A NEUROSURGICAL STUDY OF FRONTAL LOBE INFLUENCE UPON THE CARDIOVASCULAR SYSTEM

MASAMITU NAKAJIMA

1st Department of Surgery, Nagoya University School of Medicine
(Director: Prof. Yoshio Hashimoto)

I. PREFACE

During all operations, especially neurosurgical procedures, attentions should be focused upon physiological changes of the patients. Moreover, it has been found that neurosurgical patients whose preoperative tests did not suggest any pulmonary or circulatory disorders show sudden cardiocirculatory changes on occasional instances. When this situation occurs, we must discontinue the operation causing a further burden to the patient and subsequent delay of the convalescence. In order to overcome similiar problem during brain surgery, it is imperative to monitor all organic observations such as pulse rate. body temperature, blood pressure, ECG, reflex photoelectric plethysmograph (R.P.P.) and so on. Such observations enable the surgeon to be aware at all time of the patient's changes and various responses during the operation.

Radical and sudden physiological changes of the patients of neurosurgical operations have been observed especially when operations are performed in the motor area of cerebral cortex, callosal convolution, the Brodmann's 8th areas of frontal lobe, and orbital surface of frontal lobe which are considered the higher centres of the autonomic nervous system. Most of the research pertaining to the higher center of the autonomic nervous system are developed from animal experiments which were done by electro-physiological methods. The application of the conclusion made from animal experiments upon human neurophysiology requires extreme caution because of the difference of degree of encephalization, especially as the cerebral cortex is highly organized in human brain.

My primary intention in this thesis is to report and discuss this matter from my own clinical neurosurgical experiences with experimental observations using the neurophysiological parameters. My observations were made on the cases in which the operation was performed by elevating the frontal lobe to operate on the posterior orbital surface. These cases were chosen because of the following conditions: (a) this operation has few ill side effects during operation and postoperative; (b) operation techniques are fully developed;

Received for publication December 8, 1962.

and (c) during all operations, the spatula was in same position on the orbital surface which caused changes to the blood pressure, pulse rate, and R.P.P.

II. A REVIEW OF BIBLIOGRAPHIES

The first observation was made from by Willis in 1664 when he suggested that the function of the autonomic nervous system was controlled by a higher central nervous system. He assumed that this was in the cerebellum. Since then, there was no further reports of this kind until the latter part of the 19th century, when the representation of the autonomic nervous system in the cerebral cortex was established gradually, *i.e.* Guller (1856), Brown-Séquard (1863), Chevalier (1867) respectively. They pointed out that a vasomotor disturbance was associated with the hemiplegics following apopletic disorder.

Hughlings Jackson (1873–1874) deduced from clinical observation that autonomic activities must be represented at all levels in the central nervous system. Eulenberg and Landois (1876) observed contralateral cutaneous temperature change following vascular or other lesions of the precentral areas of the frontal lobes. Gower (1886) recorded the vasomotor and trophic changes by cerebral cortex disorder.

Spencer (1894) observed the elevation of blood pressure, changes in respiration, and other reactions in monkeys by a stimulation of the orbital surface of the frontal lobe.

Sollier (1897) assumed that cardiac and gastric centers existed in the superior parietal lobe. Howell and Austin (1899–1900) reported blood pressure changes in response to cortical stimulation. Bechterew (1911) stated that most cerebral cortex areas had autonomic nervous function. Many other workers confirmed these reports, and later on, during the following half century, many reports have appeared from anatomy, phisiology, pathology and clinical sources.[53]

From these reports, it proves that various parts of the brain, especially, the premotor and orbital areas of frontal lobes, the cingulate gyri, parts of the thalamus, the hypothalamus, and certain nuclei in the brain stem, have a close connection with the function of autonomic nerve. Also, Kennard (1949),[42] Maclean (1950),[49] Chapman (1950),[12] Kaada, Jasper (1952),[35] Mulder (1954)[54] etc., reported that the autonomic nerve function exists in the temporal lobe.

The fact that the orbital surface of the frontal lobe has a close connection with the autonomic nervous function stems from the fact, as previously mentioned by Spencer (1894),[72] that a stimulation to this part caused a vasomotor effect. Smith (1938)[71] observed a respiratory affect by stimulation to this same part of a dog. Bailey and Bremer (1938)[4] confirmed that by a stimulation to the central end of vagus nerve, electrical activity occurred in the orbital surface of the frontal lobe. Also Bailey and Sweet (1940)[3] followed up these observations by studies of monkeys and cats and findings that by stimulation of the posterior parts of the orbital surface of the frontal lobe (areas 13, 14), control of breathing, elevation of blood pressure, and decrease of stomach tonus were noted. They then assumed that the cortical representation of the vagus nerve was probably located in these areas. Ruch (1943)[63] proved that by mutilation of these parts in a monkey, an increase in activity and polyphagia had occurred. Livingston *et al.* (1948),[48] Delgado and Livingston (1948),[15] Chapman *et al.* (1949),[11] Sachs *et al.* (1949),[64] Kaada (1951),[36] Dell (1952),[17] Maclean *et al.* (1953),[50] all confirmed the existence of the autonomic nervous function in the same part. Significantly, Livingston *et al.* (1948)[48] reported that by a stimulation to the orbital surface of the frontal lobe, changes in blood pressure and respiration will occur in human beings and monkeys. Furthermore, in the monkey, by cutting the vagus nerve and excision of suprarenals, these effect are abolished. This report is worth noticing. To summarize these reports, these cortical areas propagate their influence on the cardiovascular system, at least in part, through interconnection with vagal nuclei in the medulla oblongata.

Davis (1951)[14] suggested that these vasomotor changes following ablation or stimulation of these orbital surface are mediated through a direct unmyelinated orbito-hypothalmic tract which interconnects the orbital gyri with the ventromedial and lateral hypothalmic nuclei both in men and monkeys.

Kondo (1952)[44] recorded the change of photoelectric plethysmograph (P.P.) during the operation and after the operation to these areas and also reported vasomotor changes to the upper and lower limbs on the opposite side. Okinaka (1953)[61] observed in a dog that there are several kinds of autonomic nerve action in these areas.

Takeuchi (1959)[74] observed a decrease to the pulse rate at preoperation, postoperation, and when the operation was performed to these areas.

III. EXPERIMENTAL METHOD

The hydraulic influence of the whole circulatory system cannot be disregarded when observing the changes of cardiac rhythm and vasomotor responses. I have observed by continuous recordings of ECG, R.P.P., skin temperature, and blood pressure, many kinds of reactions which occur during neurosurgical procedures especially to the orbital surface of the frontal lobe.

1) *Conditions of Patients in Study*

Since changes in pulse rate were very important in this study, patients who had operation near the pituitary gland, and had no cardiocirculatory or respiratory disorder on the preoperative tests, were selected. These patients were selected from those hospitalized during the past 6 years in the First Surgical Clinic (Professor Hashimoto).

The recordings of ECG, R.P.P., and skin temperature were taken at the operating table with the patient in supine position 30 minutes prior to anesthesia to the time of complete recovery from anesthesia. The operation room was air-conditioned with constant temperature and humidity.

For anesthesia, a light ether anesthesia by EMO apparatus was mainly used.[60]

2) *Experimental Apparatus*

a) Electrocardiograph-Manufactured by Nihon-Koden Co. 2 channels, 3 channels, or multiplex monitor recorder.

b) Photoelectric Plethysmograph (P.P.)

Reflex Photoelectric Plethysmograph (Hertzman-Takagi) manufactured by Fukuda Electron Co.

c) The measurement of Skin Temrerature

Micropyrometer manufactured by Eko Seiki with copper constantan thermocouple was placed on the left and right second toe pad.

d) Blood Pressure-by Riva-Rocci's haemadynamometer.

3) *Orbital surface approach of the frontal lobe*

If a lesion could be approached from the left or right side, as a rule, a right craniotomy was performed, and the pituitary gland was approached by paramedian approach.[37) 62)]

The cortex is stimulated by electrical stimulation, thermal stimulation, and mechanical stimulation. However, since this is a clinical experiment, mechanical stimulation by brain spatula on cotton cloth dampened with 20°C physiological salt solution was selected.

IV. EXPERIMENTAL RESULTS

1) *Change of pulse rate*

a) *Preoperation*

The average preoperative pulse rate is according to Table 1.

TABLE 1. Pulse Rate Before Operation

Pulse rate/min. → Diseases ↓	51-60	61-70	71-80	81-90	Total
Pituitary adenoma	5	7	7	0	19
Suprasellar tumor	1	1	0	0	2
Craniopharyngioma	1	1	2	2	6
Optico-chiasmal arachnoiditis	3	10	7	2	22
Retro-bulbar tumor	0	2	1	0	3
Others	1	2	2	0	5
Total	11	23	19	4	57

Cases of pituitary tumor, craniopharyngioma, and suprasellar tumor in which pressure is made in certain way to the orbital surface of the frontal lobe, the average pulse rate of preoperation was as follows: below 60/min-7 patients (26%), above 71/min-11 patients (40%), and approx. normal range. 61–70/min-9 patientes (34%).

On the contrary, cases of optico-chiasmal arachnoiditis and optic nerve injury was as follows: below 60/min-4 patients (13%), above 71/min-12 patients (40%), and 61–71/min-14 patients (47%).

b) Changes of pulse rate during the operation

In the diseases previously listed in Table 1, the neurosurgical technique by paramedian approach[37,62] to the pituitary area is used as shown in Figure 1. That is, when the dura mater is cut horizontally at the pole of frontal lobe, the brain spatula is inserted parallel to the falx as shown in Figure 1 and pressure is applied to the posterior orbital surface. The cotton cloth is placed between the spatula and brain surface to protect the frontal lobe. After the cerebrospinal fluid, which is continuously produced, is constantly sucked, we can reached to the depths and the optic chaisma appears to the operation field.

To show the changes of the pulse rate during the operation, 57 cases (Table 2) were studied.

As shown in Table 2, these changes can be separated into three types.

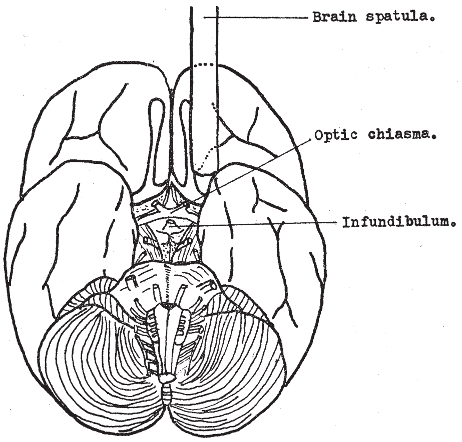


FIGURE 1. Elevation of the posterior orbital area by a spatula during frontal craniotomy (para-median approarch).

