On the Changes in Respiratory Movements Caused by Electrical Stimulation of Hypothalamus in the Cat

By

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Although the central nervous system which participates in the respiratory movements has been considered to be localized over the considerably large areas of the brain, those which take direct part in the respiratory centers of the automatic rhythmicity, the so-called primary respiratory centers, are in the pons and medulla oblongata out of the brain stem, especially in the formatio reticularis. Researches have been conducted on this subject by many scholars such as Pitts (1939) and others\(^{123}\). Various investigations have been reported concerning the role played by the cerebral cortex (Smith 1936 and others\(^{9-6}\)) and the mesencephalon (Lea\(^{**}\) and others\(^{997-99}\)) on the primary center. Further, since Hering and Breuer (1868)\(^{10}\), numerous studies have been taken up on the influences of the peripheral nervous system, the main constituent of which is the vagal nerve, upon the central nervous system.

Since 1960 the present authors have been pursuing researches on the autonomic centers, centering the attention upon the blood pressure and the respiratory movements, covering the whole range of the brain stem of the cat from the hypothalamus to the medulla oblongata. A part of our results has already been published\(^{133}\) concerning the changes of the blood pressure and the respiratory movements caused by electrical stimulation of hypothalamus in cats. The parts played by the hypothalamus of diencephalon upon the primary respiratory centers have been observed in more cases since then, about which comparatively fewer researches have been reported; the following will be the description on considerably clear-cut observations obtained in regard to the acceleratory and inhibitory responses.

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Materials and Methods

Materials used were matured cats, weighing 1.8–4.5 kg, most of which being 2.0–2.5 kg. For anesthesia mainly 30 mg/kg nembutal was subcutaneously injected, but in accordance to the conditions of the cats, intramuscularly or intraperitoneally injected. When the narcotic effects turned out insufficient so that the experimental procedure was hard to handle, ether was used additionally. The cranium of the anesthetized cat was placed in the stereotaxic instrument, Horsley-Clarke (Todai Noken type), after the cat had been inactivated in voluntary movements by the injection. Then, the cat's body was turned 180 degrees so as to keep it supine; 3–5 cm of its anterior neck skin was cut at the middle, letting the trachea be exposed, and cutting two or three pieces of cartilagines tracheales under cartilago cricoidea at their middle; into the opening was inserted the tracheal cannula with gum tube which forks to an open tip and a closed one. The closed tip was connected with the tambour so as to make it possible to record the respiratory current on the kymograph, while by the pendency method the abdominal movements by respiration was so contrived as to be recorded on the kymograph from the abdominal wall.

As for the electrical stimulation, the Universal Electric Stimulator (STW-I Model) designed by Hatakeyama (1951) was used in two ways combined: one with the same temporal durations and intervals in each rectangle wave and the 3.3, 33, 66, 330 cps frequency; and the other with the intensity of 0.1, 0.5, 1.0, 3.0, 5.0 v. Each stimulation lasted 10 secs. Concentric needles electrode (bipolar) with external coat of 0.25 mm and centric enamel wire of 0.1 mm was used as the electrode of stimulation.

The site of stimulation points covered the whole area of the hypothalamus from the regio preoptica to the corpus mammillare based on the Jasper's and Kojima's atlases, not necessarily a such specifically limited part as the nucleus or the fibre; in other words, the site extends three dimensions—rostro-caudal, right-to-left, and vertical—with the point-intervals of 1.0–1.5 mm in a network way. Each cat was stimulated at 6 to 10 different points so as to range, first, from the superficial region near the cortex cerebri, then, gradually to the deeper brain base.

After having given stimulations, physiological salt solution was injected through aorta ascendens by cutting open the atrium dextrum; and after the blood was removed 10% formalin solution was
perfused in the same way through whole body for fixation.

Serial frozen sections of 30 to 10μ were made, which were cut off in the frontal direction in which stimulating electrodes were inserted, after removing the brain fixed for 24 hours. The sections were stained by Nissl's method, and were ascertained of the traces of the electrodes by microscopic examination.

