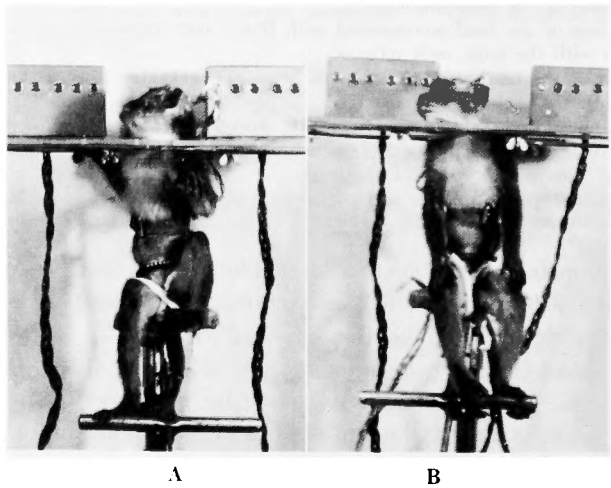


Fig 7 Monkey C. A, Response evoked by an electrical stimulation of point C11 of area 6a after bilateral ablation of area 1. Contraversion of head accompanied with flexor and extensor synergies of all four limbs identical in pattern with the tonic neck reflexes is seen. B, Response evoked by stimulation of point C11 after bilateral section of the upper three cervical posterior nerve roots. Contraversion of the head is no longer followed by response of the limbs.

Table 6. Results of Stimulation of Area 6a in Monkey with Bilateral Ablation of Area 4 and with Bilateral Destruction of the Fastigial Nucleus.

Code address of Monkeys and Electrodes	Responses of Monkey to Stimu- lation of Area 6a after Bilateral Removal of Area 4			Responses of Monkey to Stimulation of Area 6a after Bilateral Destruction of Fastigial Nuclei					
	Stimula- tion Voltage (V)	Responses		Stimula- tion Voltage (V)	Responses				
		Head	Four Limbs		Head	Upper Limbs	Lower Limbs		
						Right	Left	Right	Left
Dr 5	1.0	C	M	1.0	C	F			
Dl 3	1.0	C	M	1.0	C				
Dl 5	1.0	C	M	1.0	C				
Er 4	1.0	C	M	1.0	C	F			
Er 6	1.0	C	M	1.0	C				
El 2	1.0	C	M	1.0	C	E			
Fl 2	1.0	C	M	1.2	C	E			
Fl 3	1.0	C	M	1.2	C				
Fl 5	1.0	C	M	1.0	C				
Gl 1	1.0	C	M	2.0	C	E	F	E	F
Gl 4	2.0	C	M	2.0	C				
Hr 3	2.0	C	M	2.0	C	F			
Hl 3	2.0	I	M	2.0	I	E	F	E	F
Hl 4	2.0	C	M	2.0	C				
Ir 4	1.2	C	M	2.0	C				
Il 2	1.2	C	M	2.0	C				
Il 3	1.5	C	M	2.0	C	E	F	E	
Jr 3	1.2	C	M	2.0	C				
Jl 3	2.0	C	M	2.0	C	E	F	E	
Jl 6	2.0	C	M						
Kr 3	2.0	C	M	2.0	C	F			
Kl 6	1.2	C	M	2.0	C				
Lr 2	1.2	C	M	2.0	C				
Ll 2	1.0	C	M	2.0	C				

Code Address of Monkeys and Electrodes : Large letters stand for monkey, small letters for side of hemisphere, and number for electrode number. C : Adversive movement of the head.

I : Ipsiversive movement of the head. M : Tonic neck reflexes. E : Extension. F : Flexion.

1. Symptoms following the second operation.

In all 9 monkeys, volitional activity which had been regained after bilateral ablation of area 4 was completely abolished for about 3 days after the second operation, bilateral destruction of the fastigial nucleus. Several days thereafter, the animals were able to propel themselves in crouching position. Finally, the animals became able to walk in ataxic fashion with gross aberration of movement, frequently fell down. They could not run or climb during the course of experiment.

2. Results of an electrical stimulation of area 6a.

The results of this experiment were summarized in Table 6. As shown in this table, in stimulation of 11 of the 24 points, turning of the head was no longer accompanied

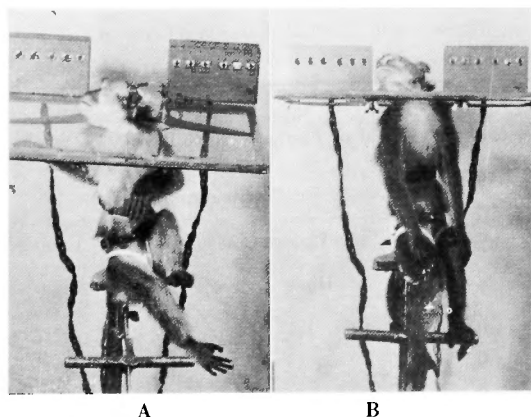


Fig. 8 Monkey F. A, Response evoked by stimulation of cortical point F15 after bilateral ablation of area 1. Contraversion of the head accompanied with flexor and extensor synergies of four limbs identical in pattern with the tonic neck reflexes is seen. B, Response evoked by stimulation of cortical point F15 after bilateral destruction of the fastigial nucleus. Contraversion is no longer followed by response of the limbs.