TABLE 2. Change of Pulse Rate-During the Operation

Change of Pulse → Rate → Diseases ↓	Type 1	Type 2	Type 3	Total
Pituitary adenoma	11	8	0	19
Suprasellar tumor	1	1	0	2
Craniopharyngioma	3	2	1	6
Optico-chiasmal arachnoiditis	13	8	1	22
Retro-bulbar tumor	2	1	0	3
Others	3	1	1	5
Total	33	21	3	57

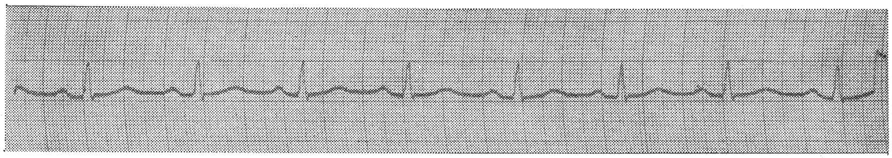
Type 1. The change decreases slowly or the change suddenly decreases and then slowly decreases.

Type 2. Almost no change of pulse rate is observed during the operation, or pulse rate increases temporarily.

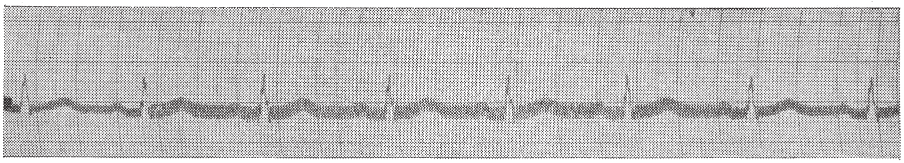
Type 3. During the operation, change in pulse rate increases slowly.

From our cases, it was confirmed as follows; Type 1–58%, Type 2–36%, and Type 3–5%. In this group, differences due to age were not noticed.

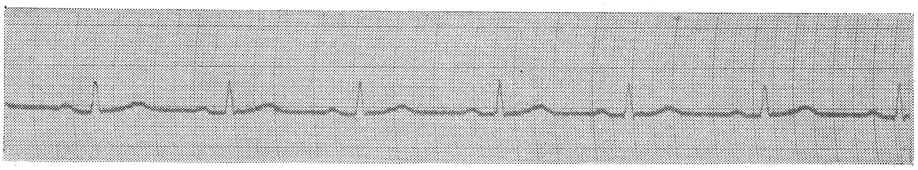
The change in the pulse rate during the operation were influenced by the following conditions: (a) intratracheal intubation[2,9,58]; (b) action by anesthesia itself; (c) a change of general condition of the body which occurs



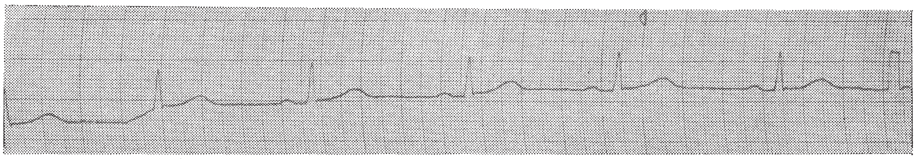
a.m. 9°30′ Skin incision. Bp. 106–90 mmHg. Paper speed: 4 cm/sec.



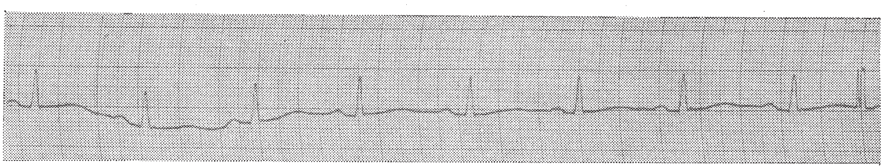
a.m. 10°20′ Elevation of the posterior orbital surface. Bp. 110–72 mmHg.



a.m. 10°40′ Pituitary tumor was removing. Bp. 118–80 mmHg.



a.m. 10°50′ Pituitary tumor was removed. Bp. 119–80 mmHg.



a.m. 11°20′ Operation was finished. Bp. 116–80 mmHg. 1 sec.

FIGURE 2. A part of continuous recording of ECG during right frontal craniotomy for pituitary tumor.

during the operation[29) 34) 56) 70) 82)]; (d) bleeding; and (e) blood transfusion. It should be emphasized that Type 1 consist of 58%.

Figure 2 shows section of continuous recording of ECG of a right crani-

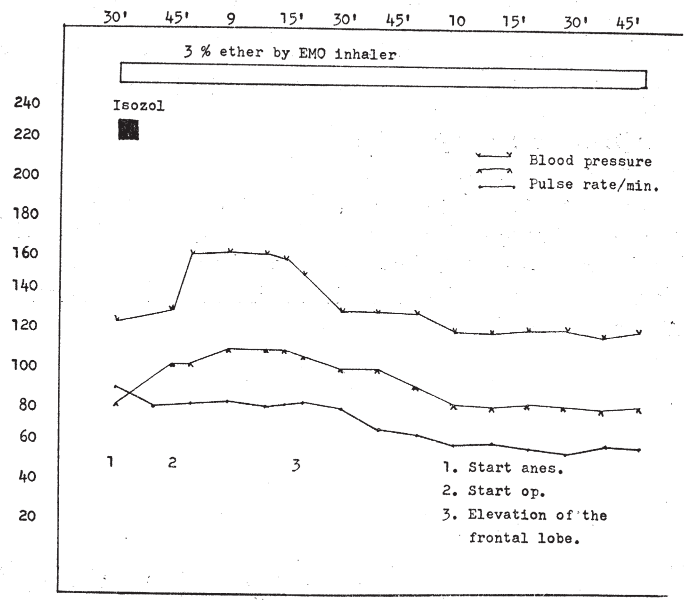


FIGURE 3. Anesthesia record of right frontal craniotomy. K. M. 20 y.o male. Optico-chiasmal arachnoiditis.

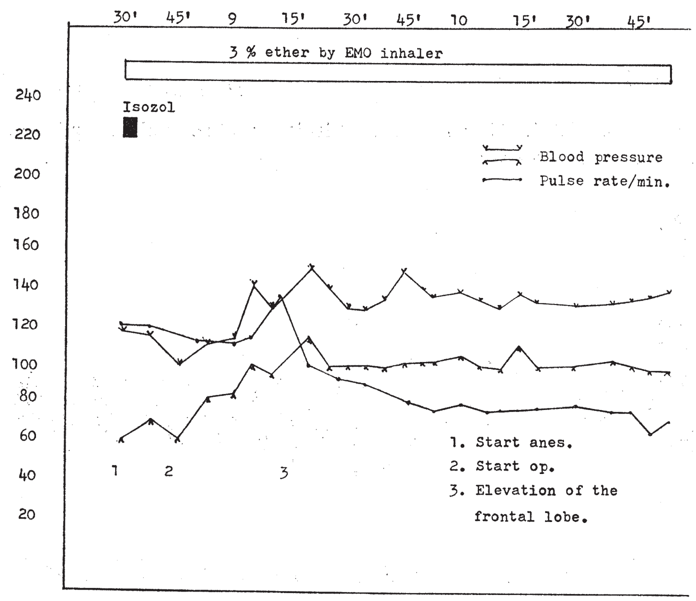


FIGURE 4. Anesthesia record of right frontal craniotomy. U. K. 32 y.o. female. Pituitary adenoma.

otomy in which a pituitary tumor was removed. A decrease in the pulse rate was noticed approximately 20 minutes while the frontal lobe was elevated.

Figures 3 and 4 are records of anesthesia during the operation of optico-chiasmal archnoiditis and hypophysial tumor. A considerable decrease of pulse rate was noticed.

It is noted that there is a distinctive decrease in the pulse rate when a firm wide pressure is applied to obtain a wide field of operation.

c) Change in pulse rate-postoperative

The change in pulse rate is as follows:

Figure 5 shows the case of hypophysial tumor. It shows the course of a patient who had a tumor removed completely by right craniotomy. In spite of a continuous fever of 37–38°C, for six days after the operation there was a distinctive decrease in the pulse rate from the second day after the operation and lasted for two weeks.

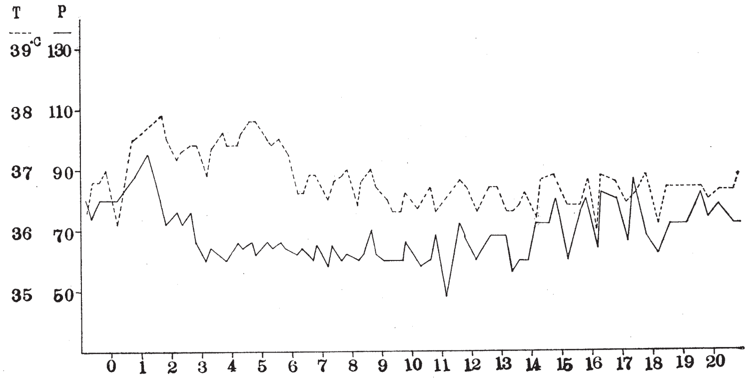


FIGURE 5. T. K. 26 y.o. male. Pituitary chromophobe adenoma. Right frontal craniotomy.

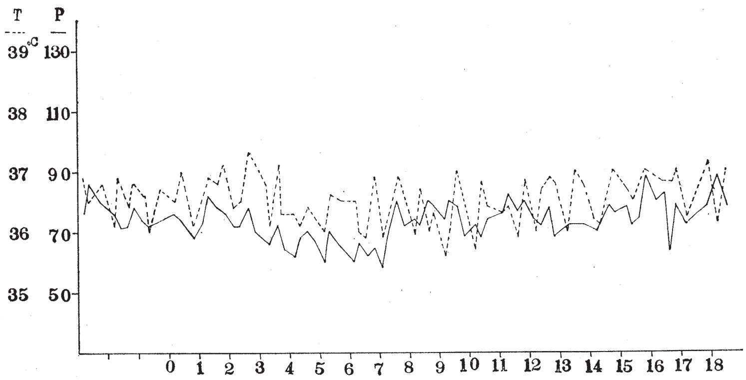


FIGURE 6. F. M. 34 y.o. female. Optico-chiasmal arachinoiditis. Right frontal craniotomy.

Figure 6 represents a patient who complained of a disorder of visual acuity caused by optico-chiasmal arachnoiditis. A right craniotomy was performed in order to remove the arachnoid membrane. Although there was no pyrexia after the operation, a decrease in pulse rate was noticed during the first postoperation week.

Figure 7 represents a case of optico-chiasmal arachnoiditis, a right craniotomy was performed to remove the arachnoid membrane. In spite of pyrexia of 38–39°C continuously for twelve days postoperative, there was no increase in pulse rate, and on the contrary, a slight fall in pulse rate was noticed. The pulse rate returned to the preoperation level on the second day.

