

## SOME ASPECTS OF NEUROLOGICAL RESEARCH IN THE UNDERSTANDING OF THE FUNCTIONS OF THE BRAIN.\*

By Arumugam Krishnamurti

(Department of Anatomy, Faculty of Medicine, Singapore 3)

### The Master, Ladies and Gentlemen

At the very outset, I would like to thank the Singapore Academy of Medicine for inviting me this evening to deliver the 1966 Galloway memorial lecture, which I consider is a generous honour bestowed on me.

Sir David James Galloway, for those who do not know him, is one of the great Scotsmen of his time. Arriving in Singapore in the year 1885 at the age of 27, he rendered outstanding professional as well as public service in this part of the world till he died in Johore Bahru in 1943 at the age of 85. To people in this part of the world he is better known as the grand old man of medicine.

By a strange coincidence, last week, I accidentally came across this book titled "Functions of Brain". When I opened this book, to my surprise I found that this book was presented as a Christmas gift to then Dr. D. J. Galloway by one Allen in the year 1888. It looks as though I am enacting the incident that took place in Sir Galloway's life because I am delivering the lecture on "Some aspects of the functions of brain" in the Allen lecture theatre during the Christmas season.

Most of us have some aesthetic appreciation of the body's form. Few of us take the time to understand the inner structure and functions of the body. As far as the inner structure and functions of the brain are concerned, they are far more complex than any computer or mechanical device invented by man. It has been estimated that there are about 9-10 billion neurons in the cerebral cortex alone. You all know that the neuron has a cell body and many processes. Whether we will ever understand completely the intricate relationship between them on the one hand, and between a highly complex organ such as the brain and the immeasurable thought process associated with it on the other hand, is a moot question. Nevertheless, scientists and clinicians are constantly working on this problem in the hope of some day solving the mysteries in the design of the human brain.

As early as 1600 B.C. the Egyptians were aware of the organ 'brain' and have attributed certain functions to it. At one time it was thought that the head contained spirits and the exposure of the skull was considered as the most spectacular practice to permit the flight of spirits from the heads of persons suffering from epilepsy, migraine, melancholia and paralysis. From such concepts we have arrived at the present day knowledge of the nervous system. It is only within the last 200 years that most of the advances in neurology have taken place. The sum total of what we know about the brain to date represents a confluence of the contributions of both clinicians and research workers. The contributions of the research workers were essentially based on the results obtained from animal experiments by employing various methods of investigations such as: morphological, histological, ablation and electrophysiological techniques and a wide variety of animals have been used as an experimental subject. It is needless to mention that it is necessary to resort to animal experiments either to confirm the observations made on human patients or to find the missing link in the data available on the nervous system of man.

Now I will deal with each one of the methods of investigation briefly:

### MORPHOLOGICAL STUDIES

The earliest recorded study on the correlation of morphology and function is by Gall (1758-1828) who lectured in Vienna on the configuration of the bony skull as an interpreter of the underlying brain as well as the mental and emotional characteristics of an individual.

The morphological features of the brain indeed can give a clue on the development of the olfactory bulb or the visual cortex and consequently on the development of the sense of smell or the visual sense. The olfactory function gradually loses its importance while the visual function gradually gains importance as we ascend in the scale of evolution. It is a known fact that we receive far more information about the external

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environment through our visual sense than any other sense organ. It is also a known fact that the sense of smell has practically lost its significance in man with probable exception of those professions like—to quote an example—where one uses his sense of smell to assess the quality of brandy.

Part of our brain in Earth's story is a creation of yesterday, a late arrival even in our own lately arisen stock. Long earlier the brain already had the several great receiving stations it has today. But the primeval brain, though it received several sets of signals did little towards combining them together. The vast expansion of the brain which is newly arisen is a gigantic combination mechanism for them. This vast expansion of the brain had to be accommodated within a limited space and so fissuration started to appear on the cortex. The fissuration is predominantly horizontal in primitive mammals, arcuate in carnivores and ungulates while the fissuration is more vertical with only relics of the other pattern in higher primates including man. To start with, the corpus callosum on the medial side and the basal ganglia on the lateral aspect act as counter-pressure sites against the increasing distension of the hemisphere. This leads to the original longitudinal cortical folding as seen in the primitive mammals such as the sloth and musk deer. Later, this becomes complicated in the posterior part of the hemisphere by the formation of a temporal lobe which in turn depends on the parietal association cortex and the simultaneous fan-like display of the insular cortex. This leads on the one hand to the arcuate pattern and on the other hand to the coronal pattern. The development of the frontal association cortex and the visual cortex also play a significant role in the formation of the coronal pattern seen in higher primates including man (Le Gros Clark, 1947).

