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# Projections from the Cortical Larynx Area in the Squirrel Monkey

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**Summary.** The projections from the cortical vocal fold area were studied in five squirrel monkeys (Saimiri sciureus) with the aid of the autoradiographic tracing technique. The location of the cortical vocal fold area was determined by exploring the exposed frontal cortex with roving electrodes while examining the larynx for vocal fold adduction. The following projections were found: To the orbital cortex (area 11), dorsomedial frontal cortex (areas 6 and 8), Broca's area (area 44), lower fronto-parietal cortex (areas 6, 4, 3 and 1), fronto-parietal operculum (area 50), insula (areas 14 and 13), caudatum, putamen, claustrum nucl. reticularis th., nucl. ventralis anterior, nucl. ventralis lateralis, nucl. ventralis posteromedialis, nucl. centralis inferior, nucl. centralis lateralis, nucl. medialis dorsalis, nucl. pulvinaris medialis, griseum pontis, nucl. parabrachialis medialis and lateralis, nucl. tr. spinalis n. trigemini and nucl. tr. solitarii.

A comparison of this projection system with a previous mapping study for vocalization (Jürgens and Ploog, 1970) revealed that there are two areas yielding vocalization when electrically stimulated which receive direct projections from the cortical larynx area, namely, the cortex around the anterior sulcus cinguli and the parabrachial nuclei at the pons-midbrain transition. The possible relevance of these structures for vocalization is discussed.

**Key words:** Cortical larynx area – Vocalization – Squirrel monkey.

## Introduction

The present study is an attempt to further specify the brain structures relevant for vocalization. In earlier papers (Jürgens et al., 1967; Jürgens and Ploog, 1970; Jürgens, 1971) brain maps were presented for the squirrel monkey in which all brain structures yielding vocalization when electrically stimulated were delineated. From these studies the question arose of whether the electrically-elicited calls have to be regarded as primary motor responses or, on the contrary, as secondary responses due to stimulus-induced motivational changes. A possible approach in answering this question was, in our opinion, to

