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Projections from the Pontomesencephalic Tegmentum to the Cranial Nerve Nuclei in the Rat

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Sheila Keane

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Irena Grofova, PhD

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PROJECTIONS FROM THE PONTOMESENCEPHALIC TEGMENTUM TO THE CRANIAL NERVE NUCLEI IN THE RAT

By

Sheila Keane

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ABSTRACT

PROJECTIONS FROM THE PONTOMESENCEPHALIC TEGMENTUM TO THE CRANIAL NERVE NUCLEI IN THE RAT

By

Sheila Keane

The purpose of this study was to determine whether the nucleus tegmenti pedunculopontinus (PPN) links the output nuclei of the basal ganglia to the cranial motor nuclei. Unilateral injections of an anterograde tracer Phaseolus vulgaris-leucoagglutinin (PHA-L) were placed in the PPN and the distribution of labeled fibers in the pontomedullary cranial nerve nuclei was charted. Results of these experiments demonstrated distinct crossed and uncrossed projections from the PPN to the facial nucleus, but only modest bilateral projections to the hypoglossal, ambiguus, dorsal motor vagus, and solitary nuclei. Since the PPN-facial projection exhibited two different distribution patterns in the facial nucleus, additional experiments utilizing retrograde transport of lectin-conjugated horseradish peroxidase (HRP-WGA) from the lateral or medial portions of the facial nucleus were carried out. These latter experiments did not substantiate the existence of PPN-facial projection and demonstrated that facial afferents actually originated from several structures surrounding the PPN.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

Am	ambiguus nucleus
AP	area postrema
CG	central gray
Cnf	cuneiform nucleus
cp	cerebral peduncle
g7	genu facial nerve
GiA	gigantocellular reticular nucleus, pars alpha
IC	inferior colliculus
icp	inferior cerebellar peduncle
IO	inferior olive
IRt	intermediate reticular nucleus
KF	Kolliker-Fuse nucleus
LC	locus coeruleus
ll	lateral lemniscus
LPB	lateral parabrachial nucleus
LPGi	lateral paragigantocellular reticular nucleus
LRt	lateral reticular nucleus
LSO	lateral superior olive
LVe	lateral vestibular nucleus
Me5	mesencephalic trigeminal nucleus
me5	mesencephalic trigeminal tract
ml	medial lemniscus
Mo5	motor trigeminal nucleus
MPB	medial parabrachial nucleus
MVe	medial vestibular nucleus
PCRt	parvicellular reticular nucleus
PN	pontine nucleus
PPNc	pedunculopontine tegmental nucleus, pars compactus
PPNd	pedunculopontine tegmental nucleus, pars dissipatus
Pr5	principal sensory trigeminal nucleus
py	pyramidal tract
Rmes	mesencephalic reticular nucleus
RN	red nucleus
RPc	reticularis pontis caudalis nucleus
RPo	reticularis pontis oralis nucleus
RR	retrorubral nucleus
RRF	retrorubral field
rs	rubrospinal tract
SC	superior colliculus
scp	superior cerebellar peduncle
SNc	substantia nigra, pars compacta
SNr	substantia nigra, pars reticulata
SO	superior olive
Sol	nucleus of the solitary tract

ABBREVIATIONS (continued)

sol	solitary tract
sp5	spinal trigeminal tract
Sp5o	spinal trigeminal nucleus, pars oralis
SPTg	subpeduncular tegmental nucleus
SpVe	spinal vestibular nucleus
Tz	nucleus of the trapezoid body
tz	trapezoid body
VLL	ventral nucleus of the lateral lemniscus
vsc	ventral spinocerebellar tract
xscp	decussation of superior cerebellar peduncle
3	oculomotor nucleus
4	trochlear nucleus
6	abducens nucleus
5n	trigeminal nerve
7	facial nucleus
7n	facial nerve
10	dorsal motor nucleus of vagus
12	hypoglossal nucleus

INTRODUCTION

The nucleus tegmenti pedunculopontinus (PPN) was first described in the human caudal mesencephalic tegmentum as being "bounded medially by the superior cerebellar peduncle (scp), laterally by fibers of the medial lemniscus, and dorsally by the nucleus cuneiformis and subcuneiformis (Olszewski & Baxter '54). These authors further identified two subdivisions of the nucleus on the basis of cellular density. The smaller pars compacta "occupies the dorsolateral portion of the caudal half of the nucleus" and the "remainder of the nucleus constitutes the pars dissipata". In subprimate species, the nucleus is less clearly defined. Delineation of the PPN and its subdivisions has been variously made on the basis of cytoarchitectural features (Spann & Grofova '89), cytochemistry (Rye et.al '88, Woolf & Butcher '86), and basal ganglia input (Moon-Edley & Graybiel '83, Nauta & Mehler '66). The functions and connections of the PPN have not been fully established.

The PPN has widespread connections with the basal ganglia, thalamus, and limbic structures and has been implicated in a wide variety of functions including motor control, sleep-wake cycles, respiration, locomotion, chewing, and other rhythmic behaviors (Garcia-Rill & Skinner '88) and sensory modulation (Hylden et.al. '85, Katayama et.al. '84, Basbaum & Fields '80, Carstens et.al. '80).

The role of the PPN in the control of movement is well supported by both anatomical and physiological data. Convincing evidence exists that the PPN receives substantial input from several nuclei of the basal ganglia (Grofova et.al. in press, Spann & Grofova '89, Jackson & Crossman '83, Gerfen et.al. '82, Beckstead et.al. '79, Granata & Kitai '89, Carter & Fibiger '78, Nakamura et.al. '89, Noda & Oka '86, Garcia-Rill et.al. '83, Moon-Edley & Graybiel '83, Larsen & McBride '79, Nauta & Cole '78, Parent & DeBellefeuille '82, Beckstead & Frankfurter '82, Kim et.al. '76) and ascending efferents of the PPN return these basal ganglia projections (Woolf & Butcher '86, Jackson & Crossman '83, Saper & Loewy '82, Gerfen et.al. '82, VanDerKooy & Carter '81, Garcia-Rill et.al. '83, Moon-Edley & Graybiel '83, Gonya-Magee & Anderson '83, DeVito & Anderson '82). In addition, physiological experiments have identified a "midbrain locomotor region" in the decorticate cat (Mori et.al. '80) and rat (Garcia-Rill '87) which is located in the pedunculopontine region and includes the PPN (Garcia-Rill '86). Furthermore, lesions of the PPN in the rat have been associated with impaired motor function (Kilpatrick & Starr '81), and clinical studies have shown an association between PPN cell loss in humans and movement disorders related to progressive supranuclear palsy (Zweig et.al. '85, '87) and Parkinson's disease (Zweig, et.al. '89, Jellinger '88).