Figure 8 is a case of optico-chiasmal arachnoiditis in which a left craniotomy was performed. For four days after the operation, a slight pyrexia was noticed with no change in pulse rate. When the fever return to normal, a decrease in pulse rate was noticed from the fourth to the nineth postopera-

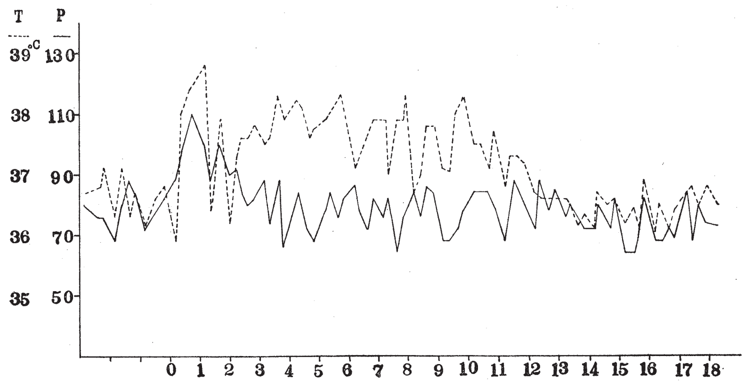


FIGURE 7. K. M. 23 y.o. male. Optico-chiasmal arachinoiditis. Right frontal craniotomy.

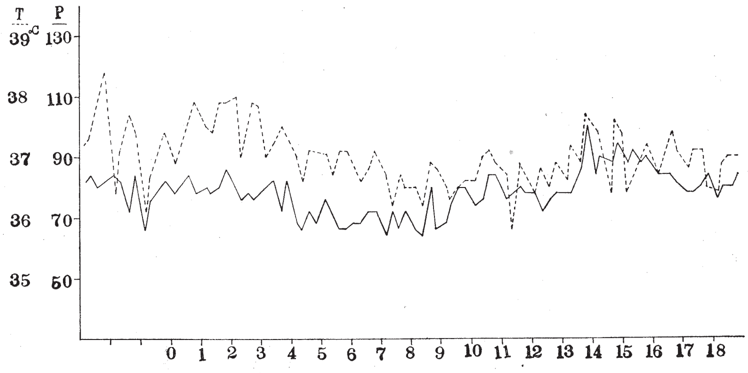


FIGURE 8. U. K. 26 y.o. female. Optico-chiasmal arachinoibitis. Left frontal craniotomy.

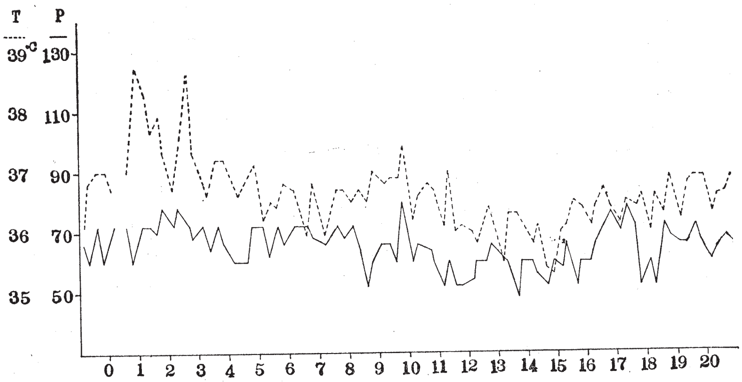


FIGURE 9. A. N. 28 y.o. male. Pituitary chromophobe adenoma. Right frontal craniotomy.

TABLE 3. Changes in Pulse Rate-Postoperation

Change in Pulse → Rate → Diseases ↓	Type 1	Type 2	Type 3	Total
Pituitary adenoma	7	8	4	19
Suprasellar tumor	0	1	1	2
Craniopharyngioma	2	1	3	6
Optico-chiasmal arachnoiditis	9	9	4	22
Retro-bulbar tumor	1	0	2	3
Others	1	3	1	5
Total	20	22	15	57
%	35	39	26	100

tive day.

Figure 9 is of a patient of hypophysial tumor. A right craniotomy was performed and the tumor was totally removed. Despite pyrexia, after the operation, no change was noticed in the pulse rate. However, between tenth and sixteenth day after the operation, a tolerable bradycardia was noticed which seemed to be caused by the operation.

Table 3 describes the changes in the pulse rate after the operation which were studied from all the cases: they fall into three catagories.

Type 1. A decrease of the pulse rate for seven-ten days after the operation as compared with the preoperation figure. Among them various subtypes were noticed.

Type 2. In spite of pyrexia or no pyrexia, no change of pulse rate after the operation was noticed.

Type 3. An increase of pulse rate was recorded postoperatively.

According to this table, 35% is type 1 and had decrease of pulse rate. On the other hand, 26% had increase and 39% had no change in pulse rate in spite of pyrexia or no pyrexia.

The cases of "decrease" and "no change" constitute the maiority of 74% and this trend is seen for seven-ten days after operation which is the recovering period. This means that there is a direct connection between the mechanial pressure to the posterior orbital surface and postoperative bradycardia. There were no differences noted whether the craniotomy was performed on either the right or the left side.

d) Cases suffered from a distinctive irregular premature beats during the operation.

Case 1. Y. K. Age 35, Male

The chief complaints were headache, nausea, vomiting and confusion. No serious illness in family history or anamnesis. Present history is eight months before this hospitalization, a diagnosis of lung infiltration was given. Headaches were occurring from this time. Two months before this hospitalization, the headaches gradually increased, and nausea and vomiting had started to occur. One month ago, he was hospitalized at a certain hospital with a possibility of brain tumor. A lumbar puncture showed 400 mm c.s.f.. On routine chest X-ray, an abnormal shadow was noticed at the right hilum of the lung. He was transferred to this department with a possibility of metastasis to the brain from lung cancer. As stated at time of hospitalization.

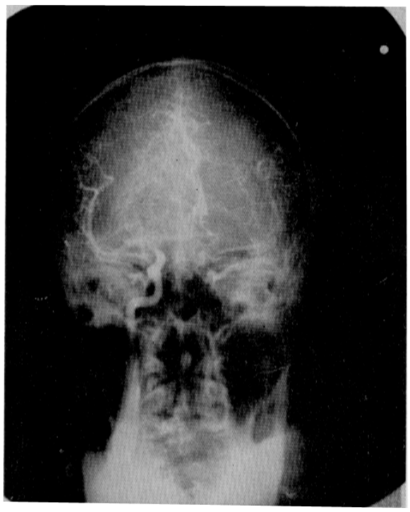


FIGURE 10

FIGURE 11

FIGURE 10 and 11 are cerebral angiograms of case 1. They demonstrate a metastatic lesion in right deep frontal lobe.

he was suffereing from confused state, severe headaches, nausea and vomiting. He showed positive neurology on examination and advanced choked disks were noticed in the retina. On cerebral angiography, a metastatic lesion was demonstrated deep in the right frontal lobe (Figures 10 and 11). A right craniotomy was performed. For anesthesia, nitrous-oxide anesthesia was used with Isozol.

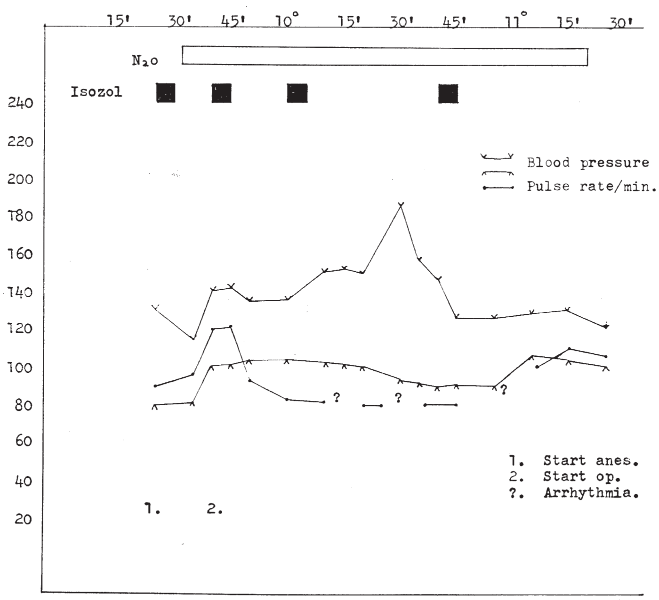


FIGURE 12. Anesthesia record of right frontal craniotomy.
Y. K. 35 y.o. male. Intracranial metastasis of lung cancer.

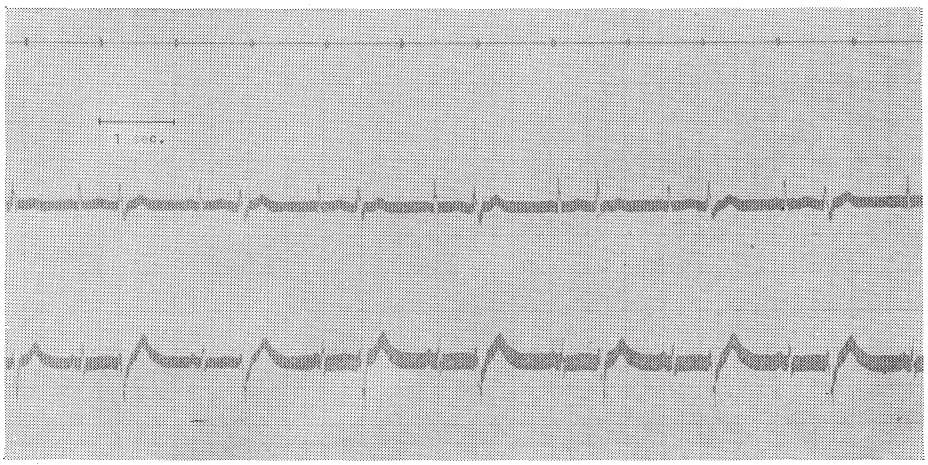


FIGURE 13. A part of continuous recording of ECG during right frontal craniotomy.

During the craniotomy as the orbital surface and callosal convolution was reached to remove the tumor, arrhythmia, bradycardia, and high blood pressure occurred. So whenever this operation was discontinued for a few moments, the pulse rate increased and arrhythmia disappeared. This was experienced repeatedly three times during the operation.

The record of anesthesia and ECG is shown in Figures 12 and 13.

Case 2. F. T. 36 years old, Female

Her main complaints were headaches, nausea, vomiting and gait disturbance. In her family history, there were persons who died from high blood pressure, apoplexy, and intestinal maligant tumors. She had diphtheria and pneumonia in childhood and pneumonia at twenty five years of age again. Headache began two years before entering the hospital. She had nausea and vomiting once every few (2-3) months.

At a certain hospital three months before she entered this department, she was told she had no abnormality. However, from that time, she complained of severe headaches. Gradually, the nausea and vomiting became more frequent occurring several times a day. Soon she had headaches continuously, especially severe in the morning. Her balance became unstable three weeks before entering the hospital, and she began to fall over backwards.