In passing, when recording the abdominal movements and the respiratory current, by means of kymograph, the ink writing was made use of in the later stages of the experiments, utilizing transducer and electromanometer. As has been referred to in the introduction, the object of this series of our experiments was not limited to the observation of the respiratory movement changes only. It was extensive enough to cover the blood pressure, the endopressure in cardia, and that of the EMG; further it ranges EEG (chiefly the lobus frontalis and the lobus parietalis), and EMG of the skeletal muscles of extremities (as the upper limbs, the m. biceps and the m. triceps of the humerus; as to the lower limbs, the m. quadriceps and the m. biceps of the femur). Both EEG and EMG were simultaneously recorded partly or wholly.

Results

Changes seen on the respiratory movements (the respiratory current and the abdominal movements), which were caused by electric stimulation, turned out to be not simple, but rather complicated. That is, there were observed high or low frequency in the curves both of the respiratory current and of the abdominal movements, difference in the amplitude and varied forms of waves; some change occurred after the stimulation and others during the stimulation; moreover, those changes themselves were manifold: the respiratory frequency, for example, showed a decreasing tendency during the stimulation and an increasing tendency after the stimulation. If those complicated changes should be classified into as many different and independent units as the variety of phenomena requires, the number of the units would amount to an uncontrollable extensiveness, and the result would be for us to lose the criterion of the evaluation. Such being the case, the respiratory frequency has been picked up as the indicator for our classification, excluding, for the moment, the mid-stimulation and post-stimulation phenomena, and those concerning the amplitude. Table 1 has thus been made.

All the changes observed in it are divided into three categories:
Table 1. Three patterns of changes in respiratory movements according to increase and decrease of respiratory frequency by stimulation. Three symbols in left column are marked in serial transverse brain maps (Fig. 1-7). Underlines to respiratory curves are shown the stimulation.

acceleration, inhibition and reversal. The case, where the pre-stimulation respiratory frequency has been heightened by the stimulation, is classified as the ACCELERATION, regardless of larger amplitude (a and b in the Table 1) or smaller one (c and d in the Table 1), and is recorded in the transverse frontal section of the brain map with the symbol ⬤. The other case, where the frequency is lowered contrary to the above, is classified as the INHIBITION, regardless of smaller amplitude (e and f in the Table 1) or larger (g and h in the same table), and is recorded in the brain map with the symbol ○. These four patterns occurred both during and after the stimulation: post-stimulation changes such as b and h in the Table 1, were often seen but the ones like d and f were rare. At any rate, those which occurred during the stimulation, such as a, c, e, and g in the Table 1, were overwhelmingly more in number than those which occurred after stimulation. If any change is observed which
satisfies any one of the abovementioned conditions of stimulation (the combination of rectangle waves, frequency 3.3-330 cps and the intensity of 0.5-5.0 v), it is recorded as either a accelerotory point or the inhibitory one in each of its stimulation position. Besides abovementioned changes, however, when the frequency or intensity was low, some changes turned out to be inhibitory or acceleratory; when the frequency or intensity high, inhibitory responses turned out to be acceleratory and vice versa (as in i and j in Table 1). Those changes are classified as the REVERSAL RESPONSES, and are recorded in the brain map with symbol of \( \oplus \). These kinds of responses were fewer than the acceleratory and inhibitory points.

The criterion for the abovementioned classification of three patterns was the qualitative difference in each case, but there were observed quantitative differences in homogeneous changes, that is the difference in strength. The frequency of respiration, which forms the standard of qualitative changes, might be further extended and employed as the indicator for the quantitative changes, but, considering the lack of a certain, definite measure, or rather an indicator, the authors had recourse to their instinct and, for the present moment, recorded on the brain map using the larger or smaller symbols, as has been described, in accordance with the degrees of changes. By the lack of standard we mean the heterogeneity of cats' individual differences, those of respiratory changes by means of nembutal anesthesia (concerning this problem a systematic investigation has been conducted, though the results have not yet been published), and the variability of change due to the stimulation such as the reversal.

Fig. 1 shows typical case of ACCELERATION both in the frequency and the amplitude of respiration caused by the stimulation. The stimulation condition on the left of the Fig. is 4.0 v, 33 cps and that on the right 3.0 v, 33 cps; the higher the voltage (left) the larger the frequency and the amplitude. The stimulation point is at the nucl. dorsomedialis hypothalami.

Fig. 2 is an INHIBITION example in which both the frequency and the amplitude of respiration decreased by the stimulation. In this case the inhibition is generally of the similar degree, regardless of the stimulation voltage or frequency. The stimulation point is at the area hypothalamica dorsalis.