The pathways by which the PPN affects motor behavior are currently under investigation. Descending PPN efferents

include projections to the ventromedial pontomedullary reticular formation (Grofova et.al. in press, Nakamura et.al '89, Mitani et.al. '88, Rye et.al. '88, Moon-Edley & Graybiel '83, Jackson & Crossman '83). This reticular region contains neurons projecting to the ventral horn and cranial motor nuclei (Vertes et.al. '86, Jones & Yang '85, Zemlan et.al. '84, Travers & Norgren '83, Holstege & Kuypers '82, Martin et.al. '81, Peterson '80). In addition, sparse projections from PPN to the spinal cord have been reported in the rat (Spann & Grofova '89, Rye et.al. '88, Goldsmith & VanDerKooy '88). Considering its many connections with the nuclei of the basal ganglia, the PPN is well situated to function as a relay nucleus for descending basal ganglia influence on lower motor structures.

While PPN efferents to the reticular formation and spinal cord have been documented by several authors, investigations of PPN projections to the cranial motor nuclei are lacking. The purpose of the present study is to determine the projections from PPN to the pontomedullary cranial motor nuclei.

MATERIAL AND METHODS

A total of 15 male Sprague-Dawley albino rats weighing 300-350 g were utilized for this study. Eight animals received unilateral injections of Phaseolus vulgaris-leucoagglutinin (PHA-L) in the nucleus tegmenti pedunculopontinus (PPN), while seven received unilateral injections of wheat-germ-agglutinin conjugated horseradish peroxidase (HRP-WGA) in the facial nucleus. Both surgeries and perfusion were performed under deep anesthesia (sodium pentobarbital, 50-100 mg/kg, i.p.), and atropine sulfate solution (0.7 mg/kg) was administered i.m. prior to the surgery in order to prevent brain edema. Injections of both tracers were made iontophoretically using glass micropipettes with an inside tip diameter of 15-35 μm, and a positive 7s pulsed 5 μA current. The stereotaxic coordinates were derived from the atlas of Paxinos and Watson ('86).

PHA-L Experiments

Micropipettes filled with a 2.5% solution of PHA-L (Vector Labs) in 10mM Tris buffer (pH 8.0) were inserted vertically through the ipsilateral hemisphere and tectum of the midbrain. Single iontophoretic depositions of PHA-L were made for 30-40 minutes. Following a survival period of 10 to 14 days, deeply anesthetized animals were perfused through the heart with a sodium phosphate buffered saline solution

followed by a fixative consisting of 4% paraformaldehyde and 0.2% glutaraldehyde in 0.15M sodium phosphate buffer. The brains were immediately removed and stored overnight at 4°C in fixative. The following day, the brains were divided into a caudal block containing the caudal pons and medulla, and a left and right rostral block including the forebrain, midbrain, and rostral pons. Serial sectioning was done at 30 μm on a vibratome in the coronal (caudal block) or sagittal (rostral block) plane. Sections were collected in Tris buffered saline and processed for PHA-L immunohistochemistry using a biotin-avidin (Vector Labs) protocol by Gerfen & Sawchenko ('84). Immuno-reacted sections were mounted onto gelatin-chrom-alum-coated slides, air-dried, dehydrated, and lightly stained with cresyl violet. The sections were examined on a Leitz Orthoplan microscope, using bright-field illumination for the localization of PHA-L injections and the presence of labeled nerve fibers and terminal fields. The localization of the PHA-L deposit in the PPN was charted on a standard map of sagittal sections through the pontomesencephalic region containing the lateral and medial halves of the PPN. The distribution of the labeled fibers and plexuses in the cranial nerve nuclei was documented on projection drawings and photomicrographs of selected sections.

HRP-WGA Experiments

Single unilateral injections were made in the medial or lateral portions of the facial nucleus using a 2% HRP-WGA solution in Tris buffer delivered iontophoretically for 15 to 25 minutes according to Graybiel & Devor ('74). In order to minimize leakage of HRP-WGA along the needle track, the micropipette remained in situ for 10 minutes after the injection, and reversed polarity was applied during its withdrawal.

After a 24-48 hour survival period, deeply anesthetized animals were perfused intracardially with a fixative consisting of 1% paraformaldehyde and 1.25% glutaraldehyde in 0.15M sodium phosphate buffer. The brains were blocked into right and left halves, and serial sections were cut sagittally at 30-50 μm on a freezing microtome or vibratome. HRP-WGA histochemistry using the chromogen tetramethyl benzidine (TMB) was performed according to Mesulam ('82) . Some of the sections were additionally stabilized with ammonium molybdate (Olucha et.al. '85). Reacted sections were mounted on gelatin-chrom-alum-coated slides and lightly counterstained with neutral red.

Sections were analyzed in bright-field illumination for the presence of retrogradely labeled cells in the PPN and surrounding regions. The distribution of labeled cells was documented on projection drawings in representative cases using major blood vessels and fiber tracts as landmarks. Cell

counts for all retrogradely labeled mesopontine nuclei were taken from alternating sections, and the numbers of labeled cells contained in a specific nucleus was pooled from all inspected sections.

The borders of the PPN and its subnuclei were identified according to previously established criteria (Spann & Grofova '89). For clarity, the delineation of all other relevant structures was taken from the atlas of Paxinos & Watson ('86).

RESULTS

Before describing the experimental results, the normal morphology of the pedunculopontine region will be considered briefly. The PPN represents a portion of a continuous cell column surrounding the ascending limb of the superior cerebellar peduncle (scp) at the pontomesencephalic junction. It consists of two subdivisions: 1) the pars compacta (PPNc) composed primarily of larger cholinergic neurons; and 2) the pars dissipata (PPNd) containing a considerable portion of smaller non-cholinergic cells. While the boundaries of the PPN and its subdivisions are well-defined in primates, the outlines of the PPN in carnivores and rodents are less clear. Consequently, there is little consistency in the literature regarding the delineation of this nucleus or its subdivisions in the rat brain. In the present report, we adhere to the definition of PPN based on cytoarchitectural features described in a previous study (Spann & Grofova '89).