On neurological examination she was confused and advanced choked disks were noticed in her retina. Left hemiparesis, left facial nerve paresis, and left Babinski's test were positive. From the above mentioned symptoms, a possibility of right frontal tumor was considered. A right side cerebral angiography was taken, and a space taking lesion was suspected in the deep frontal lobe (Figures 14 and 15). A right frontal craniotomy was performed

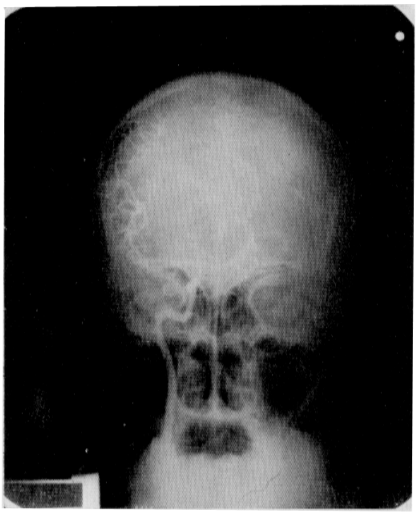


FIGURE 14

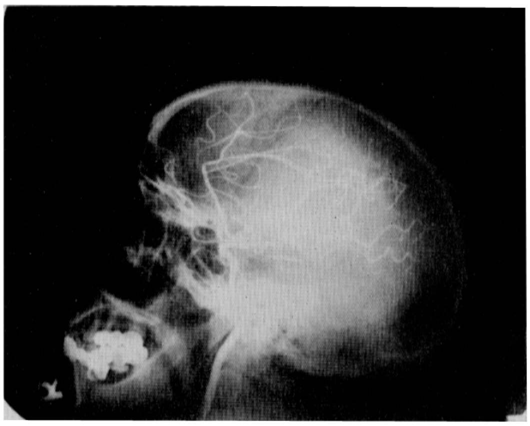


FIGURE 15

FIGURES 14 and 15 are cerebral angiograms of case 2. They demonstrate a brain tumor in right deep frontal lobe.

with nitrous oxide anesthesia. The biopsy showed that the tumor was malignant glioma, so therefore a right frontal lobectomy was performed. When the operation reached the callosal convolution of inner hemisphere and at the bottom of the orbital convolution, suddenly a ventricular tachycardia occurred and her pulse rose to 200/min, her blood pressure became impossible to record.

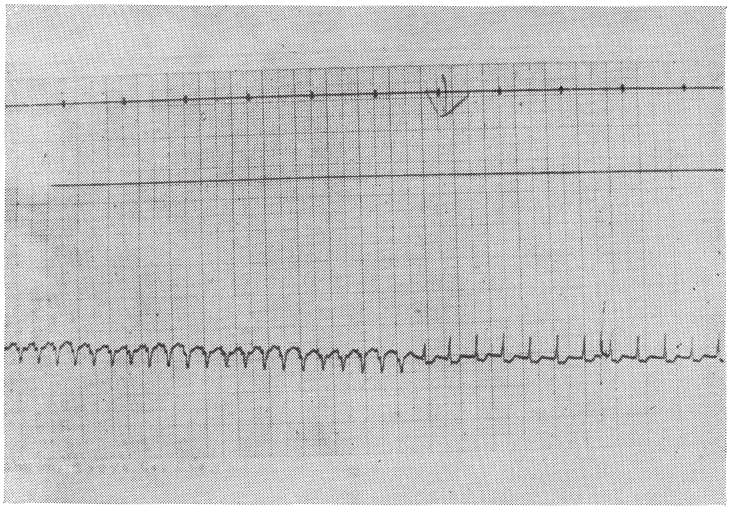


FIGURE 16. A section of ECG during right frontal craniotomy of case 2.

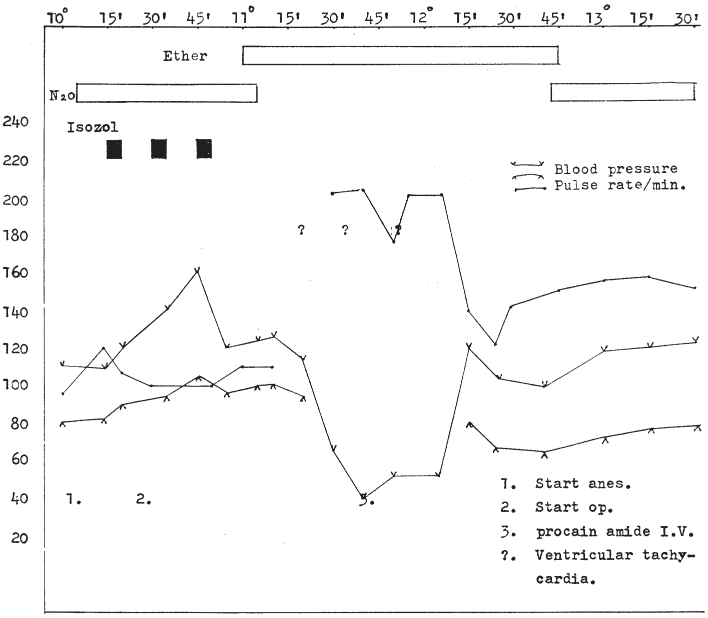


FIGURE 17. Anesthesia record of right frontal craniotomy. F. T. 36 y.o. female. Right frontal lobe tumor.

Figure 16 shows the ECG. Nothing serious happened when procain amide was given intravenously. At first nitrous oxide was used for anesthesia; however, since the tachycardia occurred, ether and oxygen was used. The nitrous oxide anesthesia is not harmful to the human being, and it is said that no reaction occurs to the body.

This case and case 1 show that the reaction was caused by a direct attack to the brain. Figure 17 shows the anesthesia record of this case.

Case 3. Y. S. 18 years old, Male

Main complaint is left visual disorder. Unremarkable family history and anamnesis were noted. As present hisory, at thirteen years old, he stopped growing and his left visual acuity was 0.3 which was impossible to remedy, then gradually his disorder of visual acuity increased. At seventeen years old, his left vision was reduced to perception of hand movements at one foot. From that time, an incrementum of subcutis occurred and his breast became like a female's and also a year ago his pubic hair decreased.

Ophthalmological findings:

Visual acuity of right was 0.9 and of left was hand movements at one foot. His visual fields showed temporal hemianopsia on right side and left was impossible to record. Fundi oculi showed an atrophied papilla in left eye and normal in right.

Skull X-ray showed an enlarged balloon type sella turcica as well as an erosion of posterior clinoid processes.

From a neurologic standpoint, nothing abnormal was noticed except the visual disturbance. The diagnosis of pituitary tumor was made and a right craniotomy was performed with light ether anesthesia by EMO inhaler,[60] and a removal of pituitary tumor was by paramediam approach. When the pressure to the posterior orbital plane with the brain spatula was applied, frequent

FIGURE 18. A part of continuous recording of ECG during right frontal craniotomy for pituitary tomor.

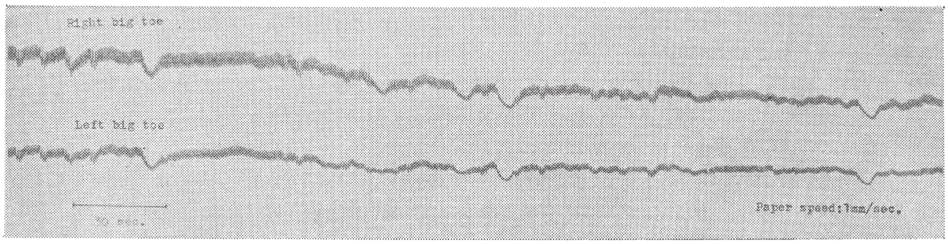


FIGURE 19. A part of continuous recording of RPP during right frontal craniotomy for pituitary tumor.

supraventricular extrasystole was noticed. ECG shown in Figure 18. Figure 19 is R.P.P. which was recorded simultaneously as which time a frequent irregular pulse was recorded.

Case 4. T. I. 51 years old Female

Her main complaints were right sided hemiplegia and speech disturbance. Unremarkable family history and anamnesis. Brief history of her illness is as follows; onset of illness was in the Feburary of 1959 when she noticed difficulty of speech and tinnitus, and she was told she had encephalomalacia at that time. She fell in the June of 1960 and became hemiplegia on right side ever since. She had attacks of convulsion of right limbs in the July of 1960 and speech disturbance progressed. She began to have headache in the summer and vomiting in the fall of same year. From the neurologic standpoint, sensorium was clear on appearance, but almost completely aphasic motorwise and sensory as well. She showed disorientation of right and left although this could be a part of her apraxia and not that of the Gerstman's syndrom. She demonstrated almost complete right hemiplegia including lower two-thirds of the face on that side. Advanced papilledema bilaterally. E.O.M. not impaired. From the above mentioned statement, a possiblity of brain tumor at left central area was considered. Left carotid angiograms show enormous tumor staining over left Rolandic area (Figures 20 and 21). A left parieto-frontal craniotmy was performed under EMO ether anesthesia, and convex meningioma was removed completely. During the craniotomy, when the Rolandic area was reached in order to remove the tumor, marked tachycardia occurred which continued for next thirteen days (Figure 22) in spite of various treatments, until she regained consiousness fully.

2) *The Change of Reflex Photoelectric Plethysmograph* (*R.P.P.*)

A research of peripheral circulation using the photoelectric plethysmograph (P.P.) has become epochmaking since Hertzman (1938)[23] *et al.* had invented the R.P.P. recorder. In Japan, many researches were reported since Kobayashi (1937)[24] had originated the P.P. recorder. Ishikawa, etc.[32][33][45] reported cases of many kinds of disorder of in peripheral blood circulation by using the P.P.

At the First Surgical Department (Prof. Hashimoto) Tsuzaki[77] and Fujimura[23] reported the influence on the P.P. when different ways of surgery

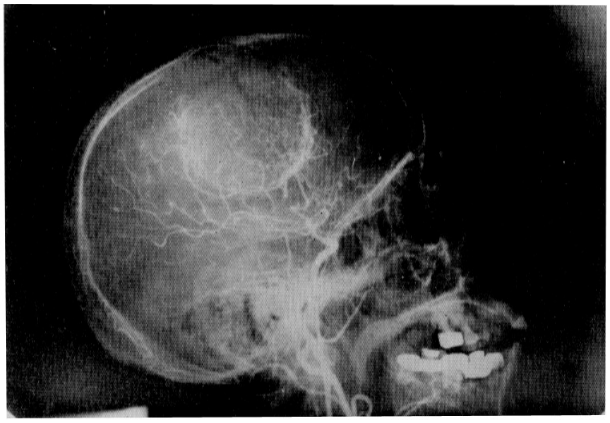


FIGURE 20

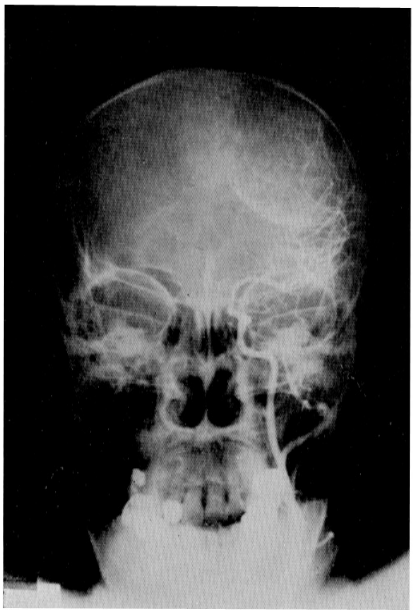


FIGURE 21

FIGURES 20 and 21 are cerebral angiograms of case 4, and they demostrate a big brain tumor over Rolandic area.

to the sympathetic nerve were made. Kamiya etc.[38,59] reported the relationship between the brain surgery and P.P. Saegusa[65,66] studied the correlation of ECG and P.P. and also reported the pulse wave transmission time.