Fig. 3 presents an example in which the response turned out to be REVERSAL in accordance with the stimulation conditions in
Fig. 2. A typical case of inhibition in respiratory movements caused by stimulation. A symbol ○ by arrow in brain map (left side) is a point of stimulation. The abbreviations in the map are explained in Table 2.
Fig. 3. A typical case of reversal in respiratory movements caused by stimulation. A symbol by arrow in brain map (left side) is a point of stimulation. The abbreviations in the map are explained in Table 2.
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spite of one and the same stimulation point. The left side stimulation condition is 2.0 v, 66 cps which increased the respiratory frequency, while the right side one is 3.0 v, 3.3 cps which reversely decreased it. The stimulation point is at the commissura Gasseri near the brain base of pars anterior hypothalami.

Those are what seem typical of changes. Now let us observe the whole cases. Change symbols of various size are dotted on the maps of the serial transverse sections which are of the same direction along which the stimulation electrodes were put, covering from the rostral (anterior) side to the caudal (posterior) side of the hypothalamus (Figs. 4 and 5); in other words, they run from the rostral side to the caudal in the order of the Fig. 4 A-C and Fig. 5 D-F. The numbers on the lower left corners of the diagrams correspond with those which were contrived by Kojima, extending from the rostral side to the caudal side, ranging the whole length from the hypothalamus to the medulla oblongata, the intervals between any

Table 2. Abbreviations for all figures.

<table>
<thead>
<tr>
<th>Acb—Nucl. accumbens</th>
<th>Mi—Nucl. corporis mamillaris lateralis</th>
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<tr>
<td>AD—Nucl. anterior dorsalis</td>
<td>Mm—Nucl. corporis mamillaris medialis</td>
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<td>aHd—Area hypothalamica dorsalis</td>
<td>NCM—Nucl. centralis medialis</td>
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<td>AM—Nucl. anterior medialis</td>
<td>NPr—Nucl. prothalamicus</td>
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<td>AV—Nucl. anterior ventralis</td>
<td>PC—Nucl. paracentralis</td>
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<td>CA—Commissura anterior</td>
<td>PMm—Pedunculus corporis mamillaris</td>
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<td>CC—Corpus callosum</td>
<td>Pt—Nucl. parataenialis</td>
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<tr>
<td>Cd—Nucl. caudatus</td>
<td>PVA—Nucl. periventricularis anterior</td>
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<tr>
<td>Ch—Chiasma opticum</td>
<td>PVH—Nucl. periventricularis hypothalami</td>
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<tr>
<td>CL—Nucl. centralis lateralis</td>
<td>R—Nucl. reticularis thalami</td>
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<tr>
<td>DBB—Diagonal band of Broca</td>
<td>RE—Nucl. reuniens</td>
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<td>En—Nucl. entopeduncularis</td>
<td>ST—Stria medullaris</td>
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<td>fcd—Fundus caudati</td>
<td>Sch—Nucl. suprachiasmaticus</td>
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<tr>
<td>Fil—Nucl. filiformis</td>
<td>SM—Nucl. supramamillaris</td>
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<td>Fx—Fornix</td>
<td>SO—Nucl. supraopticus</td>
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<td>Gx—Commissura Casseri</td>
<td>Spt—Septum pellucidum</td>
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<td>H1 and H2—Fields of Forel</td>
<td>ST—Stria terminalis</td>
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<td>Ha—Hypothalamus anterior</td>
<td>STh—Nucl. subthalamicus</td>
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<tr>
<td>Hdm—Nucl. dorsomedialis hypothalami</td>
<td>TMT—Stria mammillo-thalamicus</td>
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<td>HL—Hypothalamus lateralis</td>
<td>TO—Tractus opticus</td>
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<tr>
<td>Hp—Hypothalamus posterior</td>
<td>VA—Tractus mammillo-thalamicus</td>
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<tr>
<td>Hvm—Nucl. ventromedialis hypothalami</td>
<td>VM—Nucl. ventralis anterior</td>
</tr>
<tr>
<td>IAM—Nucl. interoanteromedialis</td>
<td>VM—Nucl. ventralis medialis</td>
</tr>
<tr>
<td>LD—Nucl. lateralis dorsalis</td>
<td>VL—Nucl. ventralis lateralis</td>
</tr>
<tr>
<td>LP—Nucl. lateralis posterior</td>
<td>VPM—Nucl. ventralis posteromedialis</td>
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<tr>
<td>MD—Nucl. medialis dorsalis</td>
<td>ZI—Zona incerta</td>
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<tr>
<td>MFB—medial forebrain bundle</td>
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of the two numbers being about 250μ, and the smaller the number
the nearer the rostral side.