Moreover, it may be mentioned that the cortical sulci, as a rule, separate physiological subdivisions of the cortex, *i.e.*, separate functional areas of the cortex. This has been demonstrated by both histological and electro-physiological techniques. Therefore, an increase in the cortical fissuration tends to suggest an increase in the physiological subdivisions of the cortex.

## HISTOLOGICAL STUDIES

The discovery of the giant pyramidal cells by Betz, the description of six layered cortex by Baillarger and the introduction of biological staining techniques by Gerlach in the latter part of the 19th century gave an impetus to the cyto-architectonic studies, *i.e.*, parcellation of various

functional areas of the cortex based on histology. This method was undertaken by several investigators like Brodmann, Economo, Vogts and others. Unfortunately, over-enthusiasm on the part of the latter investigators has resulted in the division of the human cortex into some hundred different areas. This provoked severe criticisms from investigators like Lashley & Clark (1946) and Sholl (1956). Despite some of its drawbacks, the value of cytoarchitectural studies has been clearly outlined by Le Gros Clark.

The principal feature of the motor area is the increase in size and number of pyramidal cells in the ganglionic layers while the sensory areas of the cortex show as a rule an increase in the granule cells especially in the inner granular layer. This inner granular layer exhibits a further subdivision by the presence of the band of Gennari in the visual area.

It may be said that the term cortex—aptly called master of destiny—is the term applied to the thin layer of gray matter on the surface of the cerebral hemisphere. It has been estimated that the total cortical area in man is between 200,000 to 250,000 sq. cm. About two-thirds of this area is buried in the depths of the fissure.

The cortical regions are classified in various ways:

Based on phylogeny and ontogeny three major subdivisions are described. Archicortex, Paleocortex and Neocortex. Archicortex is the term applied to the hippocampus, paleocortex is the term applied to the pyriform cortex and the neocortex makes up the major portion of the cerebral cortex in man.

Based on morphology, the term allocortex is applied to cortical regions which do not show the six basic layers. Archi- and paleo-cortices are examples of allocortex. The term isocortex is applied to those cortical regions which show a six layered pattern—example being neocortex. This neocortex falls into two major groups depending upon the nature of cells present in these six layers: an agranular cortex such as the motor cortex and a granular cortex such as the sensory cortex. Konicortex is yet another term widely used for such sensory areas as the visual, auditory and somesthetic because of the presence of densely arranged small cells.

## ABLATION STUDIES

There are certain significant features of destroying cortical lesions. As Sir Hughlings Jackson expressed it, the cortex is very tolerant of destroying lesions. If such a lesion be very restricted it may be symptomless, and when

productive of symptoms these are apt to be minimal in range and severity and to be capable of high degree of restoration. This so called tolerance of the cortex to destroying lesions and the high degree of recovery that occurs after a destroying lesion are all incompatible with the theory of an exclusive representation in certain fixed points of the cortex. Research work directed on these lines lead to the discovery of the so-called second area (motor II, somatic sensory II, auditory II and visual II) and the concept of duality of cortical organization was propounded by Rose and Woolsey about 20 years ago. Further probing into this problem revealed the presence of many more areas around the primary one which are referred to as fringe areas. The primary zone receives direct afferent input while the fringe area, in addition, receives cortico-cortical connection from the primary field. The duplicity of centres can then explain, at least in part, why a focal lesion in certain parts of the cortex does not produce the expected results.

#### ELECTROPHYSIOLOGICAL STUDIES

The discovery of electrical excitability of the cerebral cortex by Todd (1840) and by Fritsch and Hitzig (1870) opened the era of experimental neuro-physiology and this technique was improved upon by Sherrington, Cushing, Penfield and his associates in the early part of this century.