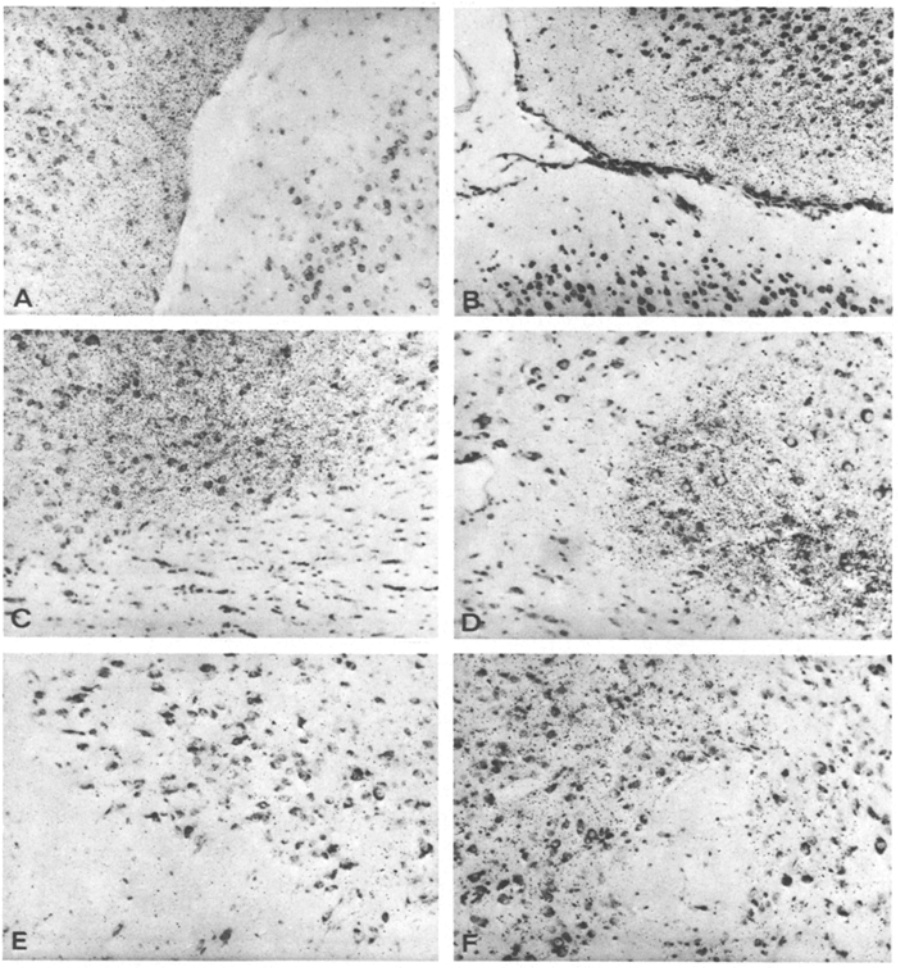


**Fig. 1.** Photographs of some of the terminal fields drawn in Fig. 2A–C. (A) Cortex around the sulcus orbitalis with labelled lateral bank and unlabelled medial bank (AP 20). (B) Cortex around the sulcus cinguli with labelled dorsal bank and unlabelled ventral bank (AP 18.5). (C) Putamen. Heavy labelling just above the anterior commissure (AP 11). (D) Nucl. ventralis postero-medialis (AP 6.5). (E) Nucl. parabrachialis lateralis. Weak activity above the brachium conjunctivum; the latter is at background level (AP–1). (F) Nucl. tractus solitarii. No label in the tractus solitarius itself (AP–4)

study the projections from the cortical larynx area, for we can be sure that the vocal fold movements elicitable from this area are not produced indirectly by a motivational change. A direct connection of the cortical larynx area to a particular vocalization area can be interpreted, therefore, as an indication of a close functional relationship of the latter with basic phonation-coordinating or -initiating processes.

## Methods

In five squirrel monkeys (Saimiri sciureus) anesthetized with α-chloralose (70 mg/kg, dissolved in propylene glycol) the exposed left or right frontal cortex was explored with a monopolar stainless steel electrode (0.15 mm in diameter) for vocal fold movements. The stimulus parameters used were: biphasic rectangular pulse trains of 5 sec, 70 Hz, 1 msec pulse duration, 4 V. After having found an effective locus the electrode was withdrawn and 0.5–1.2 µl $^3$H-leucine (33 µCi/µl) was injected at that site with the aid of a micromanipulator-driven microsyringe. The injection time was 20 min. After a survival time of 10 hours, 4, 14 and 22 days, respectively, the animals were sacrificed, perfused with 4% formaldehyde, embedded in paraffin and sectioned at 10 µ in the frontal plane. The sections were deparaffinized, hydrated and coated with Kodak NTB3. After an exposure time of about 8 weeks the sections were developed (Kodak D19), fixed (Superfix) and stained (toluidine blue 0). Microscopic evaluation was carried out with a combined transmitted light-dark