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RESPIRATORY AND VASCULAR RESPONSES IN MONKEYS FROM TEMPORAL POLE, INSULA, ORBITAL SURFACE AND CINGULATE GYRUS*

A PRELIMINARY REPORT

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INTRODUCTION

ATTENTION has recently been focused on the finding of vascular and respiratory responses resulting from stimulation of the cortex of the posterior orbital surface (4, 8, 12, 17) and the anterior limbic region (10, 19, 22) of the frontal lobe of monkey. Physiological neuronography has shown reciprocal and restricted firing between the posterior orbital surface and the cortex of the temporal pole (3). Also, cytoarchitectural studies in the macaque have indicated a close resemblance between these two areas (5). The finding of respiratory responses from stimulation of the anterior insula (20) provided a link between the frontal and temporal lobe. Because of these relationships it was decided to stimulate the cortex of the temporal pole and to study vascular and respiratory responses. In view of the positive results obtained from stimulation of the temporal pole in the present experiments, and the similarity of these responses from all of the above-mentioned regions, an investigation of the possible continuity of these responsive areas was undertaken.

MATERIALS AND METHODS

Stimulation experiments were carried out in 8 monkeys (6 *Cercopithecus aethiops pygerythrus* and 2 *Macaca mulatta*) anesthetized intraperitoneally with 0.5 cc. sodium amytal per kg. body weight (with 0.2 cc. Dial-Urethane per kg. added when necessary). One animal was anesthetized with Chloralose. A solution of 50 per cent glucose was given intravenously shortly after the animal was anesthetized in doses of 4 gm. of glucose per kg. body weight. This resulted in marked shrinkage of the brain which aided considerably in the exposure of poorly accessible regions. Subcutaneous injection of physiological saline solution was usually given every two hours.

A linear scalp incision was made, extending from the vertex over the temporal region to well below the zygoma. The zygoma and entire temporal muscle were resected. A burr hole in the temporal bone was enlarged to expose the entire frontal and temporal lobes. When necessary the exposure was extended well past the midline, giving access to the medial surface of the hemisphere. The rim of the orbit was removed, permitting retraction of the ocular bulb so as to spare any unnecessary manipulation of the cortex. The insula was exposed by blunt dissection of the pial layers and temporary packing with cotton patties

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separating the temporal from the fronto-parietal operculum. After such packing the exposure maintained itself for short periods, necessitating only the most gentle retraction. The depths of the various sulci were explored with the same technique. When occasional venous oozing resulted from the dissection it was arrested by gentle packing. The uncus was easily reached from above after the insula was exposed. By packing and by the use of gravity the ventral surface of the uncus and the hippocampal gyrus were visualized. The medial surface of the frontal lobe was explored by both this method and by resection of one lobe, giving unobstructed access to its opposite.

A square-wave stimulator recently designed by A. Mauro (13) was employed. The frequency (0.5–1000/sec.), pulse duration (0.5–10 msec.), and intensity could be varied independently of one another. Bipolar silver electrodes insulated except for the tips were used. Respiratory movements were recorded by means of a pneumograph placed around the thorax and abdomen and connected to a Marey tambour writing on a kymograph, or through a tracheal cannula connected to the tambour.* Arterial pressure was recorded from the femoral artery by the use of a mercury manometer.

RESULTS

Electrical excitation of the temporal pole and uncus partly or completely inhibited *respiratory movements*. The inhibition was mainly of amplitude, although the rate of respiration at times also decreased. This decrease affected the inspiratory phase predominantly and respiratory arrest occurred with the thorax in the expiratory position (Fig. 1). Such arrest was not maintained for more than 25–30 seconds, after which period the respiratory movements reestablished themselves despite continued stimulation. At times the apnea was interrupted by a deep inspiration.

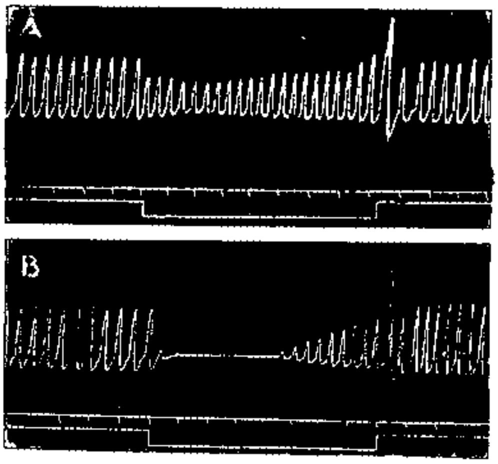

FIG. 1. Pneumograph records of inhibition of respiratory movements resulted from electrical stimulation of subcallosal region in monkey (recorded by means of pneumograph placed around the chest). Stroke upwards indicates inspiration. Time 5 sec. A: Weak stimulus (Int. = 3 volts, F. = 40 per sec.; sigma = 10 msec.). Note inhibition predominantly of inspiratory phase. B: Stronger stimulus applied to same cortical point (Int. = 7 volts, F. = 40 per sec., sigma = 10 msec.). Complete respiratory arrest with thorax in expiratory position.