The rat PPN is located medial to the nuclei of the lateral lemniscus and lateral to the decussation of the scp. It is caudally contiguous with the lateral and medial parabrachial nuclei (LPB and MPB) and is rostrally adjacent to the retrorubral field (RRF) and retrorubral nucleus (RR) as defined by Paxinos & Watson (1986). The PPN borders ventrally on the nucleus reticularis pontis oralis (RPo), and dorsally on the cuneiform (Cnf) and mesencephalic reticular

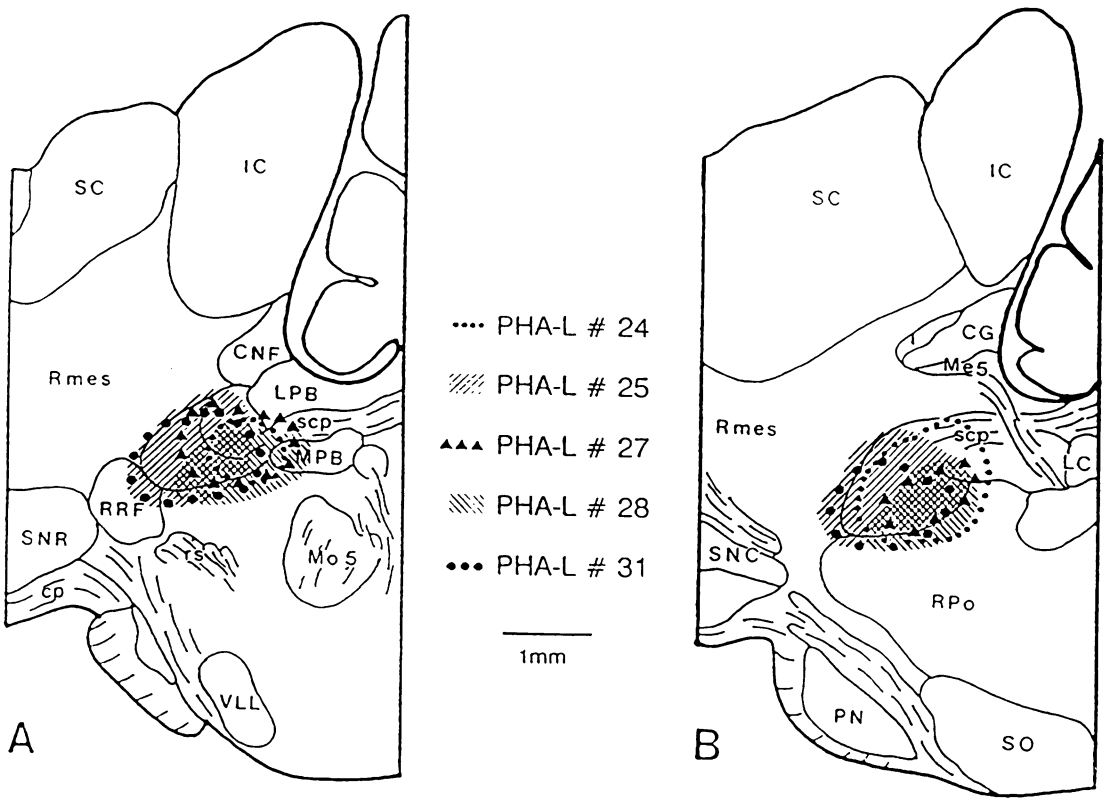


Figure 1: PHA-L Injection Sites

Schematic representation of PHA-L injection sites involving the lateral (A) and medial (B) halves of the PPN in cases in which labeled fibers could be traced to the facial nucleus and to the medullary cranial nerve nuclei

(Rmes) nuclei. While both divisions of PPN can be distinguished in the rat, the PPNd comprises the bulk of the nucleus. The PPNd is particularly prominent medially and appears to receive a substantial input from the substantia nigra pars reticulata (Spann & Grofova '88).

PHA-L Experiments

PHA-L injections were directed toward the PPN region receiving afferents from the substantia nigra (i.e. the medial two thirds of the PPNd). Out of eight cases, five showed excellent anterograde labeling as well as precise localization of the injection in the PPNd. These five cases represent the core material for the present report. The remaining three cases yielded less intense labeling and provided complementary data.

While centered in the medial portions of PPNd, all PHA-L injections involved the entire mediolateral extent of the PPN (Fig. 1). Two zones of different labeling intensity were observed at the injection sites; a central zone in which the DAB reaction product obscured the cytoarchitecture, and a peripheral zone in which single neurons exhibiting Golgi-like labeling could be discerned. In all animals, a variable number of labeled neurons were observed in the surrounding nuclei. However, fiber tracts passing through the injection site were always free of label (Fig.2). The absence of labeling was particularly striking with regard to the scp

Figure 2: Bright-field Photomicrographs of PHA-L Deposits in the PPN.

A-C: Illustrate the extent of PHA-L injection in case PHA-L #25. The injection extended somewhat beyond the lateralmost border of PPN (C) and the tracer was taken up by a few cells (arrowheads) in the RR. More medially, single labeled cells can be seen in the RRF and in the rostral MPB (arrowheads in B). Unstained fibers of the scp traverse the medial (A) and middle (B) regions of the PPN (arrows).

D: The center of PHA-L injection in case PHA-L #28. A few Golgi-like labeled cells are present in the MPB (arrowheads).
Scale bar: 0.5mm

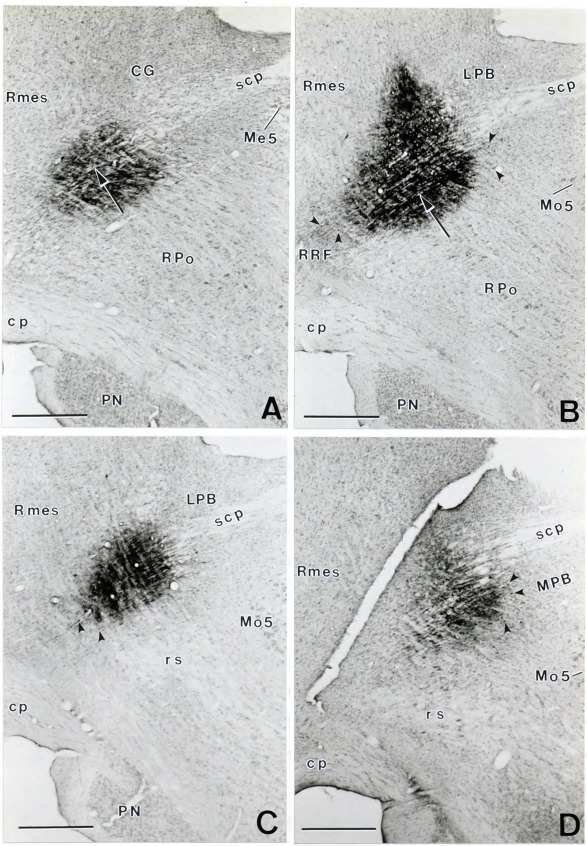

CG
scp
Rmes
Me5
RPo
cp
PN
A
Rmes
LPB
scp
Mo5
RRF
RPo
cp
PN
B
Rmes
LPB
scp
Mo5
rs
cp
PN
C
scp
Rmes
MPB
Mo5
rs
cp
D

Figure 2

which was inevitably included in the central zone of all PHA-L injections.