Yet another road was opened to the experimental exploration of the activity of the brain, when the spontaneous electrical activity in the brain was recorded by Caton (1875) and Berger (1929). This led to the localization of sensory areas of the brain by recording the evoked potentials through an electrode placed in the respective areas of the cortex and applying appropriate external stimulus. It is this method of study that will serve as an introduction to my talk this evening and it is my intention to confine myself to those areas of the brain which receive afferent impulses from the skin surface of the body (with special reference to tactile sensibility).

#### PATHWAYS MEDIATING TACTILE IMPULSES TO THALAMUS AND CORTEX

The following are the receptors or sense organs found in the skin subserving tactile stimulus.

- a) Meissner's corpuscles found in the papillary spaces on the deep side of the epidermis in certain regions of the body like fingers, palm, toes, sole of foot, lips, tongue, nipple, clitoris and penis etc.

- b) Merkel's disks—these are cup-like nerve endings in contact with modified epithelial cells.
- c) Free nerve endings in stratified squamous epithelium of the skin and lips.
- d) Nerve terminations around hair follicles.

Fibres conducting tactile sensibility are medullated fibres and their cell bodies are in the dorsal root ganglion of the spinal nerves as well as ganglia in relation to 5th, 7th, 9th and 10th cranial nerves.

The central process of the neurons situated in the dorsal root ganglion enter the spinal cord through the medial division of the dorsal root. Within the ipsilateral dorsal funiculus, these central processes bifurcate into a long ascending and a short descending fibre. These fibres and numerous collaterals from them terminate in cell bodies of the posterior gray column over 6-8 segments of the spinal cord. This arrangement provides the anatomical background for the central overlap of these sensory impulses. Consequently this pathway serves to conduct less specific tactile sensibility.

From these cell bodies in the posterior gray column the fibres cross in the ventral white commissure and ascend as the ventral spinothalamic tract through the brain stem to terminate in nucleus ventralis posterolateralis of the thalamus. (No kind of localization pattern has been demonstrated for the ventral spinothalamic tract).

The neurons mediating more specific type of tactile sensibility ascend in the ipsilateral dorsal white column of the spinal cord without giving collaterals to the dorsal gray horn (but with possible collaterals to the ventral gray horn for reflexes) and to terminate in the nucleus gracilis and cuneatus. Such ascending fibres from sacral, lumbar and part of the thoracic spinal nerves end in nucleus gracilis while those from remaining thoracic and cervical levels end in nucleus cuneatus. It has been demonstrated in cat and raccoon that there exists a one to one relay between fibres of the fasciculus gracilis and cuneatus and the neurons in the nucleus gracilis and cuneatus.

From nucleus gracilis and nucleus cuneatus a crossed ascending path projects these tactile impulses to the nucleus ventralis postero-lateralis of the thalamus.

The 5th cranial nerve supplies the face (with the exception of a small area at the angle of the jaw) and the scalp up to vertex of skull. The small area at the angle of the jaw is supplied by C<sub>2</sub> and C<sub>3</sub>. Sometimes this is a useful fact to

know in testing for a true sensory loss as opposed to a possible hysterical condition or to malingering. The external ear is supplied by branches of 5th, 7th, 9th and 10th cranial nerves.

The central process of the cell bodies situated in the ganglia of these cranial nerves end in chief sensory and spinal nucleus of the 5th nerve. Fibres subserving more specific tactile sensibility end directly in the cells of the chief sensory nucleus whose axons partially decussate to form dorsal division of the trigeminal lemniscus. Fibres subserving less specific tactile sensibility bifurcate into two branches. One branch terminates in the chief nucleus and the other in the spinal nucleus of the 5th nerve. The axons of these cell bodies form the ventral division of the trigeminal lemniscus which crosses the mid-line to ascend to the opposite side. Both ventral and dorsal divisions of the trigeminal lemniscus terminate in the nucleus ventralis postero-medialis.

Finally, the axons of the cell bodies in the ventrobasal complex (nucleus ventralis postero-lateralis and nucleus ventralis postero-medialis) terminate in the post central gyrus of the cortex.