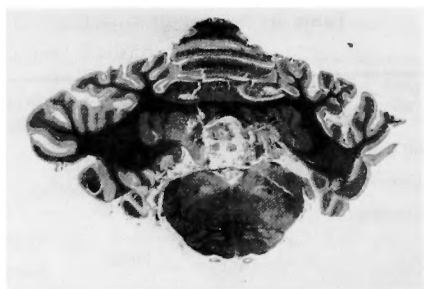


Fig. 9 Photograph showing bilateral complete destruction of the fastigial nucleus.

with response of the limbs (Fig. 8) and, in stimulation of the remaining 13 points, it was followed by reduced responses of one to four limbs. After these animals were sacrificed, the location and the extent of fastigial lesions were controlled on serial histological sections. In general, in the cases in which response of the limbs was abolished, the histological sections also proved complete destruction of both fastigial nuclei, as shown in Fig. 9. On the other hand, in remaining cases in which turning of the head was still followed by response of one to four limbs, the histological sections proved partial or no destruction of the nuclei.

DISCUSSION

When the motor and premotor areas are bilaterally removed from an adult monkey, voluntary activity is completely abolished and the animal is reduced to the high decerebrate status. However, if some part of the frontal motor area remains intact, the animal ultimately regains some degree of gross voluntary movement in all four limbs. The movements which are performed under these circumstances reveal the specific functions of the remaining part of the frontal extrapyramidal area.

It is generally recognized that faradic stimulation of area 6 $\alpha\alpha$, the posterior part of the premotor area, gives rise contralaterally to isolated movements of the individual muscles, similar in character to those obtained from area 4, and area 6 $\alpha\beta$, the rostral part of the premotor area, yields, in addition to stereotyped movements of the limbs, characteristic adverse movements of the head and trunk; turning of the head and eyes to the opposite side, with rotation of the trunk in the same direction. And also from the posterior part of area 6 $\alpha\alpha$ a specific ipsilateral area was found by BUCY. Furthermore, by making a superficial incision of the cortex between area 6 $\alpha\alpha$ and area 4, the movements of individual muscles elicitable from area 6 $\alpha\alpha$ are abolished, but certain of the sustained movements remain. In DENNY-BROWN'S experience, the only consistent movement following ablation of area 4 plus the strip region were the stereotyped flexion and extension movements of the fore and hind limbs; and from the more anterior parts of area 6 adverse

movements of head and eyes. ITO, MURAKAMI and the present author performed experimental study in which area 6a was stimulated with implanted plate electrodes under awake condition in monkey with bilateral ablation of area 4. The results of this study are summarized as follows:

1) Contraversion of the head and eyes was induced from many points diffusely scattered over area 6a and also ipsiversion of the head and eyes was evoked from only a few points of this same area. Moreover, turning of the head was frequently followed by flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes.

2) Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs were evoked from points sparsely scattered over area 6a. Furthermore, similar movements of the limbs were frequently accompanied with turning of the head. It is probable that the combined movements mentioned above are induced by simultaneous stimulation of two points having different kinds of function of which the one is capable of inducing movement of the head and the other capable of inducing movement of the limbs.

3) These cortical stimulation points of different kinds were diffusely scattered over area 6a mingled with one another, and some of them were located around area 6a, as

shown in Fig. 6.

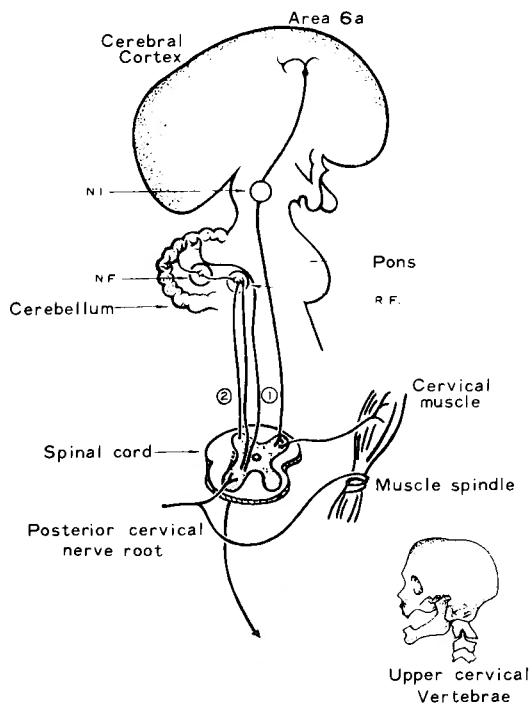


Fig. 10 Diagram showing neural mechanism responsible for turning of the head accompanied with the tonic neck reflexes. Impulses arising from area 6a are transmitted through extrapyramidal pathways from area 6a, via interstitial nucleus, to the cervical segments of the spinal cord, causing turning of the head which is followed by the tonic neck reflexes.