Let us now describe the responses of the stimulation on the
respective maps from the rostral side (the letters in brackets and
in Figs. are abbreviated, refer to the Table 2). On the transverse
section (Fig. 4, A: 22) which the commissura anterior (CA) crosses
median and appears the largest, there are observed, generally speak-
ing, many acceleratory points; between the hypothalamus anterior
(Ha) and the commissura anterior, on the dorsal sides, some inhibi-
tory points; and where it contacts with the left side commissura
anterior, acceleratory responses. And then out of the stimulation
tried at some specific nuclei, in the nucl. suprachiasmaticus (Sch)
remarkable in inhibitory responses are observed and in the nucl.
supraopticus (So) an acceleratory response though only one.

Next, on the transverse section including the commissura Gasseri
(Fig. 4, B: 23), outstanding acceleratory responses are found almost
all over the area. Only, as in the description in the typical example,
two reversal points in all are noticed in the commissura Gasseri
and a point slightly near to the dorsal to it: at a point near right
side of the tr. opticus (TO) an inhibitory response; further, just
one but an outstanding effect is seen among the stimulation in the
fornix (Fx) dorsally situated, though it does not belong to the hypo-
thalamus.

On the transverse section (Fig. 4, C: 24) which includes the
foramen interventriculare, the acceleratory effects occupy the most
part as seen in the previous transverse section, but at three points
where they make contact with the ventriculus tertius and in an
area where they come near the fornix (Fx) inhibitory points are
observed, especially in the latter area the phenomena is as conspicu-
ous as in the previous transverse section. Similarly on the nucl.
supraopticus (SO) acceleratory effects is observed as in the Fig. 4, A.
And around the nucl. periventricularis anterior (PVA) where they
touch the ventriculus tertius three inhibitory effects are observed.

On the Fig. 5, D: 26, where the nucl. ventromedialis hypothalami
(HVM) appears largest approximately at the middle of the hypo-
thalamus, acceleratory effects are perceived over the best part of
the stimulated nucleus, one right side point being conspicuous and
another on the left side slight. On the area hypothalamic a dorsalis
(aHd), dorsal to the nucleus, the stimulation on the ventro-medial
part turned out acceleratory and on the dorso-lateral part inhibitory;
farther more in the area of the nucl. filiformis (Fil) a conspicuous
Inhibitory effects are observed, and also the same conspicuous effects are found in the area where nucl. reuniens (RE) exists which belongs to thalamus, except three acceleratory effects which appear on the part where they adjoin the ventriculus. Although the following three areas do not belong to hypothalamus, two points are each inhibitory and reversal effect on the nucl. anterior medialis (AM), one point on the nucl. caudatus (Cd) is of inhibitory effect, and another point on the capsula interna (CI) is reversal.

In the following transverse section (Fig. 5, E: 28), where a part of the hypothalamus posterior (Hp) is localized at the bottom of the ventriculus tertius, inhibitory effects are observed overwhelmingly more, and only 3 out of 23 are acceleratory around and at the back of ventriculus tertius, which is said to form the medial part of the hypothalamus. On the hypothalamus lateralis (HL) which includes fornix (Fx) many acceleratory effects are observed, while on the fields of Forel (H1 and H2) and zona incerta (ZI), on the contrary, inhibitory effects are seen. So far as this section is concerned, it can be summarized as this; there are three responsive zones extending from the ventriculus tertius to the outside, and on the dorsal side all the responses are inhibitory. Taken in connection with the whole of this section, there are observed 30 out of 45 inhibitory responses, which are much more than those on the rostral side as in Fig. 4, A–C and Fig. 5, D. And 2 points on the right and left sides of the dorsal side nucl. parataenialis (Pt), though it does not belong to the hypothalamus on this section, represent those of acceleration.