In case PHA-L #25, there was a dense deposit of PHA-L throughout the entire extent of the PPN. Some cells in the Cnf were also labeled along the course of the needle track. In addition, a few PHA-L labeled cells were observed rostrally in the RR and RRF, ventrally in the RPo, caudally in the MPB, and laterally in the nuclei of the lateral lemniscus (Fig. 2). The inclusion of rostrally adjacent structures in the peripheral zone of PHA-L uptake was also observed in case PHA-L #31, where the rostroventral half of PPN was labeled in addition to individual neurons in the surrounding RR, RRF, and RPo. In cases PHA-L #28, PHA-L #27, and PHA-L #24, injections were also centered in PPN but extended somewhat caudally to include neighboring regions of the MPB and LPB. The PHA-L injection in case PHA-L #28 was the most laterally placed of these, involving the caudoventral PPN and labeling several cells caudal to PPN in the MPB and ventrally in the RPo (Fig. 2).

Projections to the Brainstem

The bulk of PPN descending projections were distributed within the reticular nuclei of the brainstem. Labeled fibers were seen descending through the pontine reticular nuclei to the ventromedial portions of the nucleus gigantocellularis (GiA and GiV). Although many fibers appeared to cross the

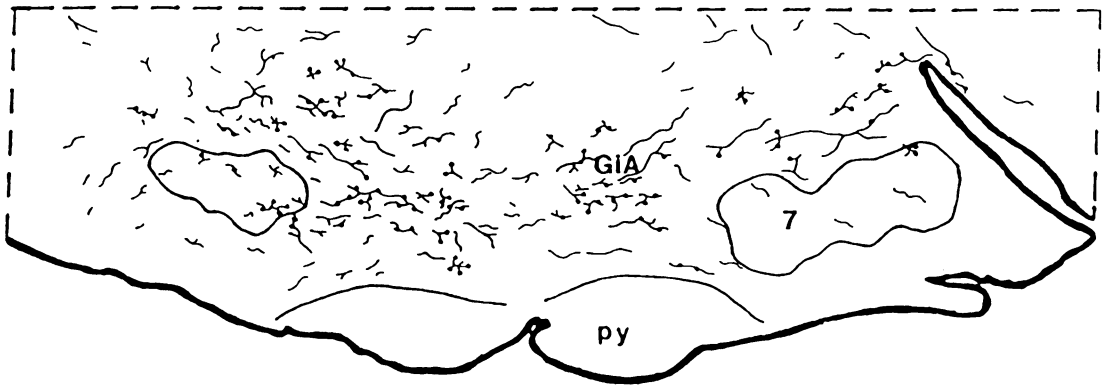
midline in the caudal pons and rostral medulla, terminal arborizations were somewhat more numerous ipsilaterally. In the pons, numerous varicose branches of the labeled fibers were seen to terminate around large reticular neurons, especially in the reticularis pontis caudalis (RPc). Projections to the medulla and spinal cord were relatively sparse. The course and distribution of these projections have been described and illustrated elsewhere (Grofova et.al. in press).

In addition to the fibers distributing to the reticular formation, PHA-L labeled fibers were also seen in several cranial nerve nuclei in the pons and medulla. No labeled fibers were found in the motor trigeminal (Mo5) nucleus. However, two distinct distribution patterns were observed in the facial nucleus. One pattern, present in all cases, consisted of diffuse labeling in the ipsilateral facial nucleus, while two cases (PHA-L #25 and PHA-L #31) additionally demonstrated a dense contralateral projection to the rostromedial two thirds of the facial nucleus. Projections to the cranial nerve nuclei of the lower brainstem were relatively sparse and were bilaterally distributed.

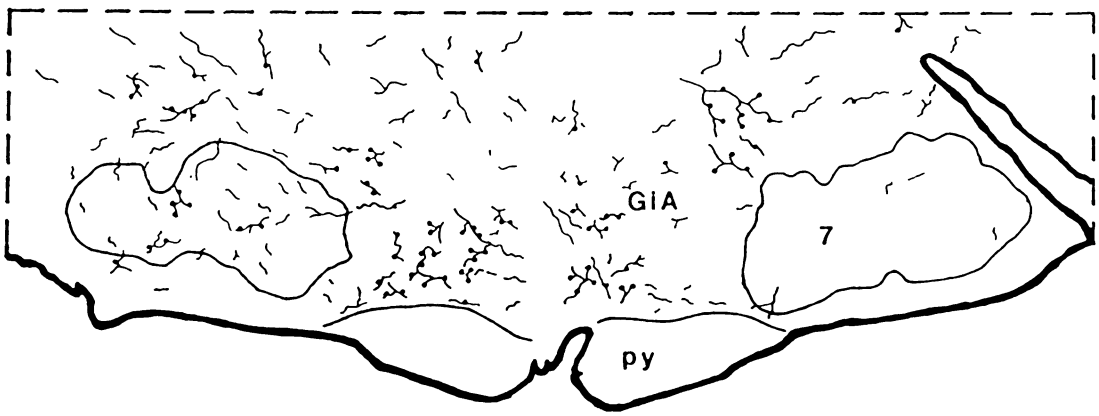
Figure 3: Distribution of Labeled Fibers in the Facial Nucleus in Case PHA-L #28

Projection drawings of coronal sections through three pontomedullary levels showing the distribution of labeled fibers in the facial nucleus and ventral reticular nuclei in experiment PHA-L #28. Labeled varicose fibers are present throughout the ipsilateral facial nucleus with greater concentration caudally.