field incident light-light field technique (Leitz Orthoplan). Thus, the silver grains were seen as white dots within a normally illuminated tissue. This technique made it possible to detect the silver grains with a rather low magnification (80 ×) and at the same time to identify the brain structures which contained the grains.

Identification of terminal fields was done qualitatively, not quantitatively (grains/mm$^2$). Only those areas were accepted which, with the naked eye, showed activity clearly above background for at least three consecutive sections. Examples of heavily, intermediately and weakly labelled terminal fields are given in Fig. 1.

## Results

As the area yielding vocal fold movements is rather large (2–3 mm in diameter) and also as the material is not homogeneous (different survival times, different injection volumes), the resulting projections differed somewhat between individuals. We decided, therefore, not to arbitrarily select a single case for representation, but to superimpose the projections of all five animals and to map out only those projection areas which are shared by at least three animals. These areas are represented in Fig. 2A–C. Deviations from this representative will be mentioned in each case.

### *A) Intrinsic Cortical Projections*

The injection site is shown at AP14 (Fig. 2A); the area of labeled perikarya, which had a diameter of about 2 mm, is drawn in black. From here rostral projections extend ventrally to the anterolateral orbital cortex (AP 21.5), sulcus orbitalis (AP 20 and 18.5), Broca's area (AP 17 and 15.5), posteromedial orbital cortex (AP 15.5), fronto-operculum (AP 14) and insula (AP 15.5 and 14). The dorsal projections are going to the sulcus cinguli and dorsomedial frontal cortex at the level of the genu of the corpus callosum (AP 20 to 17); at the level of the injection site two projections to the lateral frontal cortex (AP 14; areas 6 and 4) can be distinguished. Posterior to the injection site terminal fields can be found in the sensory areas 3 and 1 (AP 12.5 to 9.5), in the adjacent opercular region (AP 11 and 9.5) and in the posterior insula (AP 8).