On the transverse section where the corpus mamillare appears largest, that is, the most caudal part of the hypothalamus (Fig. 5, F: 30), many acceleratory responses are observed on the ventromedial part comprising of such as nucl. corporis mamillaris medialis (Mm), its dorsal part of nucl. supramamillaris (SM) and the commissura supramamillaris (SMx). On the hypothalamus posterior which surrounds the ventriculus tertius, both responses, acceleratory and inhibitory, are seen, and on the area which includes the nucl. centralis medialis (NCM) inhibitory effects are conspicuous. As has been observed on the previous Figure, outer fields of Forel (H1 and H2), the zona incerta (ZI), the hypothalamus lateralis (HL) and nucl. subthalamicus (STh) are showing some conspicuous inhibitory effects. One point on the dorsal side of the nucl. periventricularis anterior (PVA) is inhibitory as in the Fig. 5, and another point on the nucl. centralis lateralis (CL) which belongs to the
Fig. 4. Mappings of the three levels at which respiratory acceleratory, inhibitory or reverse effects were obtained. Numbers and alphabet's letters refer to antero-posterior (rostro-caudal) stereotaxic coordinates for hypothalamus. Symbols and abbreviations are explained in Table 1 and 2.
The observations that have been made up to the present moment include those which do not belong to the hypothalamus, such as the thalamus, the nucl. subthalamicus, the capsula interna, the fields of Forel and the zona incerta. Now to make an intermediate summary concerning the whole of the hypothalamus stimulation, it can be summed up as follows. Generally speaking, on the pars anterior hypothalami rostral to the nucl. ventro-medialis hypothalami, mostly conspicuous acceleratory responses are observed except two or three cases (nucl. supraopticus, fornix and so forth); on the area where the nucl. ventromedialis hypothalami appears at the pars intermedialis hypothalami, acceleratory responses are observed on the ventral and medial sides, and inhibitory responses on the dorsal and lateral sides; caudal-ward from here, over the area from the ventriculus tertius to the lateral side, as has been mentioned above, there are ventrodorsal three responsive zones consisting of inhibition, acceleration and inhibition, and on their dorsal side inhibitory effects, but, as a whole, inhibitory responses become overwhelmingly more. Further backward where the corpus mammillare appears, the ventromedial part (including the nucl. corporis mammillaris) shows acceleration, the part around the ventriculus tertius has mixed effects, its lateral side inhibition, and the dorsal of these inhibition; the distribution is somewhat complicated.

The abovementioned observations are the correlations between the three responses (acceleration, inhibition, and reversal) and the localization of the stimulated points on the hypothalamus. There have been observed points of apnea caused by the stimulation during the experiment when the stimulation get intense and the frequency high. The Fig. 5 is one of those examples, the stimulation condition being 4.2 v, 33 cps, and the stimulation point is at the dorsal part of pars intermediais hypothalami close to nucl. filiformis and its nature expiratory apnea. Eight cases have been observed with various ways of apnea. These cases should have all been observed after having been categorized, but, since they were few in number, the criterion for the evaluation of them has been confined to the fact that the apnea, which is a problem at the primary respiratory centers on the medulla oblongata, is either inspiratory or expiratory. In the Fig. 7 the symbol \( \odot \) stand for the expiratory apnea and the \( \oplus \) inspiratory one. As may be understood in the Figure 7, only one case out of eight showed inspiratory apnea and it is situated in the fields of Forel. The other seven of the inspi-
Fig. 6. A typical case of apnea caused by stimulation. A mark © by arrow in brain map (left side) is a point of stimulation. In this case expiratory apnea was obtained. The abbreviations in the map are explained in Table 2.
Fig. 7. Mappings of the three levels at which the effects of apneas were obtained. There are two characteristic apneas; one is expiratory (symbol ©) and another is inspiratory (©). The other explanatory notes are same as in Fig. 4.
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Respiratory cases are localized rather gatheringly, that is, on the pars anterior hypothalami they are obtained on the ventral side, on the pars intermedialis hypothalami they are on the dorsal side, and on the pars posterior hypothalami it is found, though just one point, where it is contiguous to the ventriculus tertius.