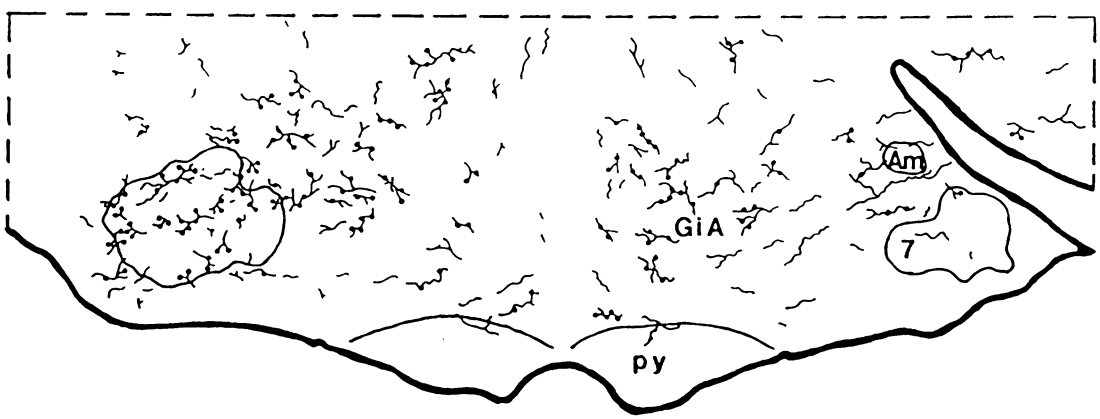
PHA-L #28



Rostral



Middle



Caudal

Ipsilateral

Contralateral

1mm

Figure 3

Projections to the Facial Nucleus

Results presented from cases PHA-L #28 and PHA-L #25 are representative of the two patterns of distribution found in the facial nucleus. In case PHA-L #28, labeled varicose fibers were dispersed diffusely throughout the ipsilateral facial nucleus with somewhat greater concentration in its lateral half (Fig. 3). Thick labeled fibers typically divided into smaller branches exhibiting multiple terminal and preterminal varicosities both in the neuropil and near the somata of lateral facial motoneurons (Fig. 4 A & B).

In case PHA-L #25, in addition to the diffuse ipsilateral facial projection which was present in all cases, a dense plexus of anterogradely labeled fibers was observed in the rostromedial two thirds of the contralateral facial nucleus (Fig. 5). Numerous varicose arborizations formed a dense terminal plexus surrounding the medial groups of facial motoneurons (Fig. 4 C & D). This contralateral projection to the medial facial nucleus was also seen in case PHA-L #31, but was not present in other cases.

Projections to Medullary Cranial Nerve Nuclei

All cases demonstrated a sparse bilateral distribution to the solitary (Sol), dorsal motor vagus (10), and hypoglossal (12) nuclei. In addition, a few thin varicose fibers in the proximity of the large motoneurons of the nucleus

Figure 4: Bright-field Photomicrographs Illustrating the Two Distribution Patterns of PHA-L Labeled Fibers in the Facial Nucleus.

A&B: Diffuse ipsilateral projection to the lateral half of the facial nucleus in case PHA-L #28. Figure A illustrates a modest number of labeled fibers (arrows) within the dorsolateral group of facial motor neurons. These fibers are shown at higher magnification in Figure B. Arrows indicate a thick fiber of an even diameter dividing in several thin branches exhibiting multiple varicosities.

C&D: Contralateral projection to the medial groups of facial motoneurons in case PHA-L #25. A dense terminal plexus of labeled fibers within the ventromedial group of facial motoneurons and LPGi is shown in Figure C. Figure D represents a higher magnification of the region outlined by a rectangle in Figure C, and illustrates numerous preterminal and terminal varicosities surrounding the cell bodies of the medial facial motoneurons (arrowheads) as well as distributing in the neuropil (arrow).
Scale bar: 0.1mm

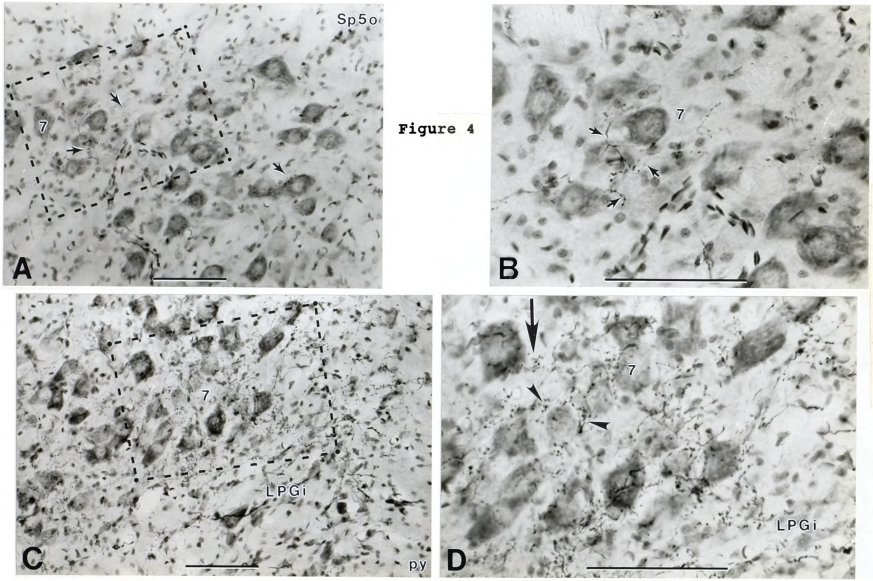


Figure 4

Figure 5: Distribution of Labeled Fibers in the Facial Nucleus in Case PHA-L #25

Projection drawings of coronal sections through three pontomedullary levels illustrating a dense plexus of labeled varicose fibers in the rostral two thirds of the medial portion of the contralateral facial nucleus in experiment PHA-L #25.