The magnitude of the response was greatly influenced by the pulse duration and the frequency of stimulation. The longer pulse durations of 10 msec. were far more effective than the shorter ones of 1–2 msec. The fre-

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* The former method of recording gives more accurate information regarding the respiratory phase in which the alterations occur than does the latter, which merely measures the intratracheal pressure (18).

quency producing the optimum effect was found to be about 40 per sec. With these optimum parameters responses were obtained with intensities of from 3 to 8 volts.

On stimulating the region from which respiratory changes were found, a rise in *blood pressure* was usually recorded, the best responses being obtained at frequencies of 40–100 per sec. However, during unfavourable conditions such as very deep anesthesia or low systemic blood pressure, the pressure had a tendency to drop in response to stimulation. At times the rise in blood pressure was followed by a secondary fall, or a fall in pressure was succeeded by a rise. In these cases the application of a stimulus of low frequency (10–20 per sec.) had a tendency to increase the amplitude of the falling phase of the pressure, whereas higher frequencies (40–100 per sec.) applied to the same point on the cortex tended to increase that of the rising phase. The variation in pressure amounted to 15–40 mm. mercury, the rise usually being of greater magnitude than the fall. The blood pressure response appeared after a latency of a few seconds. As with respiratory changes, stimulation using the longer pulse durations of 10 msec. proved most effective. Section of the trigeminal nerve (which runs close to the temporal pole) did not abolish the responses from the temporal pole.

The *responsive area* in the temporal lobe was limited to the temporal pole and uncus (Figs. 2 and 3). Posteriorly, the boundary was not sharp, the response to stimulation tapering off toward the 1st and 2nd temporal gyri and on the anterior hippocampal gyrus. Dorsomedially, the responsive area continued without interruption into the anterior temporal operculum, the anterior insula and into the posterior orbital surface of the frontal lobe. The responsive cortex of the posterior orbital surface extended to the midline and included the anterior perforated space. Anteriorly, the boundary was not sharp, the response to stimulation diminishing about one-third of the distance toward the frontal pole. Further exploration on the medial surface of the frontal lobe showed that the same vascular and respiratory responses already described could be obtained from the cortex of the anterior limbic region (as previously reported, 10, 19, 22) and also from the subcallosal region (Fig. 3). Ventrally they were elicited as far as the ventromedial edge where this region is continuous with the posterior orbital surface.

In addition, the lateral surface of the frontal lobe, including the depths of the arcuate and principal sulci, was explored, as was the "suppressor strip" surrounding the lunate sulcus. Using the parameters of stimulation which gave maximum results for the previously noted regions, inconstant respiratory changes were obtained from the cortex dorsal to the superior limb of the arcuate sulcus and ventral to its inferior limb. With high intensities (15 volts) similar responses were obtained from the depths of the arcuate sulcus, especially the posterior bank of the inferior limb. At no time were any responses obtained from stimulation of the frontal polar region, the depth or banks of the sulcus principalis, the region of the lunate sulcus, or