**Discussion**

The expression of "respiration" implies multifarious meanings or functions from the medical viewpoint, instead of simple ones. What has been pursued in our research, out of manifold functions, is into the respiratory movements which are called the external respiration, and that our concentration has been confined exclusively to the central nervous control of them. The method employed is to give electrical stimulation to various parts of the central nervous system, by which 1) the changes in the respiratory current curves and 2) the expiratory or inspiratory displacement of the respiratory middle position of the curves introduced from the abdominal movements, have been observed. These two have been our sole objectives in this series of experiment, so that the following have been excluded from our immediate interests; measurement of respiratory current, analysis of gas-change in the blood, or functional and morphological changes in pulmonary alveoli and so forth. And no observation has been tried on the influence inflicted upon the respiratory movements of the peripheral nervous system.

Such kind of researches into the respiratory center as we have had, have been conducted by various scholars since last century. And after Lumsden tried an experiment of crucial sections of the brain stem well into this century (1923), the autorhythmic primary respiratory center was inferred to be localized in the pons and medulla oblongata, but since the invention of two instruments, Hess's (1932) and Horsley-Clarke's (1908), it has been discovered that the primary respiratory center is situated within the reticular formation of the pons and medulla oblongata; going into further detail, it has been disclosed that the inspiratory center is in its ventro-medial part and the expiratory center is in its dorso-lateral side. It is true that there is an objection against these (Hoff and Breckenridge 1949), but, since the present work is not immediately concerned with the primary center, our discussion will not be extended over it until another of our detailed article on the stimulation of the medulla oblongata is scheduled to be published.
Among those parts of the brain which are considered to participate in the respiratory movements other than the pons and medulla oblongata, there are cortex cerebri (Smith and others)\(^{38}\) and th\(\i\) mesencephalon (Max Markwald 1890 and others)\(^{125,157,116}\), and various studies on the influence towards the primary center have been carried on. But comparatively fewer have been made as to the hypothalamus of the diencephalon which makes the object of our present study. Hess (1946)\(^{19}\) reports that the stimulation given on the vicinity of the commissura posterior produces acceleratory effect, that on the perifornical region, tachypnea is obtained, with the effect of displacing the respiratory middle position toward the expiratory side, and that inhibitory effects are obtained (that is, respiratory amplitude is reduced and its frequency is lessened) on three different parts, which are commissura interthalamica, hypothalamus lateralis, and the nucl. lateralis thalami localized over the area, lateral, ventral, caudal to the perifornical region. Now let us turn to the comparison of his study with ours. To begin with, the method employed will be taken up. He used the damped impulse (impulses with retarded potential rise), with both frequency and intensity of stimulation slightly different from those of ours. He explains that the reason for using such impulses by means of his own invention was that the main purpose of his study was not only to see autonomic changes but rather the behavior. At the present stage of investigation in this line, the difference of the influences upon one nerve cell (cell-body or nerve-fiber) by various electrical impulses has been analysed to a certain extent, but the difference of the stimulatory effects upon a large amount of cell-bodies or nerve fibers, which are caused by using rather a large-pointed electrode (0.25-1.0 mm) and different kinds of impulses, has not yet been well analysed.

Now disregarding the application of different types of impulses, we have to turn our attention to the comparison of effects and their positions obtained by Hess and us. He states that the perifornical region is acceleratory (which is in accordance to our classification), while our results show that, where the fornix enters the hypothalamus on the rostral side, there are observed inhibitory effects, and on the perifornical region near an area slightly rostral to the corpus mamillare on the caudal side acceleratory effects are observed. But, since ours have disclosed that inhibitory effects have been ascertained on two areas which form dorsal and medial parts to the fornix, that is, those which correspond with an area called nucl. filiformis and
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nucl. reuniens as well as the hypothalamus lateralis, Hess's observation agrees with ours. Especially what Hess calls the commissure interthalamica can be presumed to be the same with our nucl. reuniens, so that it may safely be said that Hess has got the same result with us. However, if what he calls the lateral region of the fornix should be equal to what we have named the pars intermedialis hypothalami, our observations is quite contrary to his, because there we have obtained acceleratory effect. The problem here is Hess's way of description; for example, "ventral or medial to the fornix" which is found in his expression can be interpreted, as the case may be, either hypothalamus or the thalamus, if there should occur that a reader shift the exact location in reading if slightly. Furthermore, sagittal sections are employed in his figures showing the effective points by stimulation and that in his own way; for some reason or other, he uses diagonal section (from the dorsal to the ventro-lateral). It is inconvenient for us to find the exact localization when expressed in that way, because we are liable to make a slight but important misreadings and misinterpretation. We would like to propose that some kind of international standard is set up so that every body can describe in an unified way common to all.