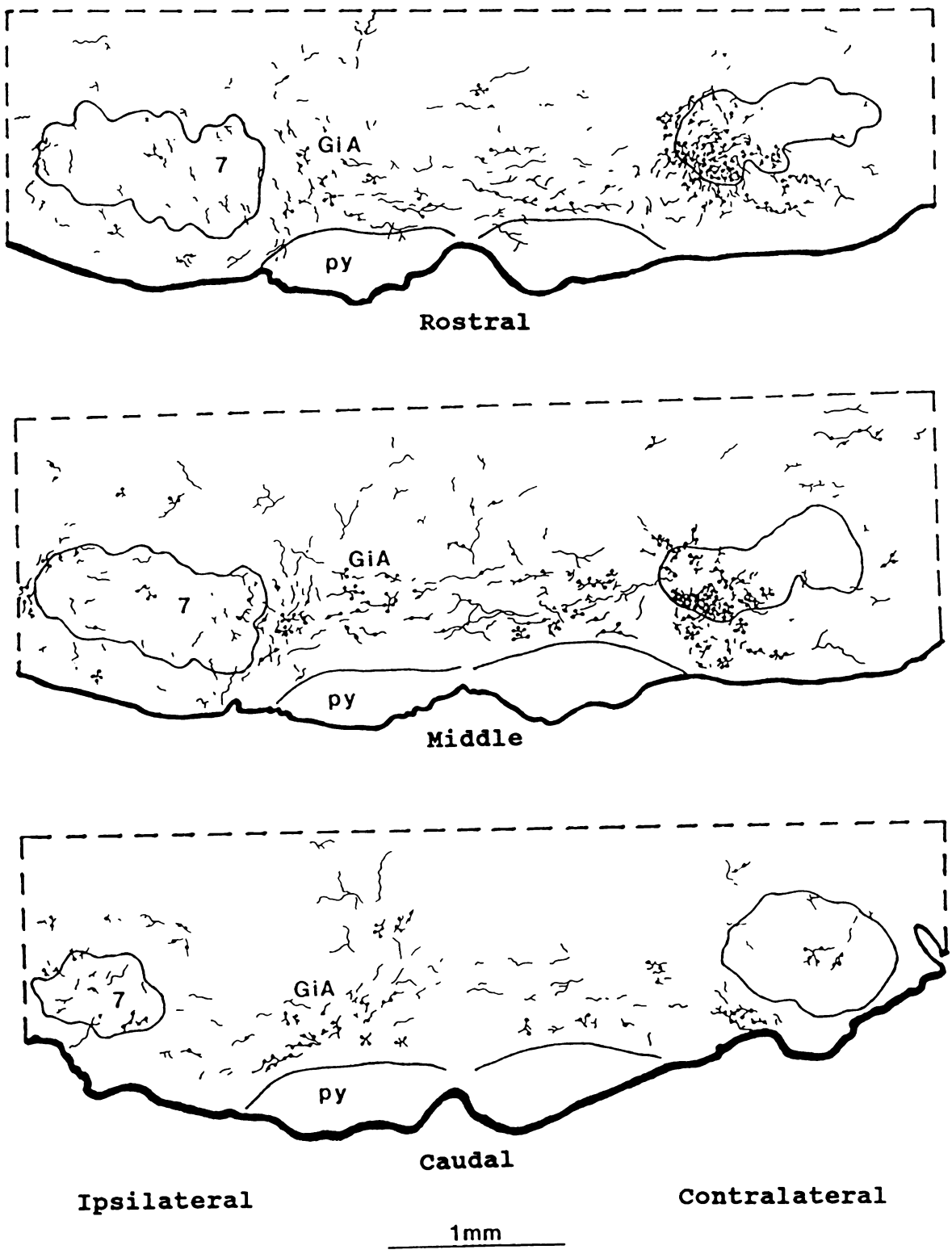

PHA-L #25
7
GiA
py
Rostral
7
GiA
py
Middle
7
GiA
py
Caudal
Ipsilateral
Contralateral
1mm

Figure 5

nucleus ambiguus (Am) were occasionally seen bilaterally (Fig. 6A).

The distribution of PHA-L labeled fibers to the caudal medullary cranial nerve nuclei are illustrated in Figure 7. Varicose fibers descended bilaterally in the hypoglossal nuclei near midline, subsequently turning and passing to the reticular formation ventrolateral to 12. Similarly, thin varicose fibers were seen coursing from midline along the borders of Sol, branching and terminating in the lateral portions of Sol and 10. While present bilaterally, varicose arborizations were somewhat more numerous ipsilaterally in the lateral regions of Sol and 10, and in the reticular formation ventral to this region (Fig. 6).

HRP EXPERIMENTS

Results of PHA-L experiments suggested a topographical organization of PPN projections to the facial nucleus, with rostral portions of PPN projecting to the contralateral groups of medial facial neurons, and caudal portions of PPN projecting ipsilaterally primarily to the lateral half of the facial nucleus. To verify this hypothesis, experiments utilizing the retrograde transport of HRP-WGA from medial (N=4) or lateral (N=3) portions of the facial nucleus were carried out.

Figure 6: Photomicrographs Showing PHA-L Labeled Fibers in the Medullary Cranial Nerve Nuclei.

A: Arrows indicate labeled fibers in the ipsilateral Am in case PHA-L #24.

B: Labeled fibers (arrows) in the ipsilateral 12 in case PHA-L #25.

C&D: A discrete plexus of fine varicose fibers in the lateral portion of the Sol ipsilateral to the PHA-L injection in case PHA-L #25.
Scale bar: 0.1mm

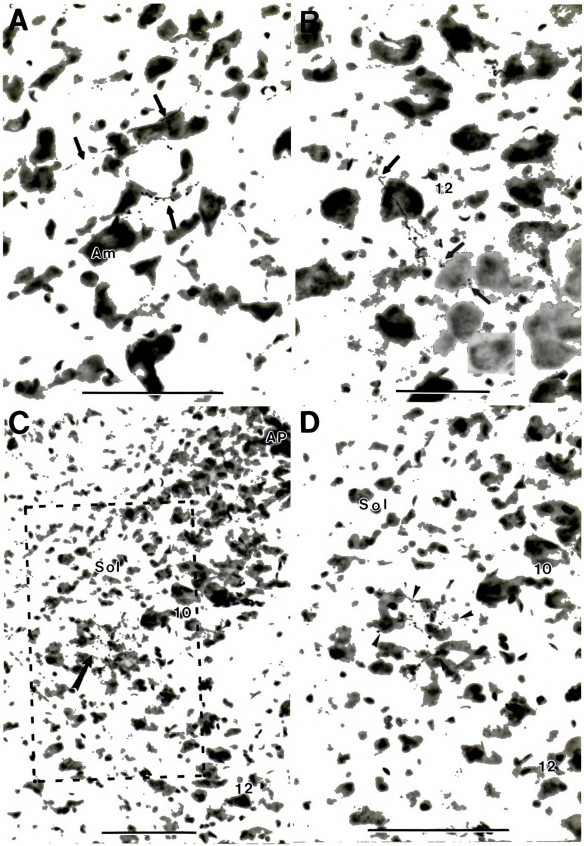


Figure 6

Figure 7: Distribution of Labeled Fibers in the Medullary Cranial Nerve Nuclei

Projection drawings of coronal sections through the dorsal portion of the lower medulla showing a relatively modest number of varicose fibers in the 12, 10, and Sol in experiment PHA-L #25.