The pattern arrangement on the somesthetic cortex is clearly evident in the Penfield and Rasmussen diagram. This is known as 'homunculus' meaning a small man. The anal and the genital areas are represented on the medial aspect of the hemisphere above the cingulate sulcus. Immediately above, is the representation of the toes continuing through foot, ankle, leg and so on up to the hip. The hip representation is separated from the upper extremity representation by a small area related to the trunk and neck. The area devoted to the hand region above all the thumb is relatively large. Then comes the region related to the face area which is also relatively large.

#### EXPERIMENTAL SUBJECT

The animal chosen as an experimental subject in the present investigation is the slow loris (*Nycticebus coucang coucang*) (Fig. 1). I am sure you are all quite familiar with this animal. This animal was used as an experimental subject for the following reasons:

1. the availability of the slow loris in the Malaysian jungle;
2. the lack of information on the nervous system of this animal and
3. the desirability of conducting experiments on an animal like slow loris which belongs to the same zoological order of primates as man himself.

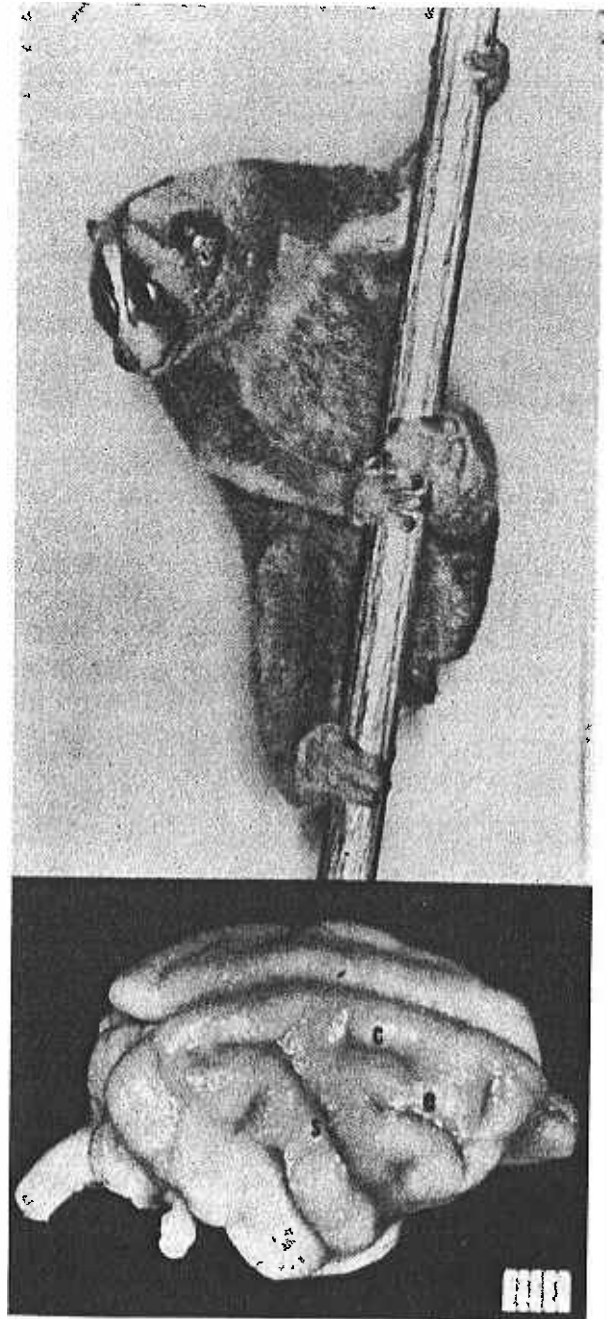


Fig. 1.

Top: Slow loris (*Nycticebus coucang coucang*)

Bottom: Brain of slow loris.

c = sulcus 'c'

e = sulcus 'e'

s = sylvian fissure.