Also at the First Physiological Department, Takagi, Ikegami, Yamada, Sakae, *et al.*, reported their general remarks and researches of R.P.P.[30,31,67,76,81]

The problem which I am interested in during brain surgery, especially in the posterior orbital plane, is whether the peripheral blood vessel make a constriction, a dilation, or no change and also if L/R difference exists.

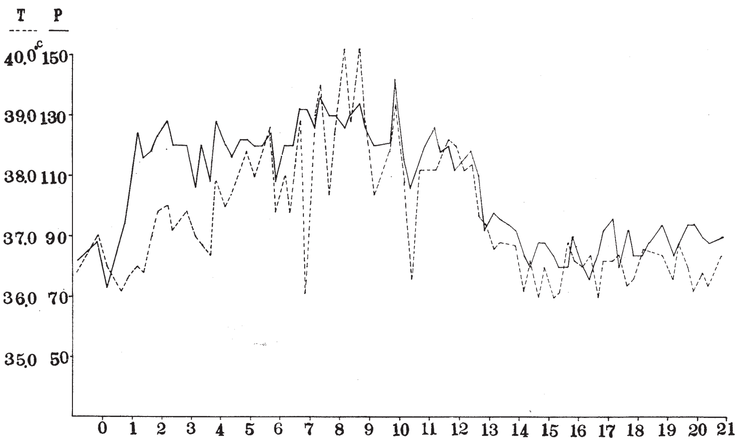


FIGURE 22. T. I. 51 y.o. female. Meningioma in left motor area.

The volume change of a finger is considered to show the circulation of skin blood vessel fairly accurately. Therefore, for this reason I have selected both L/R halluces. Of course, the results which has been reported here cannot be referred to every skin. The tonicity of the sympathetic nervous system becomes higher when it reaches the periphery, and also the arteriovenous shunt, which acts as a important part of the skin blood vessel function which are remarkably developed at the tip of the finger or toe, is distributed with numerous sympathetic nerve fibers.

Another important point we can consider is that the finger or the toe consist of only skin blood vessels. However, we cannot avoid considering the artery or the vein of an arm or a leg on the artery or vein of the finger or toe since the blood system of the finger and toe are periphery of the arm and leg. Therfore I feel that a finger skin blood vessel will represent whether there is constriction or dilation of skin blood vessel caused by a certain operation as a stimulation to orbital surface of the frontal lobe.

a) Recordings at Preoperative Status

The records were taken at the following conditions: (a) the operation room's temperature was 15°-20°C, (b) the patient was placed in supine position and made as comfortable as possible, and (c) the R.P.P. recording were taken from L/R thumb and big toe pad.

In all cases (11) cases there were no L/R differences. A number of observations on the spontaneous fluctuation in plethysmographic records have been made by Burch,[8] Hertzman,[27] Sawada,[68] Nagashima,[55] Suzuki,[73] Ishikawa,[33] etc.

The spontaneous fluctuations have been analysed only mathematically and classified into several groups without considering any physiological significance. But recently Ihara[30] found some correlations between these fluctuations and certain psychosomatic conditions and he classified them into several patterns.

In my series as reported in details by Ihara, these fluctuations run parallel with change of psychosomatic conditions.

There is an individual difference in vasomotor response elicited with a stimulation which will give a mental disturbance such as: crack sound, pain, hot, cold, mental calculation and recollection, etc.. However generally after 3 seconds of latent periods, a radical downward trend to base line and a decrease of amplitude appeared. Then a slight upward or an increase in amplitude follows. Both sides (L/R) show similar changes and it can almost be considered a duplication. In all examples, no case of vasomotor abnormality were noticed.

b) Change-During the Operation

Proceeding with the anesthesia, the spontaneous fluctuation of the base line had disappeared and flattened with the exception of the pulse wave which equalled to the heart beat and breathing wave by controlled respiration during skin incision or other procedure during operation. The fluctuation of base line were not noted except the ones mentioned above (Figures 23, 24 and 25).

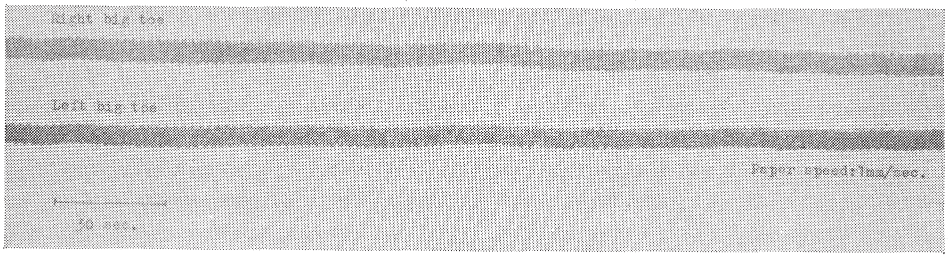


FIGURE 23. A part of continuous recording of RPP during right frontal craniotomy (before elevation of the posterior orbital surface).

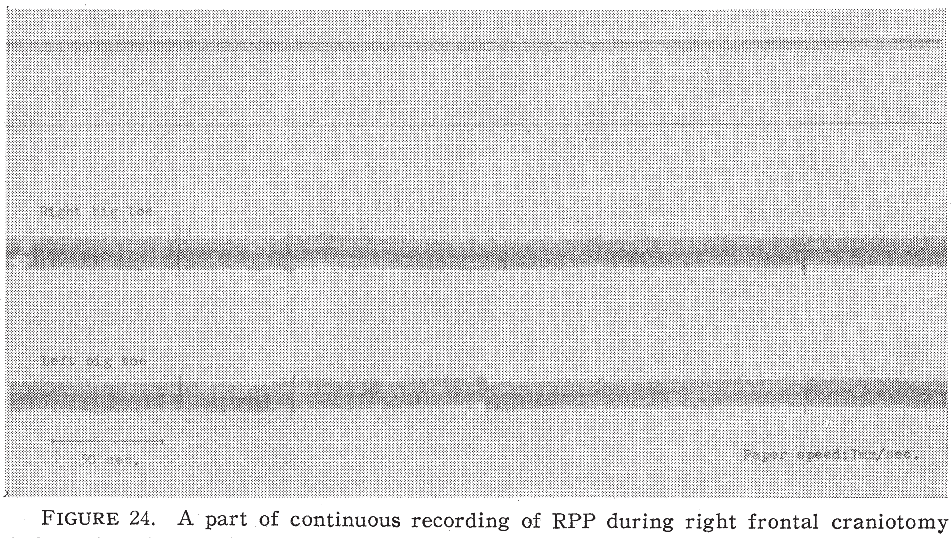


FIGURE 24. A part of continuous recording of RPP during right frontal craniotomy (before elevation of the posterior orbital surface).

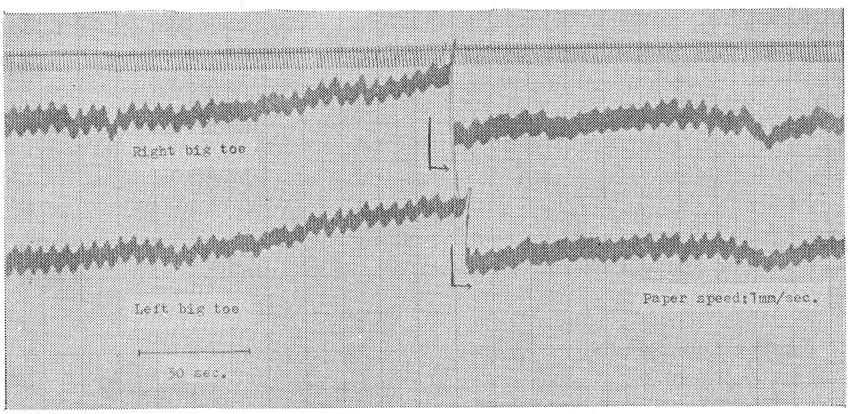


FIGURE 25. A part of continuous recording of RPP during right frontal craniotomy (before elevation of the posterior orbital surface).

At the incision of the dura mater, there is no change. However, if when the tip of frontal lobe was compressed by a brain spatula, and a cotton cloth dampened with physiological saline was introduced into the orbital plane, a radical downward trend of the base line and a decrease of amplitude occurred symmetrically and gradually it approached the basic level followed by a fluctuation of the base line with a cycle of 8–10 seconds, appears and generally a prominent fall of base line was noticed. During this time, almost no changes in blood pressure was noticed. This shows that there is a symmetrical constriction of the peripheral blood vessel especially in the arterioles (Figures 26, 27 and 28). The prominent fall of the base line and fluctuation appeared 8–10 minetes after the operation was performed to the posterior orbital plane. Then after periodically induced fluctuation, cycle of 10 seconds appeared while the operation continued and a fall of the base line is confirmed (Figures 29, 30, 31 and 32).

The frequency distribution of the cycle of the base line fluctuation when

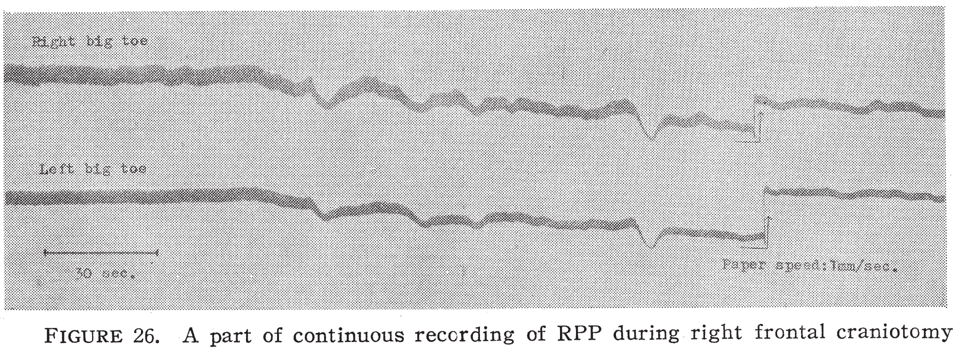


FIGURE 26. A part of continuous recording of RPP during right frontal craniotomy (a brain spatula or cotton pledget is introduced into the posterior orbital surface).