PHA-L #25

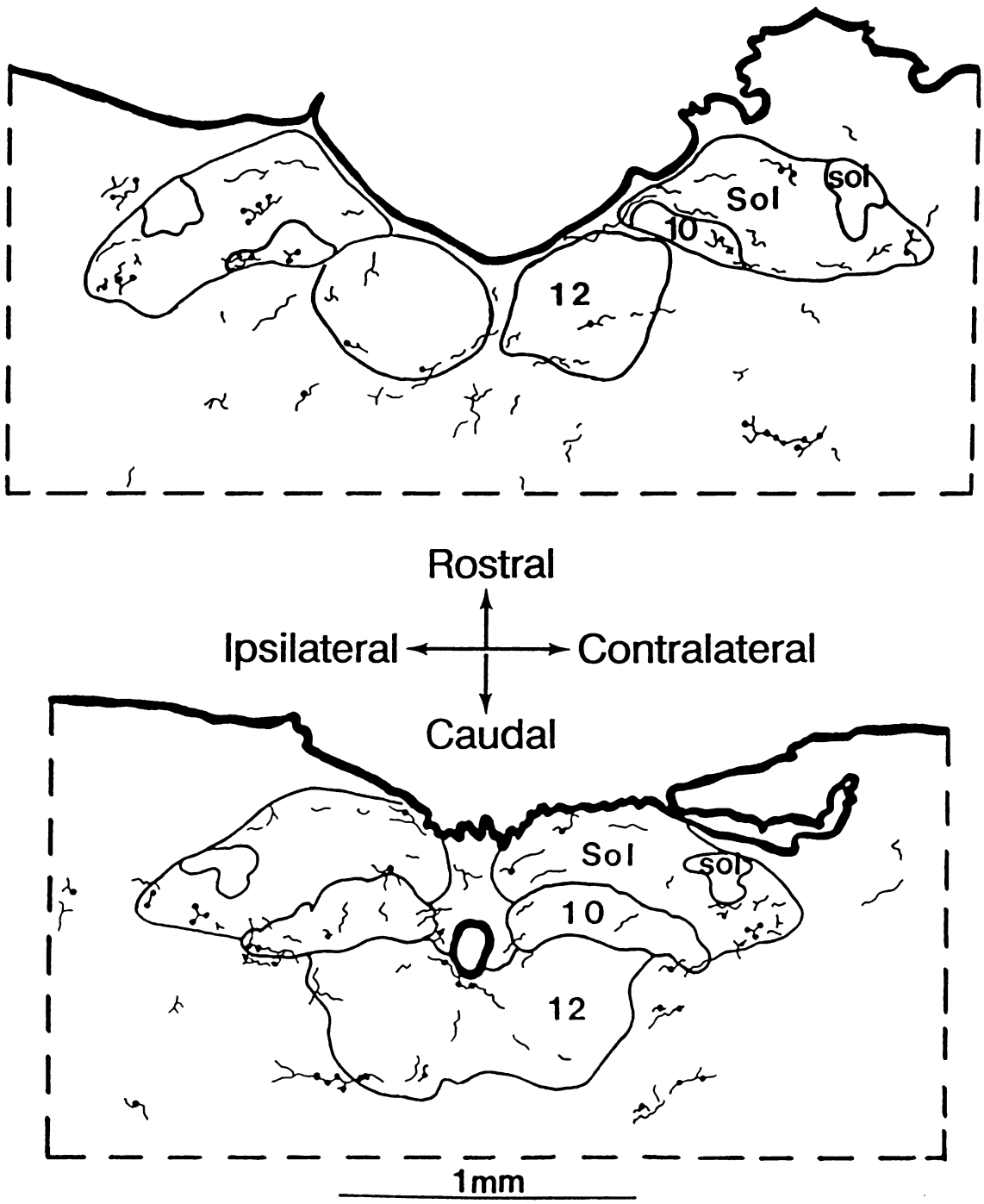


Figure 7

Lateral Facial Injections

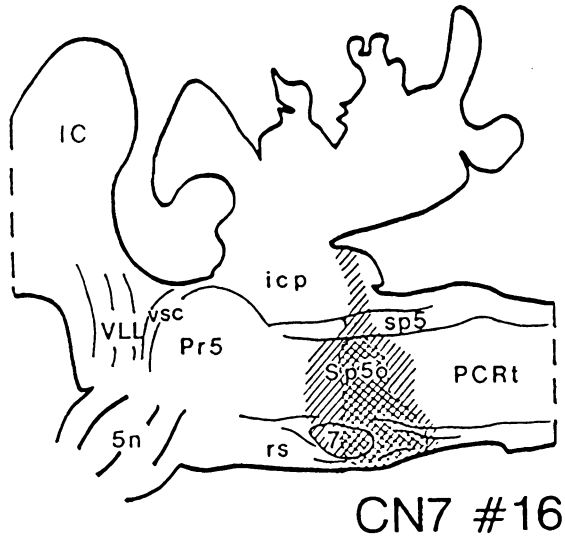
The HRP-WGA injection sites involving the lateral portions of the facial nucleus are shown in Figure 8. Dense deposits of HRP-WGA were observed in the lateral third to half of the facial nucleus in all three lateral injections. Despite all precautionary measures, HRP-WGA reaction product was also consistently present along the needle track and in portions of surrounding structures.

In case CN7 #17, the dense deposit of HRP-WGA was nearly completely confined to the lateral two thirds of the facial nucleus in its middle antero-posterior extent. A "halo" of diffused reaction product extended ventrally into the trapezoid (tz) and rubrospinal (rs) fiber tracts, and into the reticular formation caudolateral to the facial nucleus (Fig. 9A).