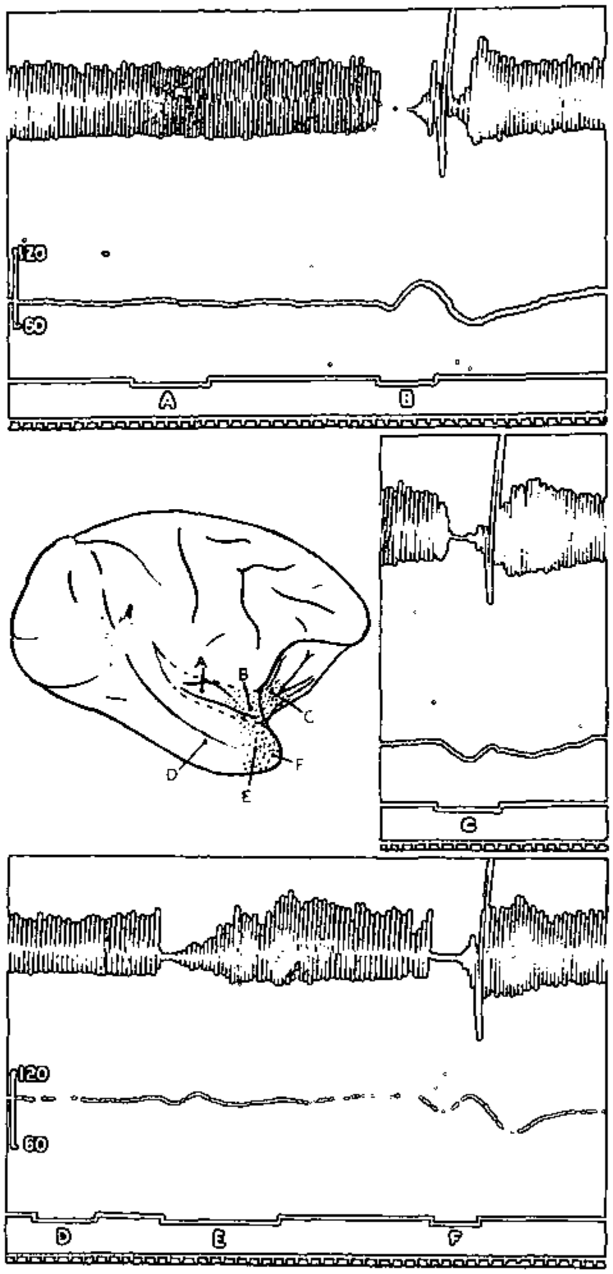

FIG. 2. Respiratory (upper record) and blood pressure responses (lower record) resulting from electrical stimulation of points corresponding to designation on brain map. Insula (A and B) visualized by separation of temporal and frontoparietal operculum. Responsive regions indicated by dots. Respiratory movements through tracheal cannula. Stroke upwards indicates expiration (see footnote, p. 348). Parameters of stimulation: Int. =5.5 volts, F. =39.5 per sec., sigma =10 msec.). Time 5 sec.

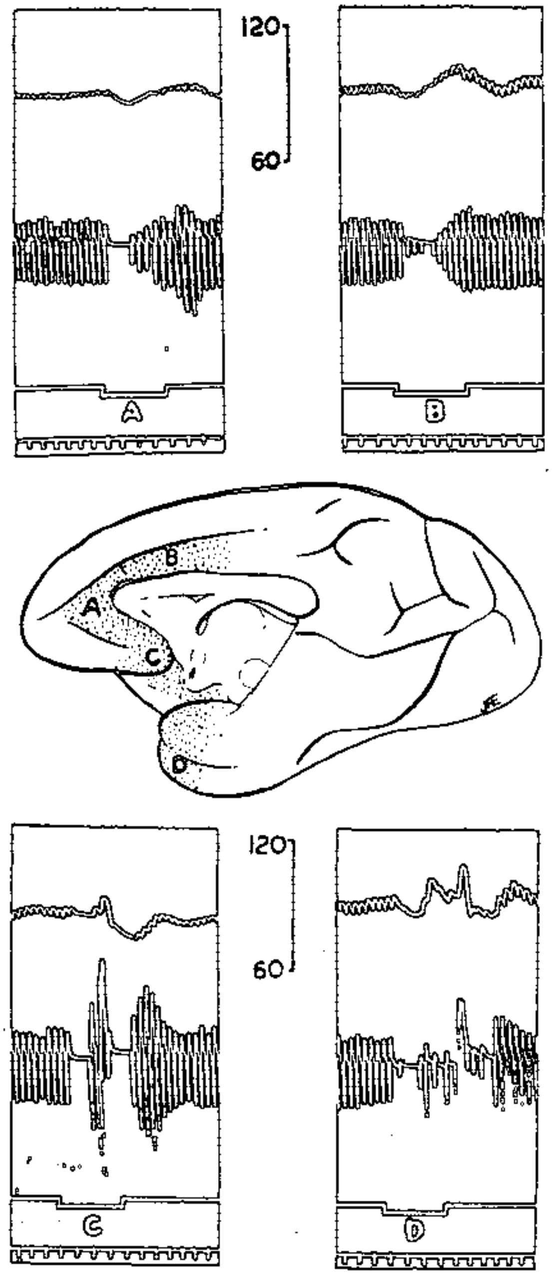

Fig. 3. Blood pressure (upper record) and respiratory responses (lower record) resulting from electrical stimulation of points corresponding to designation on brain map. Responsive regions indicated by dots. Respiratory movements recorded through tracheal cannula. Stroke upwards indicates expiration (see footnote, p. 348). Parameters of stimulation: Int. = 6 volts, F. = 39.5 per sec., sigma = 10 msec. Time 5 sec.

from the more anterior parts. Area FL also comes over onto the orbital surface as far laterally as the olfactory sulcus and thus includes Walker's area 14 (Fig. 4). According to von Bonin and Bailey (5), area FL has affinities with the allocortex and might also be placed with the mesocortex. It partly corresponds to Broca's olfactory field of man. Von Economo (9) points out the gradual change in the cytoarchitectural picture from the granular cortex on the frontal pole towards the agranular type in the posterior parts of this region in the human brain.