In this experiment, furthermore, analysis of the neural mechanism responsible for combined movements of turning of head and flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes was done. In this condition, when the head was passively immobilized, cortical stimulation induced no response of the limbs and, moreover, the responses of the limbs were abolished by bilateral section of the upper three cervical posterior nerve roots or bilateral destruction of the fastigial nucleus.

Rademaker found that the postural reflexes were well demonstrated in dogs and cats with total chronic cerebellectomy.

On the other hand, it has been realized that the cerebellum acts as a regulator of the intensity of the postural discharge.

The results of this experiment also prove that the cerebellum exert a great influence upon the postural reflexes. From these facts, it is revealed that activities of the center for the postural reflexes are released by ablation of area 4 so that turning of the head is followed by the tonic neck

reflexes (Fig. 10).

The neural mechanism of characteristic patterns of voluntary movement, posture and reflex found in spastic paralysis in man should be considered on the basis of the results obtained from these experiments. As proved by FULTON, when areas 4 and 6 are bilaterally removed from an adult monkey, the animal is reduced to the thalamic reflex status. However, if in one hemisphere some part of the agranular frontal cortex remains intact, the animal regains some degree of volitional movement in all four limbs. This is the same also in man. Volitional movements performed under this condition depend upon the integrity of the frontal extrapyramidal motor area, particularly of area 6a. As proved in this study, area 6a is made up of several small circumscribed anatomically and functionally homologous areas, each of which is capable of producing turning of head and synergic movements of the limbs. Impulses arising from respective functional units of area 6a are transmitted through the extrapyramidal pathways from area 6a, via the interstitial nucleus and reticular substance, to the same segments of the spinal cord. Therefore, when some part of area 6a is damaged, the functional deficit is easily compensated for by the part remaining intact. Volitional movements performed under this condition are flexor and extensor synergies. Moreover, as proved in this study, it is clear that the characteristic attitudes assumed by the affected extremities, such as flexion of the upper extremity and extension of the lower extremity, are induced by the postural reflexes. In spastic condition, there is a competition between the volitional activity of extrapyramidal origin and the postural reflexes.

In the next place, the function of higher centers controlling the frontal motor area may be briefly considered. It is generally recognized that both motor and premotor areas are under control of the ideomotor area located in the supramarginal gyrus of the parietal lobe, as shown in Fig. 11. The ideomotor area initiates complicated pattern of

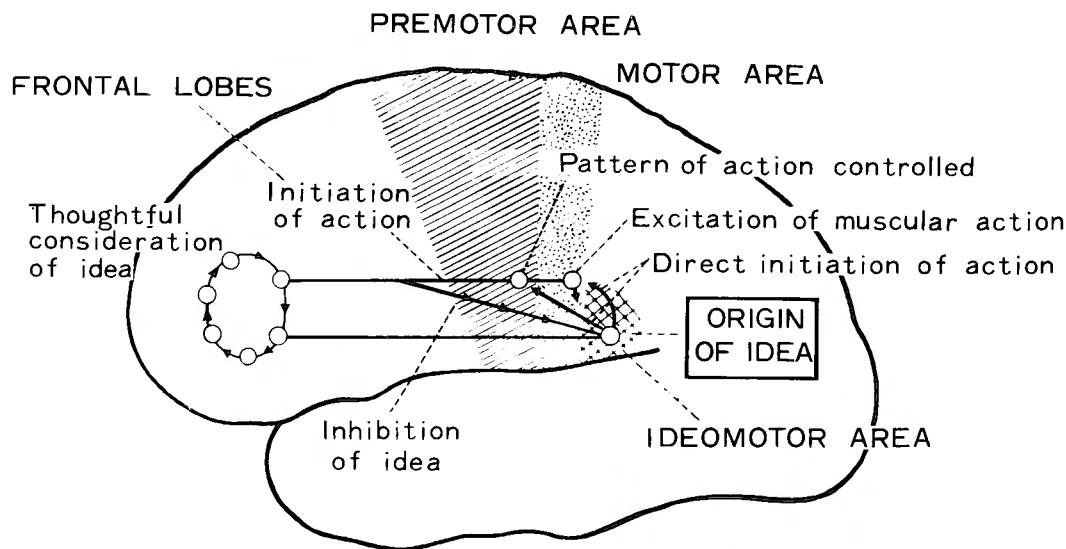


Fig. 11

The pattern of impulses in the brain for originating and controlling motor functions.

muscular activity. The premotor area probably contains many potentially oscillating circuits and, when oscillation is initiated in one of these circuits, the resulting impulses cause a particular pattern of movement to occur somewhere in the body. The prefrontal lobe operates in association with the ideomotor area and gnostic area, common integrate area in the angular gyrus, to help determine the sequence of muscular functions as well as the sequence of other thought processes of the brain.