Before considering the experimental procedure, I thought that I should make certain general comments regarding this lower primate since it is found only in this part of the world. It is commonly known in Bengal as Lajjar banar (bashful monkey) or Sharmindi billi (bashful cat) and in Malaysia as Kukung (lazy or shy) or Keraduku (monkey with its head resembling a duku fruit). Luijaardt sloth is the name given to this animal by a Dutch voyager Seba in 1734, who mistook this animal for a kind of a sloth, a sluggish arboreal endentate found in America. In 1765 Buffon, a French taxonomist, recognised

the true nature of this animal and coined a new term 'loris' for this animal. So this became Paresseux loris in French, Plump lori in German and slow loris in English. It is interesting to note that the English meaning of the word loris which is sloth (Webster, 1951) has defeated the very purpose of Buffon's attempt to coin a new term 'Loris' to differentiate these lower primates from sloth.

The zoological term given to slow loris is *Nycticebus coucang coucang*. The word is derived from the Malay word *Kukung* and *Nycticebus* is a composite of two Greek words, 'Nyctos' meaning night and 'cebus' meaning a long tailed monkey which uses its tail for prehensile purposes. Though the slow loris is a nocturnal animal it has neither a long tail nor uses its tiny tail as a prehensile organ. However, like the common name slow loris, the zoological term *Nycticebus* has also been generally accepted and is now in taxonomic use.

The present study was conducted on the brain of 30 slow lorises, all of them collected from Malaysia. The general topographical anatomy of the brain was studied on 18 brains. The animals were anaesthetized and perfused through the heart with formol saline. The brain was removed from the skull and photographed from standard views. These brains were used for the macroscopic study of the sulci, gyri as well as the internal structure.

The morphological study (Krishnamurti, 1966) revealed the following:

1. The visual system as a whole is well developed in slow loris as revealed by the large lateral geniculate bodies, the presence of a posterior horn of the lateral ventricles and a well marked retrocalcarine fissure.
2. The cortex of slow loris exhibits a general sagittal sulcal pattern. However, as a progressive feature, there are two coronally orientated sulci. The sulcus lunatus limiting the visual area anteriorly and the vertical portion of sulcus 'e' separating the motor from the somatic sensory areas.

The cytoarchitectonic studies were carried out by embedding the brain in celloidin, cutting serial sections and staining them for cell bodies. This permitted the parcellation of the various areas of the brain based on the architecture of the cell bodies.

The cytoarchitectonic studies (Sanides and Krishnamurti, 1967) revealed the following interesting features:

1. The insular and limbic cortices represent more primitive stages of cortical development whereas the neocortical regions show a fully developed isocortex. Therefore, the insular and the limbic fields are thought to be phylogenetically more ancient than the neocortex and therefore the second somatic sensory area appears as an older level of cortical control than the classic representation.
2. The somatic sensory cortex studied in detail in the present investigation, shows the following partitioning: area proK (SmII), parK (2 & 1), Ks (3) and Int (3a) (Fig. 2). In man, fields 3 and 1 have been considered to be related particularly to cutaneous sensibility and field 2 to proprioception. The field 2 is sometimes regarded as a suppressor area or area 2s. Some workers believe that pain is projected rostral to tactile area.

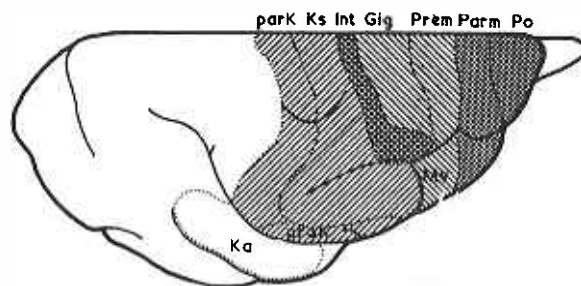


Fig. 2. The cytoarchitectonic division of the sensory and motor fields of the slow loris. Somatic Sensory Cortex include:—areas proK, parK, Ks and Int.