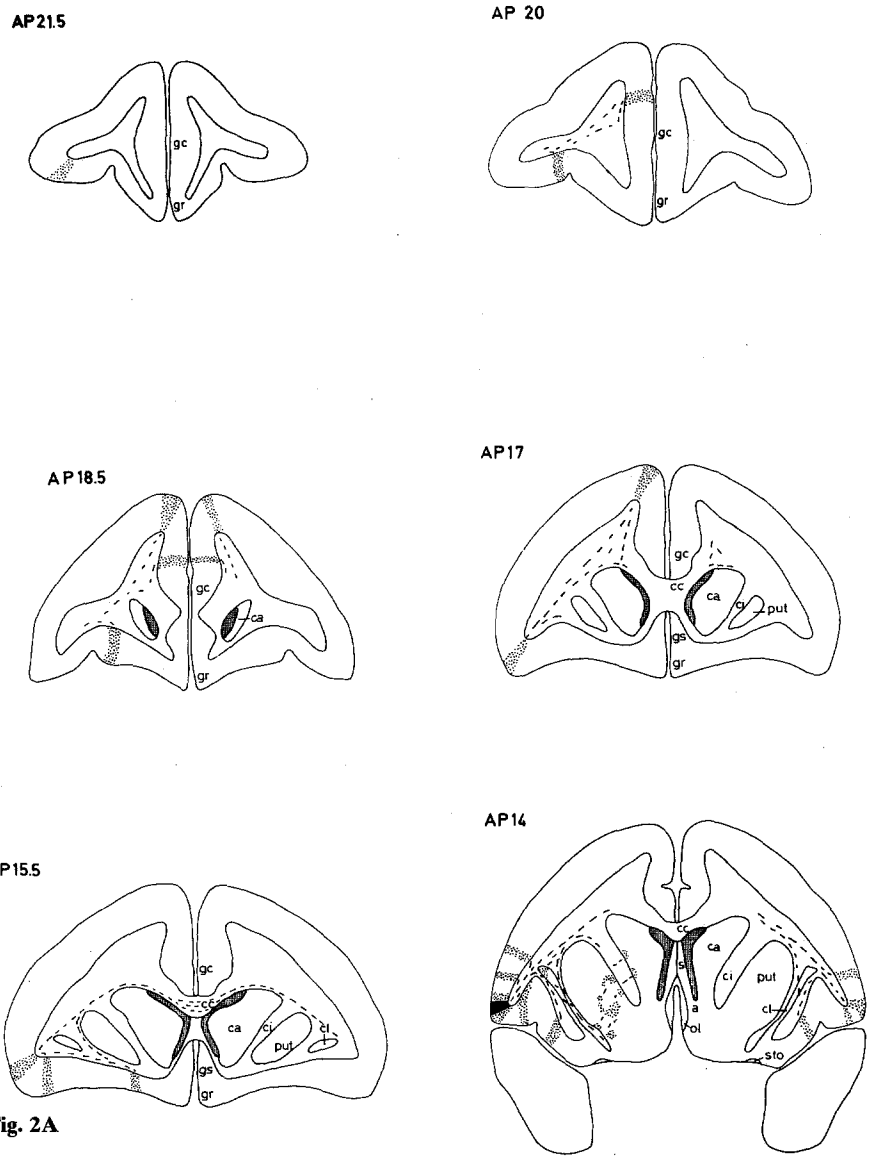


**Fig. 2A**

**Fig. 2.** (A–C). Projections from the cortical larynx area. Injection site (labelled perikarya) is drawn in black; labelled fibres are indicated by dashes, terminal fields by dots. *a* nucl. accumbens, *aa* area anterior amygdalae, *ab* nucl. basalis amygdalae, *ac* nucl. centralis amygdalae, *al* nucl. lateralis amygdalae, *am* nucl. medialis amygdalae, *an* nucl. anterior thalami, *aq* substantia grisea centralis, *bc* brachium conjunctivum, *ca* nucl. caudatus, *cb* nucl. cerebelli, *cc* corpus callosum, *ci* capsula interna, *cl* claustrum, *cm* centrum medianum, *cr* corpus restiforme, *cei* nucl. centralis inferior thalami, *cen* nucl. centralis superior tegmenti, *cin* cingulum, *coa* commissura anterior, *cop* commissura posterior, *csp* tractus cortico-spinalis, *coli* colliculus inferior, *cols* colliculus superior, *db* fasciculus diagonalis Brocae, *dbc* decussatio brachii conjunctivii, *f* fornix, *gc* gyrus cinguli, *gl* corpus geniculatum laterale, *gp* globus pallidus, *gr* gyrus rectus, *gs* gyrus subcallosus, *h* campus Foreli, *ha* nucl. habenularis, *hip* hippocampus, *hya* area hypothalamica anterior, *hyv* nucl. ventromedialis hypothalami, *in* nucl. interpeduncularis, *lm* lemniscus medialis, *lap* nucl. lateralis posterior thalami, *m* corpus mamillare, *md* nucl. medialis dorsalis thalami, *nst* nucl. striae terminalis, *nts* nucl. tractus