Next to this, Magoun and his collaborators (1938) have reported that there have been seen "panting" between the commissura anterior and the brain base, by means of thermal stimulation, and that the respiratory frequency increases as high as up to 300 per min. The location in his experiment corresponds with our Fig. 4, A., where conspicuous acceleratory responses have already been referred to in above. It will be an important problem whether this acceleratory effect be interpreted as panting or not, but it must be remembered that in some area the effect of the stimulation has gone so far as to be apnea. Still it is of profound interest that Magoun has obtained the same result as ours agrees with in respect to increased respiratory frequency, though the methods of stimulation differ. As Hess (1944) further reports that there is found a wider range of panting over the brain areas, so in our experiment we have had the observation so far as the increase of respiratory frequency alone is concerned: there are discovered zonal or collective areas where it increases not only on the pars anterior hypothalami but on the pars intermedialis hypothalami and the pars posterior hypothalami.

We have discussed and examined up to now the experimental results by Hess, Magoun and us in terms of comparison. In
consequence of the difference of the method employed and the experimental conditions utilised, it is natural that the results do not always agree with each other, so that follow-up investigations are hoped. But the present authors have the pleasure or regarding the significance of our hitherto research as being heightened the more because multiple combinations of electrical stimulations have been tried and that the hypothalamus is stimulated concentratively and in a network pattern with more of stimulation points given on it.

What seems to be important next is the problem of the mechanism in which the effect of stimulation appears. When the mechanisms in the central nervous system come to be considered, it would be unavoidable for us to have recourse to the neurone theory. Accordingly in evaluating the response that is caused by stimulating the hypothalamus, the influence of the primary respiratory center in pons and medulla oblongata has to be considered through neuronal chain. What attracts our attention here is the phenomena that the nearer to the mesencephalon the stimulation is given on the pars posterior hypothalami the more inhibitory effects are seen. It may be because of the fact that it is situated near the pneumotaxic center (Lumsden 1923, and Pitts 1946) of the pons and mecencephalon so that by the stimulation it has come into action through neuronal chains. This is, however, nothing but a surmise, and any contact of the neuronal chain has not positively been ascertained. We are opinion, even in interpreting the result of our experiment, that it would be a hasty conclusion to discuss the problem of mechanism by being supported by the idea of the neuronal chain. The reason is that it will be impossible to try the explanation of the mechanism, because of the extreme largeness of the electrode which has been used (0.25–1.0 mm), compared with the size of one nerve cell. So that a chain of nerve cell with one cell-body of the size of (1) 5–40µ and one nerve fibre of the diameter of (0.2) 1–20 does not bear the explanation of the cell. That is the reason why the discussion from the viewpoint of the neuronal chain as to the correlation between the hypothalamus and the medulla oblongata (Thomson 1950) is considered to be jumping too hasty to the conclusion.

The further development of this problem must start with the electrode-tip of at least than 20µ in diameter and, at the same time, by the help of observing the spontaneous discharges in the central nervous system, and then the hitherto conducted research results should be so analysed and reduced as to reach the neuronal chain.
Conclusion

The following results are obtained through electrical stimulation of hypothalamus in cats, with respiratory frequency as the indicator for the observation in which effects are classified into that of acceleration, inhibition and reversal.

1) In the pars anterior hypothalami, major part has been occupied by the acceleratory responses.

2) In the pars intermedialis hypothalami, acceleratory responses have been predominant on the ventro-medial part, and on the dorsal part conspicuous inhibitory responses have been obtained. On the slightly caudal side of the hypothalamus where the ventro-dorsal zone is localized including the fornix, acceleratory responses have been observed, while on almost all the other areas inhibitory responses has been ascertained.

3) In the pars posterior hypothalami, which includes corpus mamillare, acceleratory responses are found on the nucl. corporis mamillaris as well as the part dorsal to it, while on the periventricular region mixed responses and on the other parts inhibitory effects have been obtained.

4) Eight points have turned out to be apnea during the process of the stimulation. Some of them have been on the ventral to the pars posterior hypothalami, others on the dorsal of the pars intermedialis hypothalami, major part of them (seven points) being of the nature of expiratory apnea.

References