The delineation of the somatic sensory areas of the cerebral neocortex of slow loris (Krishnamurti, Welker and Sanides, 1965) was carried out further, utilizing the refined recording and stimulating techniques. For this purpose, ten animals were used. All animals were anaesthetized with pentobarbital sodium administered intraperitoneally (initial dose: 28/mg/kg/ of body weight) supplemented by additional doses to eliminate nociceptive reflexes. The hair on the head and the entire left half of the body was clipped and the trachea cannulated. The head was immobilized in a stereotaxic instrument, the exact position depending upon the region to be explored. Scalp and bone were removed over the frontal, parietal and temporal areas of the right hemisphere. An acralite dam bonded to the skull was constructed around the opening in the bone. This was filled with mineral oil to keep the cortex moist throughout the experiment. The dura was reflected and the exposed region of cortex was photographed. A millimetre rectangular grid was drawn on the photograph of the exposed brain and the location of each

electrode puncture was indicated thereon by a dot.

The exposed surface of the cortex was explored with the help of a tungsten microelectrode. The electrical activity picked up by the microelectrode was displayed visually upon the oscilloscope screen which forms a part of the recording equipment.

The Tungsten microelectrode used in the present study consists of an electrolytically sharpened tungsten wire firmly mounted in a stainless steel tubing and coated with an insulating varnish. The tip insulation is subsequently removed by passing 6 volts direct current.

### RESPONSE CRITERIA

Evoked positive slow wave recorded at cortical surface was used as an initial criterion. The final or definitive criterion however consisted of the unit cluster response recorded within the middle layer.

### MAPPING PROCEDURE

Cortex was explored systematically in mm. steps and occasionally in closer steps. At each location, the electrode tip was placed on cortical surface in order to identify the existence of initially positive slow wave.

By means of a micrometer drive assembly unit the electrode was introduced into the cortex. During the advance of the electrode into the cortex the body of animal was thoroughly stroked until a drivable group of neural units was encountered. The electrode was held in position until the peripheral receptive field which maximally activated the units was identified. This was accomplished by a jewellers tweezers, or cotton swab.

In identifying a peripheral receptive field, only that area which reliably activated neural units with minimal mechanical stimulation was recorded. These peripheral receptive fields were outlined on figurines of appropriate body parts. This procedure was carried out till the entire somatic sensory areas responsive to mechanical stimulation had been surrounded by nil punctures that were unresponsive or which exhibited different response characteristics from those in the main somatic sensory region.

The medial surface and the walls of sulci were explored by introducing the electrode at a suitable angle.

The results obtained from the mapping procedure based on the response criteria mentioned earlier show the following features:

1. The somatic sensory 'prosimiusculus' (Fig. 3) may be visualized as lying upon the somatic sensory area, the head, face and tongue located laterally and tail and hindlimb situated medially. The representation of the trunk is located at the caudal aspect of this somatic sensory region, and that for the apices of the limbs are directed rostrally.



Fig. 3. Somatic Sensory Prosimiusculus.

Within the hind paw subdivision of Sml area, the representation of the digits were found to be arranged in a regular order. The 5th digit is situated near the superomedial border of the hemisphere and extends on to the medial surface, while the first digit lies just medial to the fore paw representation and separated by the sulcus 'c'. The other digits are represented consecutively between them. The hallux has a bigger representation in comparison to the other digits.

The orientation of the fore paw is similar to that of the hind paw and the hand representation is confined to the area between the sulcus 'c' and the horizontal portion of the sulcus 'e'. The digit 5 extends onto the wall of the sulcus 'c' whereas digit I is situated nearest the head and separated from it by the horizontal portion of the sulcus 'e'. The pollex like the hallux has a wider representation than the other digits.

The head representation is limited by the compound sulcus 'e' medially and rostrally. While the sagittal portion of sulcus 'e' separates the hand and head areas, the vertical portion separates the Sml head from the motor area. Within this region the lower lip lies close to the

sagittal portion of sulcus 'e' separated from the upper lip by the tongue. The representations of the dorsal aspect of the head and neck are located close to the Sylvian fissure.

In SmI area, all responses had been found to be strictly contralateral, with the exception of a part of the face area (snout, mouth, tongue etc.). In the SmII area, the cutaneous surface from both halves of the body are represented in each cerebral cortex. The differentiation within SmII is much less than that within SmI. However, the hand representation is much bigger than that for any other body part and within this area the pollex, like SmI pollex, has the largest representation of the digits.