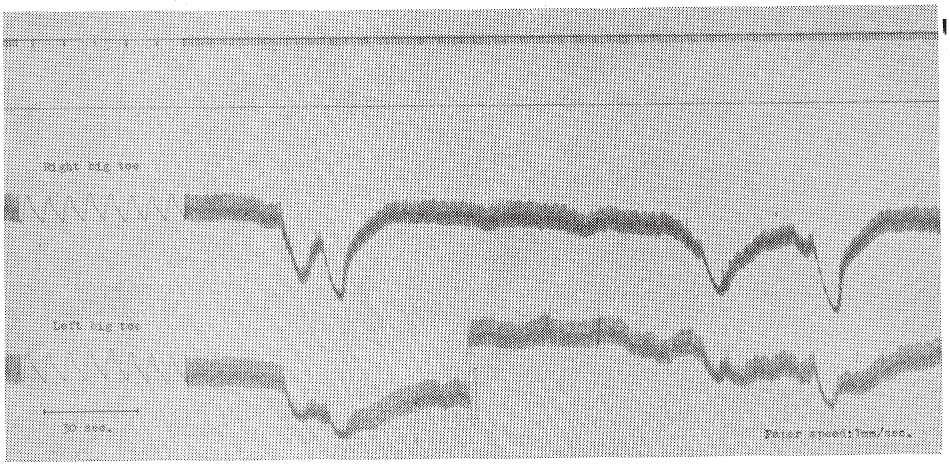


FIGURE 27. A part of continuos recording of RPP during right frontal crniotomy (a brain spatula or cotton pledget is introduced into the posterior orbital surface).

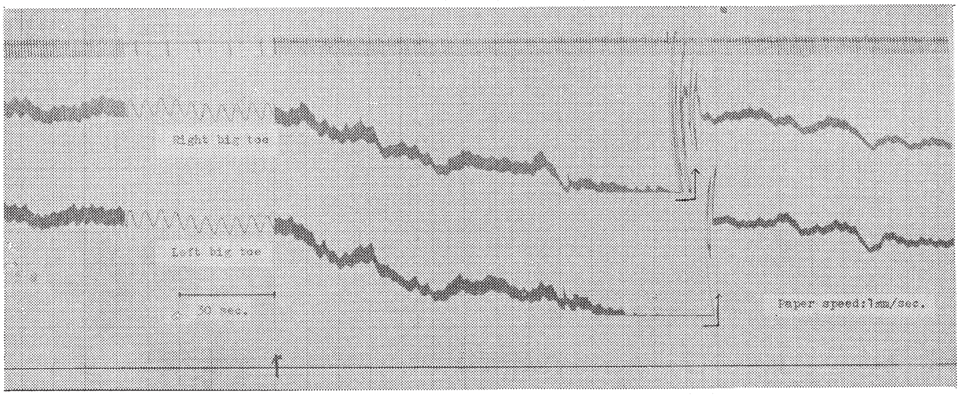


FIGURE 28. A part of cotinuous recording of RPP during right frontal craniotomy (a brain spatula or cotton pledget is introduced into the posterior orbital surface).

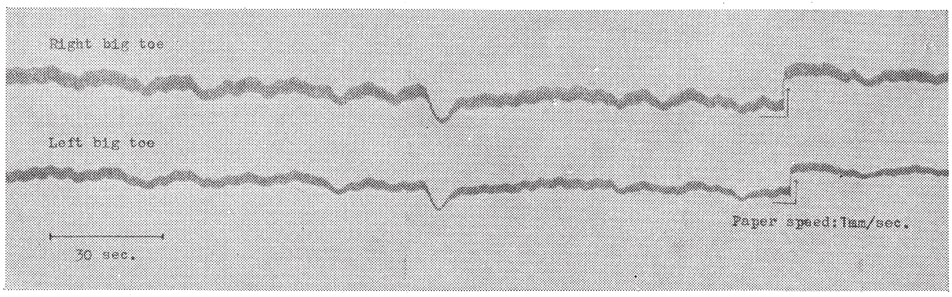


FIGURE 29. A part of continuous recording of RPP during right frontal craniotomy (elevation of the posterior orbital surface is continued).

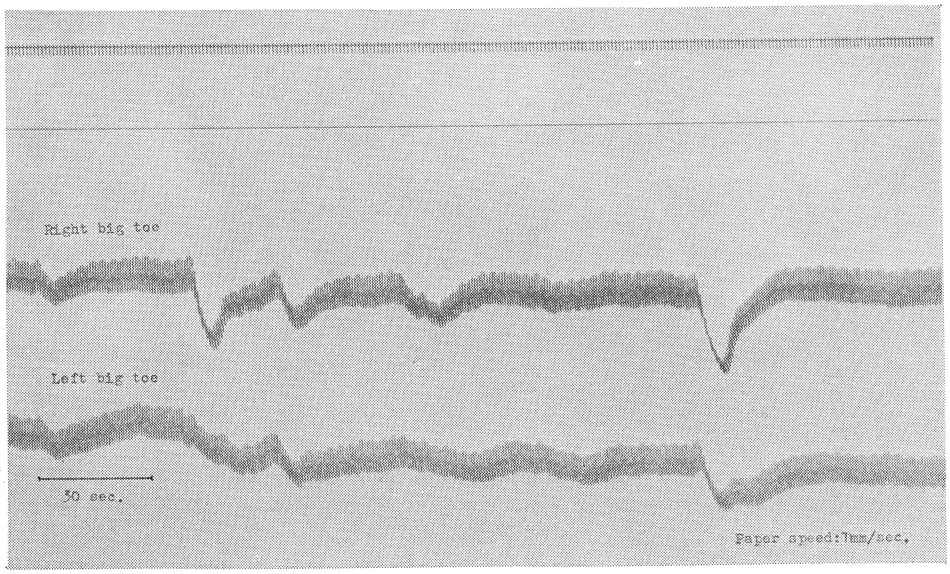


FIGURE 30. A part of continuous recording of RPP during right frontal craniotomy (elevation of the posterior orbital surface is continued).

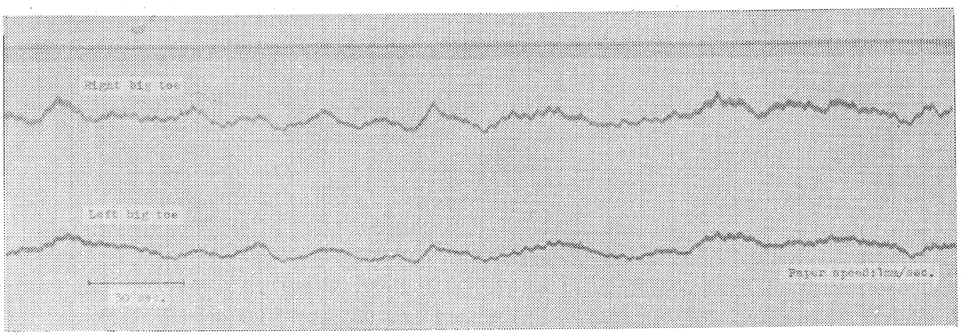


FIGURE 31. A part of continuous recording of RPP during right frontal craniotomy (elevation of the posterior orbital surface is continued).

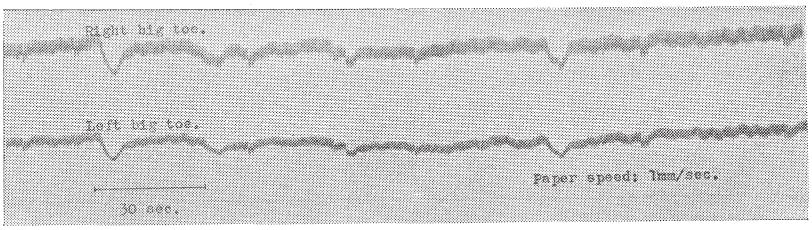


FIGURE 32. A part of continuous recording of RPP during right frontal cranitomy (elevation of the posterior orbital surface is continued).

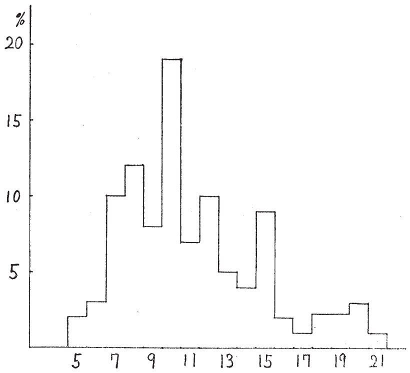


FIGURE 33

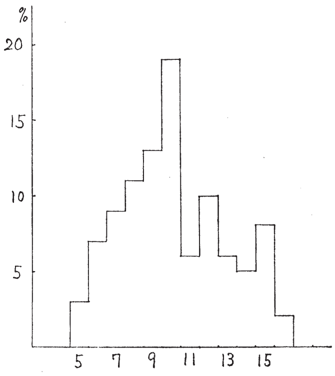


FIGURE 34

FIGURE 33. Histogram of wave period during right frontal craniotomy.
FIGURE 34. Histogram of wave period during right frontal craniotomy.

the operation is performed to the orbital plane, is shown on Figures 32 and 34. The fluctuation with a cycle of 10 seconds occupies over half of the all.

3) Change of Skin Temperature during the Operation

Immediately after the beginning of anesthesia, a slight transient upward is noticed by peripheral blood vessel dilation action of ether. However, immediately after the stimulation to the orbital plane, a comparatively rapid fall is noticed and after the pressure is withdrawn, it returns to the preoperative level gradully (Figure 35). It was confirmed that at the finger or the

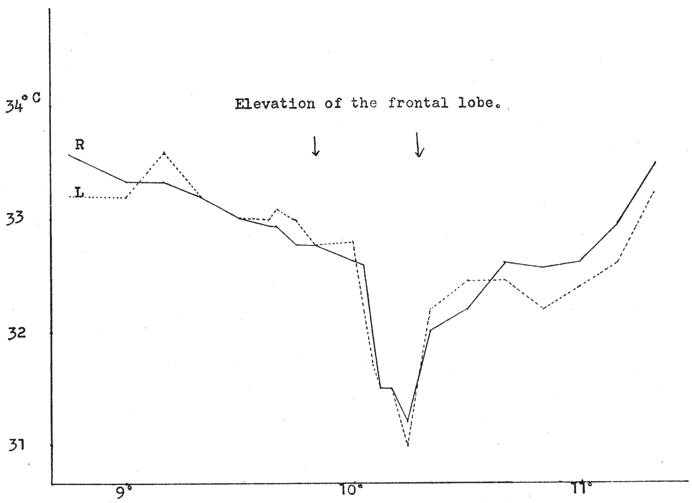


FIGURE 35. Change of skin temperature during right frontal craniotomy for pituitary tumor.

toe tip, the fall of skin temperature roughly runs parallel with the fall of the base line of R.P.P. and the fall of skin temperature occurs slightly after the change of R.P.P. The fall of skin temperature and the fluctuation and the fall of R.P.P.'s base line appears prominently for the first 8–10 minutes.