On the *orbital surface* a similar change in the cytoarchitecture from an anteriorly situated granular cortex to a posteriorly placed agranular cortex is found (5, 9, 21). This is in accord with the positive results from electrical stimulation of the posterior portions (Walker's areas 13 and 14, von Bonin and Bailey's areas FF and FL), and tends to confirm the differentiation of these areas from the frontal granular cortex.

The cortex of the *insula* has been divided into a posterior granular and an anterior agranular area (5, 7, 9). The alterations in blood pressure and respiration elicited were limited to the region of the agranular cortex and were most pronounced from the limen insulae.

Turning to the *temporal pole* there is somewhat less agreement between different cytoarchitectural studies. In *Cercopithecus* and *Hapale* Brodmann (7) failed to recognize an area corresponding to his area 38 in the human. Lashley and Clark (11) in the macaque and in *Ateles* found that the cytoarchitecture of the cortex of the temporal pole varied in their material. In the macaque von Bonin and Bailey (5) distinguish a polar area TG as homologous with von Economo's area TG in man (9). To them area TG resembles area FF (Walker's area 13) on the orbital surface, and it also reminds one of the proximity of the allocortex (1). The finding of vascular and respiratory responses on stimulation of the temporal pole supports the cytoarchitectural differentiation of the sparsely granular polar area from the rest of the cortex of the temporal lobe.

Relevant Fiber Connections. An excellent and detailed discussion of the connections of the allocortical regions involved in the present investigation has recently become available (6), and the readers are referred to this review.

Intercortical connections. The results of physiological neuronography in macaque have shown that the pyriform cortex covering the uncus is connected with the temporal pole (14). As already mentioned, there is reciprocal firing of the temporal pole and the posterior orbital surface (3). No direct corticocortical connections are known between the limbic gyrus and the other areas studied, although indirect pathways to this gyrus from the pyriform cortex (via the entorhinal area, hippocampus, mammillary bodies, anterior nuclei of thalamus) exist.

Afferent connections. The rostral limbic region receives the cortical projection from the anteromedial nucleus of the thalamus and is closely related to the posterior granular limbic cortex (16). The agranular orbitofrontal cortex may be part of the cortical projection area of the dorsomedial nucleus but this has not been proved for the monkey (15). No connections have been demonstrated between the thalamus and the temporal pole or anterior insula.

The *efferent pathways* which mediate impulses to the lower respiratory and vascular centres are unknown. The disclosure of similar respiratory and vascular responses from the rostral portions of both the dorsal and ventral part of the cingulate convolution and from adjacent areas suggests efferent connections to common subcortical centres from this extensive cortical region. This is emphasized by the fact that none of the responses from any of the areas concerned were abolished by their circumsection.

Addendum. Recent evidence indicates that in the human also the responsive areas reported here exist. Pool and Ransohoff (28) have obtained vascular and respiratory responses on stimulation of the anterior cingulate gyrus. Livingston *et al.* (27) have reported similar responses from the orbital surface. Bailey (24) has found such responses from the anterior insula and Chapman (26) from the temporal pole. The report of Elizabeth Beck (25) tends to confirm the cytoarchitectural correlations proposed.

SUMMARY

1. Results of electrical stimulation of temporal and frontal lobes and the insula of monkey with recording of vascular and respiratory responses are reported.

2. Square-wave pulses of low intensity (3 8 volts) and of varying frequency and pulse duration were used.

3. From temporal pole blood pressure alterations and respiratory inhibition were obtained. The optimal parameters of stimulation were found to be a frequency of about 40 per sec. and prolonged pulse durations (10 msec.).

4. With these optimal parameters similar vascular and respiratory responses were obtained from a continuous stretch of cortex (Figs. 2 and 3) extending through the anterior insula, the posterior orbital surface of the frontal lobe, the subcallosal region to the rostral limbic gyrus and also including basal olfactory structures (uncus, limen insulae, anterior perforated space).

5. The lateral surface of the frontal lobe (including the depths of the arcuate sulcus and principal sulcus) was explored, but even with greater intensities of stimulation (15 volts) only inconstant respiratory changes were obtained from the cortex dorsal to the superior limb of the arcuate sulcus and ventral to its inferior limb.

6. The continuous responsive region is covered either by allocortex or by agranular or sparsely granular isocortex showing characteristics of transitional cortex.

7. The relevant connections of these areas are discussed.

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Addendum

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