From this point of view, it is thought that when some part of the frontal motor area is damaged, the ideomotor area operates in conjunction with the prefrontal lobe to cause the frontal extrapyramidal part remaining intact to function effectively in the place of the part damaged.

SUMMARY AND CONCLUSION

1) In 12 monkeys (*macaca cynomologa*) with bilateral removal of area 4, area 6a was stimulated with implanted Delgado's plate electrodes under awake state. The results obtained were as follows : a) Contraversion of the head and eyes was evoked from many diffusely scattered over area 6a and also ipsiversion of the head and eyes from only a few points of this same area. Moreover, turning of the head was frequently followed by flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes. b) Various combinations of flexor and extensor synergies of the bilateral or contralateral limbs were evoked from points sparsely scattered over area 6a. Furthermore, similar movements of the limbs were frequently accompanied with turning of the head. It is probable that the combined movements mentioned above are induced by simultaneous stimulation of two points having different kinds of function of which the one is capable of inducing movement of the head and the other capable of inducing movement of the limbs. c) These cortical stimulation points of different kinds were diffusely scattered over area 6a mingled with one another, and some of them were located around area 6a. This fact suggests that area 6a is made up of several small circumscribed anatomically and functionally homologous areas, each of which is capable of inducing movements of the head and limbs.

2) In monkey in which turning of the head and eyes accompanied with flexor and extensor synergies of the limbs identical in pattern with the tonic neck reflexes was evoked, the responses of the limbs were abolished by bilateral section of the upper three cervical posterior nerve roots or bilateral destruction of the fastigial nucleus of the cerebellum. These facts prove that activities of the brain stem reticular formation are released by ablation of area 4 so that the movements initiated from area 6a are followed by the postural reflexes.

3) On the basis of these results, the neural mechanism responsible for characteristic patterns of voluntary movement, posture and reflex found in spastic paralysis in man was considered.

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和 文 抄 録

霊長類の運動領切除後に於ける前運動領の 電気刺激に対する反応

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1. 12匹のカニクイザルの両側大脳皮質分野4を切除したのち、分野6aに電極を置き、この猿を観察台に固定し、覚醒状態で於て電気刺激を行なつた。99点の刺激によつて次のような結果が得られた。i) 分野6a及びその前方部に亘つて散在する多数の点から、頭の向反運動¹⁾稀に向同運動²⁾が誘発された。又屢々この頭の回転運動に随伴して緊張性頸反射と同一型式の1肢の屈伸運動が誘発された。ii) 比較的少数の散在する刺激点から、反対側又は両側上下肢に種々の組合せの屈伸運動が誘発された。iii) 又同様の肢の屈伸運動は屢々頭の回転運動を随伴した。これは恐らく、4肢の運動を誘発する点と頭の回転運動を誘発する点が同時に刺激されておこつたと思われる。

2. i) にのべたような頭の回転運動に随伴して4肢に緊張性頸反射と同一型式の屈伸運動が誘発されるような猿に対して、上位3本の頸随神経後根の両側切断又は小脳室頂核の両側破壊を行なうと、4肢の反応が消失した。このことは、上記の4肢の反応が頭の回転運動によつて二次的に誘発される緊張性反射である

ことを証明する。

3. 上記のような種々の運動を誘発する皮質刺激点 は分野6a及びその前方部に亘つて散在し且つ互いに混在している。このことから、分野6aは頭の回転運動を誘発する点と4肢の運動を誘発する点を含むところの、解剖的及び機能的に類似の性質を有する幾つかの小領域から成り立っていると考えられる。

4. 以上の事実から、分野6aの一部が破壊された場合には、失なわれた機能はそれと類似の構造と機能を有する無傷で残つた部分によつて代償されることが出来る。又分野4が障害された場合には、失なわれた随意運動は分野6によつて代償されるが、このさい姿勢反射の中樞の機能がその抑制から解放されているために、分野6から誘発される運動に随伴して姿勢反射が誘発される。それ故に、分野4が障害された場合には、罹患肢では、錐体外路性随意運動と姿勢反射の競り合いが起ると考えられる。

5. 上記のことは、痙性麻痺に見られる特有の運動型式、肢位及び反射の神経機構をよく説明する。