The fact that the skin temperature of hullux's tip fell to 2.6°C, shows that skin blood vessel of the hullux tip, especially the arteriole, constricts with the fall of the base line and decrease in amplitude in R.P.P. In this case, there is no significant differences at both hullux tip (L/R).

V. DISCUSSION

1) Stimulation to the orbital surface of the frontal lobe

As a part of the limbic system, the orbital surface of the frontal lobe possesses the autonomic nervous function. This is confirmed by many workers since Spencer[72] reported this fact and since then, there has been no contradiction. However, as a result of various reactions, such as change in blood pressure, Spencer,[72] Bailey and Sweet,[3] Chapman[12] reports an increase while Delgado,[15] Freeman and Watt,[22] Falconer,[18] Scarff,[69] Greenbaltt,[26] etc., reports a decrease. Also similar reactions of the pulse rate and skin temperature has been observed. From these facts, I conclude that either sympathetic or parasympathetic action can be elicited with a stimulation to the same part according to the circumstance and variety or extent of stimulation.

From my study, the following results were observed: (a) no significant change appeared at both rise and fall of blood pressure, (b) the majority shows a decrease in pulse rate, and (c) when recording R.P.P. and skin temperature, a constriction of arteriole is noted.

The effects of the orbital surface of the frontal lobe to the various organs of the body and mental condition are in many way separated and the conditions of the effects are numerous.

All experimental and clinical observations which have been reported to the present indicate a firm decending autonomic pathway from the posterior orbital surface to vagus nerve through thalamus-hypothalamus-brain stem or sympathetic nerve through thalamus-hypotholamus-brainstem-spinal cord. According to Meyer, *et al.*[51) 52] and Freeman and Watt[20) 21] the fiber connection of the posterior orbital suface and hypothalamus which was up to this time considered to be the supreme center of the autonomic nervous system is mostly indirect and via relays in the medial thalamic nuclei and partly direct such as fibers in the medial forebrain bundle interconnecting hypothalamic nuclei with the preoptic and para-olfactory cortical areas in men and monkeys. Ward and McCulloch[79] report that with strychinin neurography, the orbital surface of the frontal lobe projects the posterior hypothalamic area and paraventricular nucleus.

Clark and Meyer,[13] Beck *et al.*,[5] and Wall *et al.*[78] have reported that a large, direct, unmyelinated efferent pathway passes from the orbital gyri to the ventromedial and lateral hypothalamic nuclei, both in men and monkeys. On the other hand, Bailey and Bremer[4] discovered that stimulation of the central end of a vagus nerve caused electrical activity in the orbital surface of the frontal lobe in cats, and Dell[17] and Dell and Oslon[16] claimed that they have traced ascending vagal projections to the posterior orbital gyri.

The hypothalamus acts as an important part of the autonomic nervous function, especially, the cardio-vascular system and temperature regulation system. This was first clarified by Karplus and Kreidi.[39][40][41] Since then, through many researches, it is gradually becoming clearer, *i.e.*, stimulation of paraventricular nucleus, posterior hypothalmic nuclei, ventromedial hypothalmic nuclei, and lateral hypothalmic nuclei cause a sympathetic change such as, rise in blood pressure, constriction of blood vessels, and tachycardia, etc.. By a stimulation of pre-optic, supra-optic and tuberal nuclei, a fall in blood pressure, bradycardia, etc., a parasympathetic change occurs.

From this study, a stimulation to the orbital surface of the frontal lobe, which has a close fiber connection with the hypothalmus, has a great influence on autonomic nervous system, in other words, whether sympathetic nerve function or parasympathetic nerve function will become dominant depends on the variety or extent of the stimulation or on the condition.

2) The change of Cardiac Rhythm

A stimulation of the orbital surface of the frontal lobe by a cotton cloth containing cold physiological saline and also by brain spatula pressure, in a majority of cases a trend of decrease in pulse rate was noticed. Furthermore, this trend was noticed for seven-fourteen days of postoperation which were the recovery period of brain surgery. Also in a few cases, occurrence of extrasystole was noticed.

From the above-mentioned facts, it has been confirmed that the posterior orbital surface of the frontal lobe extremely affects the cardiac rythum.

The nerves which control the cardiac rate are the vagus nerve and the accelerance nerve. The heart is based on the balance of the activity of both nerves.

The vagus nerve acts inhibitively and the accelerance nerve acts acceleratively. The rhythm of the heart is maintained by the co-operation of both nerves.

In respect to the occurrence of extrasystole, there are some reports that an occurrence will be generated by the stimulation of either vagus nerve or sympathetic nerve. However, normally an extrasystole will not occur by this only. If both nerves are stimulated at the same time, extrasystole frequently occurs.

This means that a stimulation of the accelerance nerve will accelerate the ectopic excitation; however, at the same time, it will irritate the sinus excitation, so becoming a tachycardia, it will be difficult for the extrasystole to occur. When both nerves are stimulated at the same time, the dominance of the vagus nerve is superior to the sinus node. Therefore, a sinus bradycardia will occur and a extrasystole will occur readily that is, because the interval of the heart beat will become long by vagus stimulation, it is interpreted that there will be an increase chance which makes the lower centre function to cause the extrasystole by the stimulation of acceleration nerve.[43] According to these changes of cardiac rhythm which occur during the operation, there is a possibility that these are caused by the anesthesia itself or by intratracheal intubation.[2)9)58] Furthermore, general physical changes will occur during the operation such as anoxia,[34] hyperventilation,[70)82] PH variation,[29] electrolyte especially K^+ variation,[56] bleeding, and blood transfusion. These all can be contributing factors. However, it is observed that during many cases of craniotomy which were performed under the same condition, no prominent changes occur. But at an operation of the orbital plane, these changes occur, and will continue until the neurological symptoms become normal after recovery from the operation. It is considered from these facts, that these changes occur by the direct operation to the posterior orbital surface of the frontal lobe.

As the problem of extrasystole, the explanation of its occurrence can be made when we are aware that there are representation of sympathetic and para-sympathetic nerves in the posterior orbital surface of the frontal lobe.

3) Change of Reflex Photoelectric Plethysmograph

What reflex photoelectric plethysmograph (R.P.P.) indicates physiologically has been debated very much and it is a common opinion that direct-coupled R.P.P. reveals: in the certain parts of the body: a) the difference in blood volume between inflow and outflow, b) constantly remaining blood volume, c) the diffrence in lymph fluid volume between inflow and outflow and d) constantly remaining tissue and lymph fluid volume.

Ikegami[31] compared R.P.P. with the records simultaneously taken by various other plethysmographic methods such as penetration photoelectric plethysmograph (P.P.P.), mechanico-electrical plethysmograph (M.E.P.) and so on, moreover he observed the change of numbers of capillary loops of finger nail bed under dermatoscope simultaneously as well, and concluded that the factors which influence the R.P.P. curve are the difference in blood volume between inflow and outflow, and constantly remaining blood volume in the certain parts. The blood vessels in finger and toe tips are arterioles, capillaries, venules and arteriovenous shunt. Among of them, arterioles chiefly affect the R.P.P. curve. Therefore the declination of the level in R.P.P. curve with reducing amplitude is considered to reveal decreasing of peripheral blood flow, and a rising level with increase amplitude to show increasing peripheral blood flow. In all cases no blood pressure change should occur.

It has long been noted that hemiplegics complain of coldness and sometimes of edema on the paralyzed side which is not accounted for by the immobility. Bucy[7] described a case of intensive vasospasm in the paralyzed extremities and believed that the cortical autonomic centers were paralysed, and releasing the activity of the peripheral sympathetic system. Also many investigations concerning the cortical autonomic activities have been reported.

I recognised the declination of the level in R.P.P. curve with reducing amplitude occurring on both sides simultaneouly, when the posterior orbital surface of the frontal lobe was elevated by a brain spatula or stimulated with a cotton pledget immersed in cold physiological saline. In other words, it indicates the constriction of peripheral vessels, especially arterioles, occurred on either side simultaneously. These changes are continuously recognized when the orbital surface is elevated and stimulated.

In all previous reports stimulation or destruction of the cortex elicits the vasoconstriction or vasodilation in opposite extremities, and they strictly recognize the laterality of the automonic nervous function. As an exception Narabayashi[57] reported the bilateral vasodilation in fingers and toes following unilateral stereotaxic pallidotomy.

As I investigated these changes in only clinical operations, I could not find such an accuracy as in animal experiments; however, bilateral vasomotor changes by stimulation of unilateral posterior orbital surface of the frontal lobe present a problem.

4) *The Change of Skin temperature*

The method of studying the peripheral circulation by skin temperature has been advanced by the invention of electric thermometers. Especially, this study owes much to Lewis, Pickering and Grant[46][47] of England, amongst others. There are also reports from the research team of Mayo Clinic, United States, including, Brown, and Adson,[6] Allen, Baker and Hines.[1] Furthermore White and Smithwick,[80] Freeman,[19] Gibbon and Landis[25] designed a method of recording the finger's circulatory condition by using the thermocouple. Recently, Burton[10] announced a general remarks on this matter.

Generally, the color of the skin describes the quantity of blood in the certain part. On the other hand, the temperature is regulated by quantity of blood which runs through the certain part.[75] The skin temperature is influenced by many factors such as, enviromental temperature, body temperature, metabolism, the reactive condition of autonomic nerve, and intake of food, respectively. Therefore, the skin temperature is not always in proportion to the blood quantity. However, it is considered that there is no problem to the qualitative point whether the blood quantity had increased or decreased. The blood quantity of skin is normally determined by the condition of capillary vessel's tonicity and venule. And the volume of blood stream is regulated with the degree of dilation or constriction of arteriole which carry blood to the certain part.

I had recorded the skin temperature at the same time of R.P.P. When the operation reached to the orbital surface of the frontal lobe, I noticed the fall of skin temperature of the left and right toe equally bilaterally soon after the changes in R.P.P.

After the operation to the orbital surface of the frontal lobe had been completed, it was noticed that the skin temperature returned rapidly to its preoperative level. In this case, it is not always parallel with R.P.P. changes.

VI. CONCLUSION

1) It was confirmed that there is a sympathetic and parasympathetic action at the posterior orbital surface of the frontal lobe in human beings.

2) About the change of pulse rate, there is a trend that bradycardia will occur for seven-fourteen days after operation which was generally considered as recovering period from brain surgery.