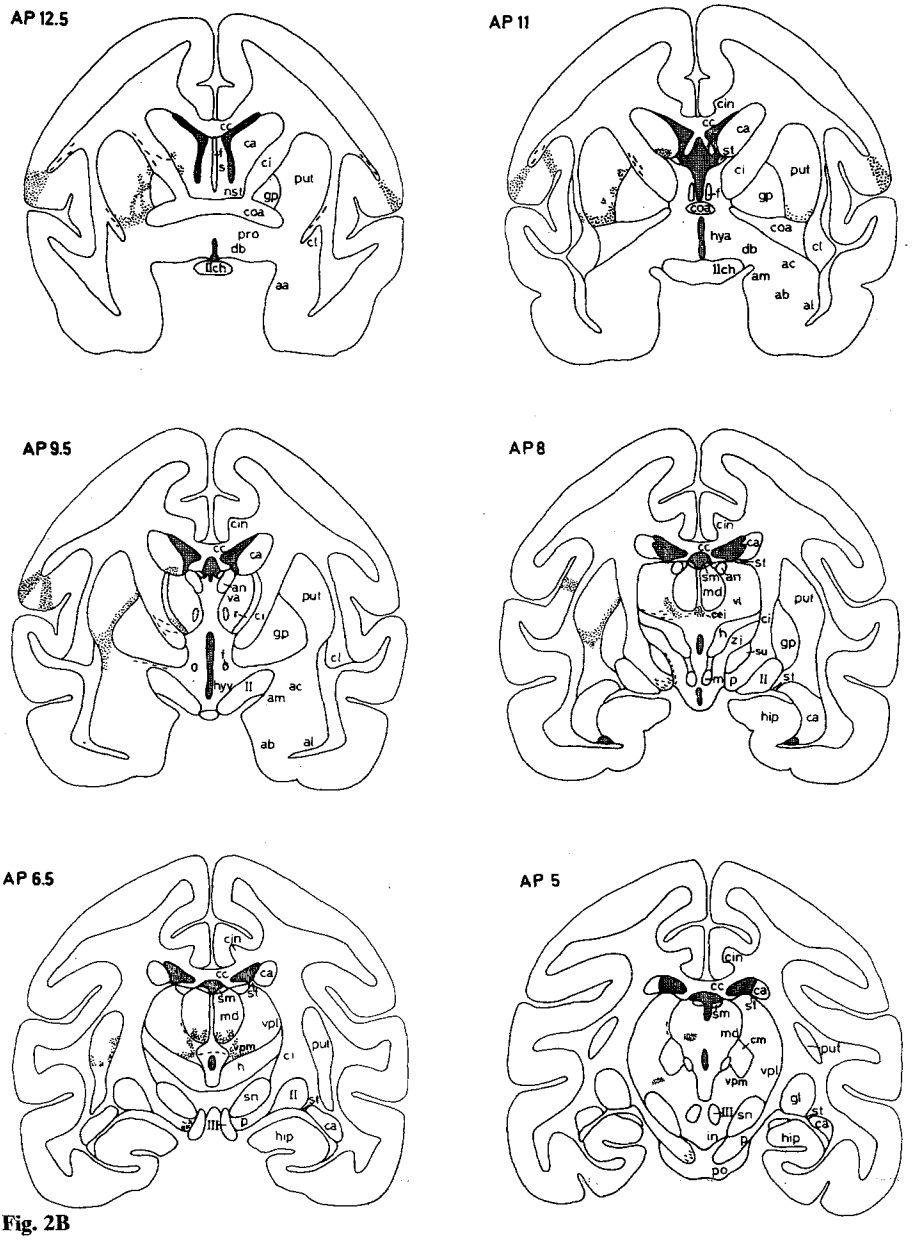


**Fig. 2B**

solitarii, *oi* nucl. olivaris inferior, *ol* fasciculus olfactorius Zuckerkandl, *p* pedunculus cerebri, *po* griseum pontis, *pu* nucl. pulvinaris thalami, *pmc* brachium pontis, *pro* area praeoptica, *put* putamen, *r* nucl. reticularis thalami, *re* formatio reticularis, *rl* nucl. reticularis lateralis myelencephali, *rub* nucl. ruber, *s* septum, *sm* stria medullaris, *sn* substantia nigra, *su* subthalamus, *st* stria terminalis, *SV* nucl. spinalis n. trigemini, *sto* stria olfactoria, *tec* tractus tegmentalis centralis, *trz* corpus trapezoideum, *va* nucl. ventralis anterior thalami, *vl* nucl. ventralis lateralis thalami, *ves* nucl. vestibularis, *vpl* nucl. ventralis postero-lateralis thalami, *vpm* nucl. ventralis postero-medialis thalami, *zi* zona incerta, *II* tractus opticus, *IIch* chiasma nervorum opticorum, *III* n. oculomotorius and nucl. n. oculomotorii, *IV* n. and nucl. n. trochlearis, *VII* nervus facialis, *VIII* nucl. cochlearis, *XII* nucl. hypoglossi