In all the microelectrode mapping studies of the somatic sensory areas of the cerebral cortex of slow loris, no overlap was found in the projections of some of those body parts that are actually separated from one another at the periphery such as head and forepaw, forepaw digits 1-5, forepaw and hind paw, and hind paw digits 1-5. Thus, under the conditions of the experiments, cells activated by head stimulation were never activated by forepaw stimulation.

The anatomical location of somatic sensory region was determined by reconstruction of tracks of the recording electrode.

There is a limit to the amount of detail that one can inflict upon an audience and some of you may well feel that I have already exceeded that limit. I turn therefore to consider the conclusions drawn from these facts of observation.

## CONCLUSION

It is noteworthy that the results obtained by the use of the microelectrode are some what different from those of macroelectrodes. In the macroelectrode mapping studies, the sensory cortex from which stimuli produced evoked potentials did not confine to the somatic sensory area, but extended well into the motor cortex whereas with microelectrode this overlap was not observed.

The present studies moreover, have revealed that sulci are found to separate physiologically distinct subdivisions.

Another interesting result which emerged from this study is that there is a large area of representation for the foot, hand and mouth regions within the somatic sensory cortex. This confirms the view that the greater degree of elaboration at the cortex is undoubtedly corre-

lated with the increased specialization and elaboration of the corresponding sensory skin receptor surface. This is consonant with the concept that the extent of projection onto the postcentral gyrus from a particular part of the body bears a direct relationship to the importance of that part of the body towards the survival of an animal.

It is not only to consider these themes that we are met here this evening, but also to honour the memory of Sir David James Galloway, the grand old man of medicine. We here, will cherish his name with a special warmth of feeling as a noble part of our own particular tradition.

Thank you.

## REFERENCES

- Berger, H. (1929): Quoted by Gibson, W.C. (1962); "Pioneers in localization of function in the brain", J.A.M.A. 180, 944-961.
- Buffon, G.L. Le C. (1765): Quoted by Hill, W.C.O. (1953a), "Early records of the slender loris and its allies", Proc. Zool. Soc. Lond., 123, 43-47.
- Caton, R. (1875): Quoted by Gibson, W.C. (1962), "Pioneers in localization of function in the brain", J.A.M.A. 180, 944-961.
- Clark, W.E. Le Gros (1947): "Deformation patterns in the cerebral cortex. In: Essays on growth and forms", Oxford, Clarendon press.
- Clark, W. E. Le Gros (1952): "A note on cortical cytoarchitectonics" Brain. 75, 96-108.
- Fritsch, G. and Hitzig, E. (1870): Quoted by Gibson, W.C. (1962): "Pioneers in localization of function in the brain", J.A.M.A. 180, 944-961.
- Gall, F.J. (1758-1828): Quoted by Gibson, W.C. (1962); "Pioneers in localization of functions in the brain", J.A.M.A. 180, 944-961.
- Krishnamurti, A. (1966): "The External Morphology of the brain of slow loris (*Nycticebus coucang coucang*)," Folia Primatologica, 4, 361-380.
- Krishnamurti, A., Welker, W.I. and Sanides, F. (1965): "Somatic sensory areas in the cerebral neocortex of slow loris (*Nycticebus coucang coucang*)", (In preparation).
- Lashley, K. S. and Clark, G. (1946): "The cytoarchitecture of the cerebral cortex of *Ateles*: a critical examination of architectonic studies". J. Comp. Neurol., 85, 223-305.  
Sholl, D. A. (1956): "The organization of the cerebral cortex". London, Methuen.
- Sanides, F. and Krishnamurti, A. (1967): "Cytoarchitectonic subdivisions of sensorymotor and prefrontal regions and of bordering insular and limbic fields in slow loris (*Nycticebus coucang coucang*)". J. Hirnforsch. 9, 225-252.
- Seba, A. (1734): Quoted by Hill, W.C.O. (1953a); "Early records of the slender loris and its allies", Proc. Zool. Soc. Lond., 123, 43-47.
- Todd, R.B. (1840): Quoted by Gibson, W.C. (1962): "Pioneers in localization of function in the brain", J.A.M.A. 180, 944-961.
- Webster, N. (1951): Webster's New International Dictionary, 2nd edition, Springfield, G. & C. Merriam.