3) The change of R.P.P. and skin temperature show that a bilateral constriction of skin arterioles occurred with the operation of unilateral posterior orbital surface of the frontal lobe.

The auther wishes to express his cardinal acknowledgement to Prof. Dr. Y. Hashimoto, Prof. Dr. K. Takagi, Dr. K. Iwata, Dr. M. Suzuki, and to other neurosurgical members of the 1st Surgical Department School of Medicine, Nagoya University for their guidance and encouragement.

REFERENCES

1. ALLEN, E. V., N. E. BARKER, AND E. A. HINES. *Peripheral vascular disease* (2nd Ed.). Philadelphia: W. B. Saunders Co., 1956.
2. ANAZAWA, Y. AND A. MIZUNO. *Jap. J. anesthesiology* **1**: 115, 1952.
3. BAILEY, P., AND W. H. SWEET. *J. Neurophysiol.* **3** 276, 1940.
4. BAILEY, P. AND F. BREMER. *J. Neurophysiol.* **1**: 405, 1938.
5. BECK, E., A. MEYER AND J. LEBEAN. *J. Neurol. Neurosurg. Psychiat.* **14**: 295, 1951.
6. BROWN, G. E., P. A. O'LEARY AND A. W. ADSON. *Ann. Int. Med.* **4**: 531, 1930.
7. BUCY, P. C. *Arch. Neurol. and Psychiat.*, **33**: 30, 1935.
8. BURCH, G. E. *Medical in Reserch* **1**: 166, 1947; *Am. Heart. J.* **33**: 48, 1947.
9. BURSTEIN, C. L., F. J. LOPINTO AND W. NEWMAN. *Anesthesiol.* **1**: 224, 1950.
10. BURTON, A. C. *Methods in medical reserach.* Chicago: Year Book Publisher, 1948.
11. CHAPMAN, W. P., R. B. LIVINGSTON AND K. K. LIVINGSTON. *Arch. Neurol. Psychiat., (Chicago)* **62**: 701, 1949.
12. CHAPMAN, W. P., K. E. LIVINGSTON AND J. L. POPPEN. *J. Neurophysiol.* **13**: 95, 1950.
13. CLARK, W. E., LE GROS AND M.MEYER. *Brit. Med. Bull.*, **6**: 341, 1950.
14. DAVIS, G. D. Quoted from Fulton, J. F., *ann. Rev. Physial.*, **15**: 307, 1953.
15. DELGADO, J. M. R. AND R. B. LIVINGSTON. *J. Neurophysiol.*, **11**: 39, 1948.
16. DELL, P. AND R. OLSON. *C.R. Soc. Biol. (Paris)* **145**: 1084, 1952.
17. DELL, P. *J. Physiol. (Paris)* **44**: 471, 1951.
18. FALCORNER, M. A. *Res. Publ. Ass. nerv. ment. Dis.* **27**: 706, 1948.
19. FREEMAN, N. E., R. H. SMITHWICK AND J. C. WHITE. *Am. J. Physiol.* **107**: 529, 1934.
20. FREEMAN, W. AND J. W. WATTS. *Res. Publ. Ass. nerv. ment. Dis.* **27**: 200, 1948.
21. FREEMAN, W. AND J. W. WATTS. *J. comp. Neurol.* **86**: 65, 1947.
22. FREEMAN, W. AND J. W. WATTS. *Lancet*, **1**: 953, 1946.
23. FUJIMURA, S. *J. Nagoya med. Ass.* **74**: 1084, 1957.
24. FURUBAYASHI C. UND M. YAMAMOTO. *Nippon. J. Clin. angiocardiol.* **3**: 28, 1937.
25. GIBLON, J. H. AND E. M. LANDIS. *J. clin. Investigation*, **11**: 1019, 1932.
26. GREENBLATT, M., R. ARNOT AND H. C. SOLOMON. *Studies in Lobotomy.* New York: Grune and Stratton, Inc.
27. HERTZMAN, A. B. *Methods in Medical Research*, **1**: 177.
28. HERTZMAN, A. B. *Am. J. Phystol.* **124**: 328, 1938.
29. HOFF, H. E. AND R. S. GRANT. *J. Neurophysiol.* **7**: 305, 1944.
30. IHARA, S. AND T. SAKAE. *Seitai no kagaku*, **9**: 378, 1958.
31. IKEGAMI, Y. *Resp. and Circul.* **6**: 881, 1958.
32. ISHIKAWA, K., S. TORADA, T. WASHIZAWA, H. KORESHIMA, K. TAKANO AND Y. MISHIMA. *Resp. and Circul.* **5**: 865, 1957.
33. ISHIKAWA, K., K. TAKEUCHI, S. TORADA, C. NAGASHIMA AND Y. MISHIMA. *Jap. J.*

Surg. Soc. **57**: 1728, 1957.
34. JACOBY, J., C. ZIEGLER, W. HAMELBERG, A. MOGG, K. KLASSEN AND F. FLORY. *Anesthesiol.* **16**: 1004, 1955.
35. KAADA, B. R., AND H. JASPER. *Arch. Neurol. Psychiat.* (*Chicago*) **68**: 609, 1952.
36. KAADA, B. R. *Acta physiol, scand.* **24**: 1, 1951.
7. KAHN, E. A., R. C. BASSETT, R. C. SCHNEIDER AND E. C. CROSBY. *Correlative Neurosurgery.* Charles Thomas publisher Co. Ltd., 1954.
8. KAMIYA, K., M. OAKU, S. AKIYAMA AND S. NAKAMURA. *Brain and Nerve.* **11**: 97, 1959.
9. KARPLUS, J. P. AND A. KREIDLE. *Pflügers Arch. ges. physiol.* **129**: 138, 1909.
0. KARPLUS, J. P. AND A. KREIDLE. *Pflügers Arch. ges. physiol.* **135**: 401, 1910.
1. KARPLUS, J. P. AND A. KREIDL. *Pflügers Arch. ges. physiol.* **143**: 109, 1912.
2. KENNARD, M. A. "*Somatic function*" pp. 243-276, "*Autonomic functions,*" pp. 293-306, In Bucy, P. C., Ed., "*The presentral motor cortex*" 2nd Ed. Urbana: University of Ilinois Press., 1949.
3. KIMURA, E. *Fuseimyaku no Rinsho.* Tokyo: Kinpodō, 1958.
4. KONDO, S., K. TAKEUCHI AND K. SHIMIZU. *Brain and Nerve.* **4**: 43, 1952.
5. KORE, H. *J. Jap. Surg. Soc.* **60**: 1932, 1960.
6. LEWIS, T. AND R. GRANT. *Heart.* **12**: 73, 1925.
7. LEWIS, T. AND G. W. PICKERING. *Heart.* **16**: 33, 1931.
8. LIVINGSTON, R. B., J. F. FULTON, J. M. R. DELGADO, E., Jr. SACHS, S. J. BRENDLER AND G. D. DAVIS. *Res. Publ. Ass. nerve. ment. Dis.* **27**: 405, 1948.
9. MACLEAN P. D. AND A. ARELLANO. *Electroenceph. Clin. Neurophysiol.* **2**: 1, 1950.
0. MACLEAN, P. D., J. M. R. DELGADO AND K. H. DRIBRAM. *Ann. Rev. Physiol.* **15**: 305, 1953.
1. MEYER, A., E. BECK AND T. MCLARDY. *Brain.* **70**: 18, 1947.
2. MEYER, A. AND T. MCLARDY. *J. ment. Sci.* **95**: 403, 1949.
3. MITCHELL, G. A. G. *Cardiovascular innervation.* Edinburch and London: E. and S. Livingstone LTD. 1956.
4. MULDER, D. W., D. DALY. AND A. A. BAILEY. *Arch. Inten. Med.* **93**: 481, 1954.
5. NAGASHIMA, C. *Nervous control of human blood vessels.* Tokyo Univ. Press. 1959.
6. NAHUM, L. H. AND H. E. HOFF. *J. Pharmacol. Exp. Ther.* **65**: 323, 1939.
7. NARABAYASHI, H., T. NAGAO AND WATANABE. *Brain and nerve.* **13**: 953, 1961.
8. NOZAKI, S. *J.J.T.S.S.* **2**: 382, 1954.
9. OAKU, M. *J. Nagoya. Med. Ass.* **78**: 330, 1959.
0. ODA, M., I. WAKAI, K. KAMIYA, S. KATO, H. FUKUSHIMA AND B. SAKAKIBARA. *Ikakikaigaku Zasshi.* **30**: 1, 1961.
1. OKINAKA, S., K. NAKAO, H. NAKAMURA, M. IKEDA, T. TSUBAKI. Y. KUROIWA AND Y. TOYOKURA. *Folia Pschia. Neur. Jap.* **7**: 141, 1953.
2. POPPEN, J. L. *An atlas of neurosurgical techniques.* Philadelphia and London: W. B. Saunders Co., 1960.
3. RUCH, T. C. AND H. A. SHENKIN. *J. Neurophysiol.* **6**: 349, 1943.
4. SACHS, E. JR., S. J. BRENDLER AND J. F. FULTON. *Brain.* **72**: 227, 1949.
5. SAIGUSA, S. AND R. ZINBO. *Nagoya J. M. S.*, **20**: 4, 1958.
6. SAIGUSA, S. *Nagoya J. M. S.* **21**: 2, 1958.
7. SAKAE, J. *Resp. and Circul.* **7**: 1125, 1959.
8. SAWADA, M. *Resp. and Circul.* **6**: 417, 1958.
9. SCARFF, J. E. *J. Neurosurg.* **7**: 330, 1950.
0. SCHERF, D., M. GOLDFORB AND R. BUSSAN. *Circulation.* **12**: 271, 1955.
1. SMITH, W. K. *J. Neurophysiol.* **1**: 55, 1938.
2. SPENCER, W. G. *Philos. Traus. B.* **185**: 609, 1894. (Cited from 53,).

73. SUZUKI, A. *Iryo.* **10**: 1012, 1956.
74. TAKEUCHI, K. *Brain and Nerve.* **10**: 171, 1958.
75. TASAKA, S. *Saishinigaku.* **10**: 926, 1955.
76. TERATA, M. *J. Physiol. Soc. Jap.* **21**: 448, 1959.
77. TSUZAKI. *Nagoya J. M. S.* **19**: 113, 1957.
78. WALL, P. D., P. GLEES AND J. F. FULTON. *Brain.* **74**: 66, 1951.
79. WARD, A. A. JR. AND W. A. MCCULLOCH. *J. Neurophysiol.* **10**: 309, 1947.
80. WHITE, J. C. AND R. H. SMITHWICK. *The autonomic nervous system.* New York: Macmillian, 1948.
81. YAMADA, S. *Resp. and Circul.* **7**: 283, 1958.
82. YOUNG, W. G., W. C. SEALY AND J. C. HARRIS. *Surg.* **36**: 636, 1954.