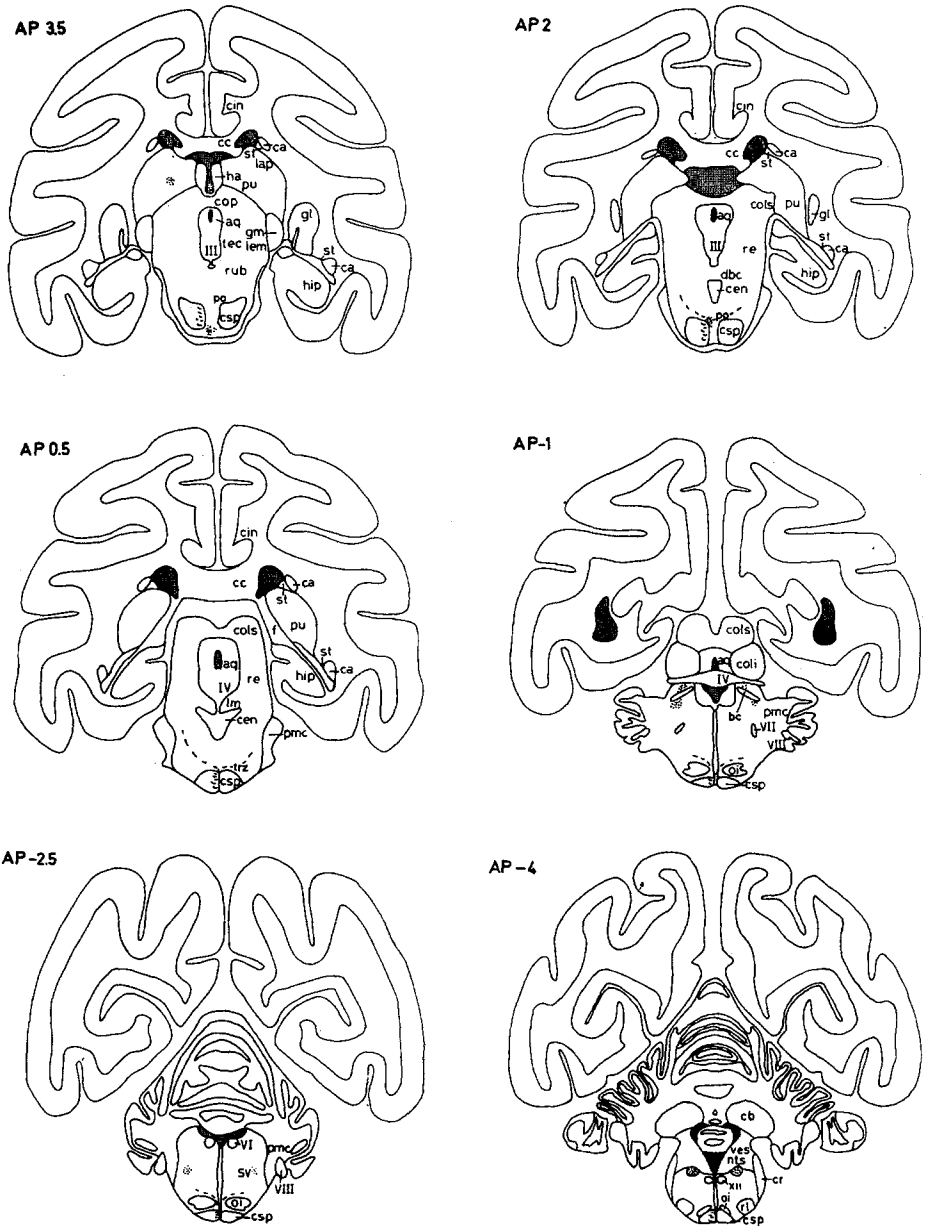


**Fig. 2C**

The only terminal fields not common to all five animals were the anterolateral orbital and dorsomedial frontal fields which were lacking in animal 3 (survival time 10 hours). Furthermore, the sulcus cinguli projection was limited to the dorsal bank of the sulcus cinguli in three animals, whereas in the other two activity was also found in the ventral bank. In the latter two animals the injec-

tion field reached somewhat further rostrodorsally than in the other three animals.

Beside these ipsilateral projections there was a heavy projection to the contralateral homologue of the injection site. Furthermore, fibres could be traced to the contralateral sulcus cinguli, dorsomedial frontal area, lateral frontal cortex (areas 6 and 4), fronto-operculum, anterior insula and to the border zone between sensory areas 3 and 1 and the fronto-parieto-operculum. In animal 3, which lacked the terminal field in the dorsomedial frontal cortex ipsilaterally, the contralateral homologue was also free of label. In one case which had an ipsilateral projection to the dorsal but not to the ventral bank of the sulcus cinguli, the contralateral projection extended only to the ventral bank but not to the dorsal one. The phenomenon that the contralateral and ipsilateral projection to two homologous areas differed slightly was encountered repeatedly.

### *B) Subcortical Projections*

*1. Telencephalon.* Within the ipsilateral telencephalon terminal fields were found in the caudate nucleus, putamen, claustrum and the most dorsolateral part of nucl. centralis amygdalae. The caudatum and putamen both received their afferents via capsula interna and capsula externa; the capsula externa fibres to the caudatum traversed the putamen in a ventrolateral-dorsomedial direction and cut the capsula interna perpendicularly. The capsula extrema also contributed to the striatum, as fibres could be followed traversing the claustrum and entering the putamen. The nucl. centralis lateralis amygdalae, like the striatum, received fibres via capsula externa and capsula interna. The latter fibres left the internal capsule at about AP9; they penetrated the lateral hypothalamus and then bent sharply lateralward towards the amygdala, passing between the globus pallidus dorsally and the tractus opticus ventrally.

The terminal fields within the caudatum and putamen did not form continuous well-delineated areas; instead, they had a patchy appearance with clusters of activity rapidly changing in their shape from section to section. The over-all distribution, however, was limited both in putamen and caudate nucleus to their ventral parts. The claustrum showed heavy labelling in the area where the fibres traversed it on their way to the internal capsule and corpus callosum; a second, much smaller claustral projection area was found at about the level of the anterior commissure. In the case of the fibres coursing through the lateral hypothalamus, which provided the dorsolateral amygdala (see above), it became unclear whether or not some of these fibres terminated in the lateral hypothalamus. More posterior there was another small contingent of fibres which left the cerebral peduncle at the level of the posterior hypothalamus and entered the bundle $H_2$ of Forel; its area of destination, however, remained unclear.

Contralaterally, only the putamen contained labelling. This terminal field, however, which received its afferents via corpus callosum and capsula externa, was very weak; it was again lacking in animal 3 (survival time 10 hours).

2. *Diencephalon.* At the level of the anterior diencephalon a large contingent of fibres left the internal capsule medially and crossed the ventral nucl. reticularis thalami, where many of them ended. The rest continued further medially, terminating in the medial part of the nucl. ventralis lateralis and the immediately adjacent zone of nucl. ventralis anterior, in the nucl. centralis inferior, ventral part of nucl. medialis dorsalis and rostromedial tip of nucl. centralis lateralis. The majority of fibres, however, ended in the medial part of the ventralis postero-medialis complex (including its parvocellular part, excluding the nucl. ventralis posterior inferior). A few fibres entered the lamina medullaris interna th. and followed it caudalward until they reached the nucl. pulvinaris medialis. This projection was lacking, however, in animal 3 (short survival time).

Contralaterally, labelling was found only in the nucl. medialis dorsalis and nucl. ventralis postero-medialis. Both projection areas received their afferents from the capsula interna ipsilateral to the injection site by fibres crossing within the thalamus.

3. *Midbrain, Pons and Medulla.* At the midbrain-pons transition a weak bilateral terminal field was found in the nucl. parabrachialis medialis and nucl. parabrachialis lateralis (AP-1). More ventrally, in the griseum pontis, fibres could be traced into cell clusters immediately adjacent to the midline; this projection also showed a small contralateral component, at least in three animals. In the posterior pons and rostral medulla, finally, a sparse projection to the nucl. tr. spinalis n. trigemini and a quite heavy projection to the rostral nucl. tr. solitarii were the most posterior projections we found. These projections were lacking, however, in animal 2, which had the most rostral injection site. Both terminal fields were bilateral, with the heavier contribution on the ipsilateral side; they ended at about the level of the rostral nucl. dorsalis n. vagi.

## Discussion

The function of the cortical larynx area in the monkey is still unclear. We only know that its electrical stimulation yields vocal fold movements – but not vocalization (Jürgens, 1974) – and that its bilateral ablation alters neither spontaneous nor conditioned vocalization (Sutton et al., 1974). In humans, on the other hand, it seems to be a well-established fact that the cortical larynx area serves speech co-ordinating functions: Lesions within this region have been reported by many authors to yield dysarthria (e.g., Conrad, 1954; Brain, 1961; Bay, 1962; Luria, 1965; Hécaen and Angelergues, 1964), and electrical stimulation of the same area has been shown by Penfield and his co-workers to yield vocalization as well as several types of stimulus-bound speech disturbances such as slurring, stuttering or speech arrest (Penfield and Roberts, 1959).

Judging from the close phylogenetic relationship between monkey and man and the results mentioned above, it appears unlikely that the monkey's cortical

larynx area is totally unrelated to vocalization processes. Following this assumption, it becomes of interest to know where there is an overlap between the vocalization-producing brain structures and the projection system outlined above. A comparison of both systems reveals that the only areas of overlap are the precallosal sulcus-cinguli region and the parabrachial region at the pons-midbrain transition. As both structures occupy an especially prominent position within the vocalization system, we think this overlap is not an accidental one, but with respect to vocalization one of functional significance. The following observations point to a significant role of the rostral sulcus-cinguli area for vocalization. Firstly, there is the study by Sutton et al. (1974) which shows that ablation of this area in the rhesus monkey abolishes conditioned vocalization, i.e., the capability of getting food reward by vocalizing; this lesion does not abolish conditionability in general, however. Secondly, the vocalizations elicitable from the sulcus-cinguli area continue as long as the duration of the stimulation – which is not the case for many other vocalization areas (own unpublished results). Thirdly, the sulcus-cinguli area is directly connected with most of the other vocalization-producing brain structures (Müller-Preuß and Jürgens, 1976). Fourthly, lesions of the rostral sulcus cinguli area in man can cause profound inertia to speak and even complete mutism (Botez and Barbeau, 1971). Fifth, stimulation just above the rostral sulcus cinguli in man – namely, the supplementary speech area – produces the same syndrome as stimulation of the cortical larynx area – that is, speech disturbances and vocalization (Brickner, 1940; Penfield and Welch, 1951; Penfield and Roberts, 1959). Our result that there is a direct anatomical connection between the cortical larynx area and the region around the rostral sulcus cinguli can be interpreted, therefore, as a further hint that vocalizations elicited from the latter area in the squirrel monkey are *primary* responses (see Introduction), despite the fact that they are accompanied by motivational changes (Jürgens, 1976).

The parabrachial area, as well, seems to occupy an outstanding position within the vocalization system. Firstly, the type of vocalization elicitable from this area, especially its caudal part, most often sounds quite artificial compared to naturally-uttered calls. This is in contrast to all vocalization areas rostral to the parabrachial nuclei (with the exception of the area ventral to the inferior colliculus) and in accordance with all structures caudal to it. Secondly, self-stimulation studies have shown that the parabrachial area is one of the few areas where, under certain stimulus conditions, vocalization can be elicited without accompanying aversive or pleasant motivational effects (Jürgens, in press). Thirdly, Car et al. (1975) found that the parabrachial area in sheep receives a direct input from the superior laryngeal nerve, which carries afferent fibres from the larynx and pharynx. Fourthly, according to Bertrand and Hugelin (1971) the parabrachial area is the only area from which electrical stimulation can synchronize respiration. Respiration, however, is an essential component of vocalization. All of these results, together with our own demonstration of a direct anatomical connection between the cortical larynx area and the parabrachial nuclei, suggest again that vocalization elicited from the latter region should not be considered a secondary response due to stimulus-induced motivational changes.

Thus, the present study accentuates two structures of the vocalization system outlined previously: One at its rostral end, namely, the anterior sulcus-cinguli region, which seems to be important for the initiative or voluntary impulse to vocalize; the other at its caudal end, namely, the parabrachial region, responsible presumably for the co-ordination of the different components involved in phonation – i.e., control of the vocal folds, respiration and oral movements.

It is worth mentioning that there is no projection from the cortical larynx area to the nucl. ambiguus – where the motor neurones to the larynx start. In contrast, we found heavy projections to all *sensory* relay stations of the oropharyngo-laryngeal region, namely, to nucl. tr. solitarii, nucl. spinalis n. trigemini, medial part of nucl. ventralis postero-medialis thalami and somatosensory facial cortex SI and SII. This corresponds to results of Kuypers (1958) in the rhesus monkey, who was also unable to find degeneration in the cranial motor nuclei after lesions in the region of the cortical larynx representation; he did find degeneration in the nucl. tr. solitarii, however. In contrast to the rhesus monkey which, in fact, possesses direct projections to the cranial motor nuclei from the motor cortex posterior to the larynx area, the cat does not seem to have any direct connections between motor cortex and cranial motor nuclei at all (Szentágothai and Rajkovits, 1958). The latter authors, who investigated the input into the cranial motor nuclei in greater detail, came to the conclusion that the motor cortex-motor nuclei connection in the cat is mainly relayed in the ventrolateral reticular formation. This conclusion was drawn, firstly, from the fact that many corticofugal fibres from the motor face area ended in the ventrolateral reticular formation and, secondly, from experiments in which lesions within that area gave rise to degenerations in the trigeminal motor nucleus, facial and hypoglossal nuclei (projections to the nucl. ambiguus were not referred to). In our own material we were unable to find terminals in the ventrolateral reticular formation; we think, therefore, that the interneurones relaying the cortical larynx efferents to the nucl. ambiguus must be looked for elsewhere. One possible candidate for such a relay station could be the parabrachial region in the rostral pons.

Finally, two further terminal fields should be mentioned, namely, one in the medial nucl. ventralis lateralis and the other in the rostral pulvinar. Both structures have become increasingly important in recent aphasia research, since it is known that stimulation as well as lesions there can interfere with normal speech abilities (Guiot et al., 1961; Hassler, 1964; Krayenbuehl et al., 1965; Schaltenbrand, 1965; Samra et al., 1969; Van Buren and Borke, 1969; Ojemann and Ward, 1971). The direct connection between the latter two structures and the cortical larynx area provides an anatomical basis for these observations.

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