No retrogradely labeled cells were observed in the PPN. Labeled neurons were identified primarily in the ipsilateral principal trigeminal (Pr5), medial parabrachial (MPB), and Kolliker-Fuse (KF) nuclei (Fig. 10). Retrogradely labeled cells of the MPB were concentrated rostrally, near the caudal border of the PPN (Fig. 11 C & D). A substantial number of labeled cells in the ipsilateral Pr5 and KF were also present at levels lateral to the PPN (Fig. 11 A & B). Fewer neurons were labeled in the ipsilateral lateral parabrachial and reticularis pontis oralis nuclei. Several labeled neurons were observed in the contralateral red nucleus (RN). In

Figure 8: Lateral Facial HRP-WGA Injection Sites

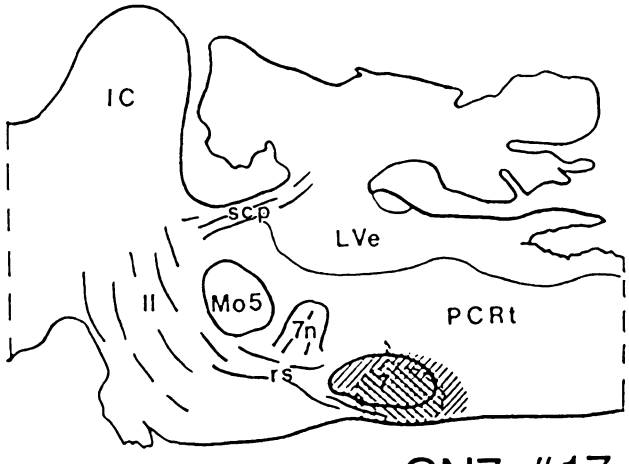
Projection drawings of sagittal sections through the center of HRP-WGA injections involving the lateral portion of the facial nucleus in three cases described in the text. The position of dense reaction product around the pipette is indicated by cross-hatching. Hatching indicates a surrounding area of lighter diffusion which may be somewhat overestimated because of use of the sensitive chromogen, TMB.



CN7 #16

CN7 #14

1mm



CN7 #17

Figure 8

Figure 9: Photomicrographs Showing Center of Injection Sites in Cases CN7 #17 and CN7 #13

Bright-field photomicrographs illustrate the center of HRP-WGA injection sites in two representative cases CN7 #17 (A) and CN7 #13 (B). The distributions of retrogradely labeled cells in the pontomesencephalic tegmentum of these two cases are shown in Figures 10 and 14 respectively.
Scale bar: 0.5mm

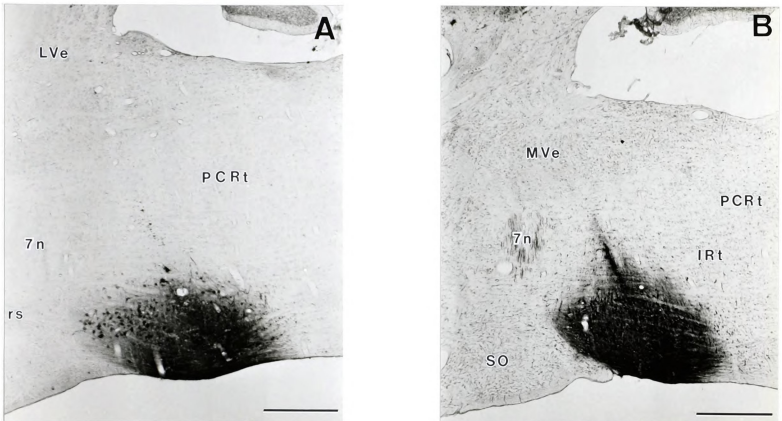


Figure 9

addition, a few scattered retrogradely labeled cells were found in the ipsilateral nucleus reticularis pontis caudalis (RPc) and contralaterally in the deep layers of the superior colliculus (SC). Results are summarized in Table 1.

Other injections of HRP-WGA in the lateral half of the facial nucleus exhibited larger diffusion of the reaction product into the surrounding tissue. In animal CN7 #16, the injection was centered at the caudolateral edge of the facial nucleus and exhibited diffuse HRP-WGA reaction product with Golgi-like labeling of neurons in the caudolateral two thirds of the facial nucleus as well as the parvicellular reticular nucleus (PCRt) dorsolateral to the facial nucleus. In case CN7 #14, the injection was centered caudal to the facial nucleus and included only the caudal half of the lateral portions of the facial nucleus. HRP-WGA reaction product in animal CN7 #14 was seen as far caudally as the rostral Am and extended dorsally into the reticular formation as well.

In these additional cases, the PPN exhibited only a few retrogradely labeled neurons. The larger and more caudally placed injection in case CN7 #14 resulted in ten labeled PPN neurons ipsilaterally, while five PPN neurons were labeled contralaterally. Case CN7 #16 demonstrated only one labeled cell in the ipsilateral PPN. Confirming the results of case CN7 #17, other lateral facial experiments also resulted in heavy HRP labeling ipsilaterally in several nuclei caudal to the PPN (including the MPB, KF, and Pr5) while the core of the

Table 1: Retrogradely Labeled Cells Following Lateral Facial HRP-WGA Injections

Case CN7#	PPN	Pr5	KF	MPB	LPB	RPo	RN	Other
#17	0 (0)	139 (2)	55 (0)	118 (3)	29 (0)	18 (0)	0 (11)	I: 5 RPc C: 4SC, 1RR, 1CG, 1Rmes
#16	1 (0)	35 (0)	4 (0)	8 (1)	0 (0)	4 (0)	0 (11)	I: 0 C: 1 SuVe
#14	10 (5)	307 (9)	16 (14)	182 (14)	92 (0)	75 (26)	2 (212)	I: 8SubLC, 1Cnf 4SuVe, 2Rmes, 1 Mo5, 1 SNR C: 23SubLC, 10SuVe, 16SC 1 Rmes, 1 CG

Table 1: Retrogradely labeled cells in the pontomesencephalic nuclei following HRP-WGA injections in the lateral portions of the facial nucleus were counted from alternating 50 micron thick sections. (Cell counts from the contralateral nuclei are in parentheses.) Retrograde labeling of the PPN is insubstantial. However, neurons are labeled ipsilaterally in several nuclei located near PPN including the medial parabrachial (MPB), lateral parabrachial (LPB), Kolliker-Fuse (KF), and principal trigeminal (Pr5) nuclei.

Figure 10: Distribution of HRP Labeled Cells in Case CN7 #17

Projection drawing of lateromedially arranged sagittal sections through the pontomesencephalic region showing the distribution of HRP labeled cells in the contralateral (A-C) and ipsilateral (D-F) nuclei surrounding the PPN in case CN7 #17. Sections illustrated in A and D are lateral to the PPN. Each dot represents one labeled cell.

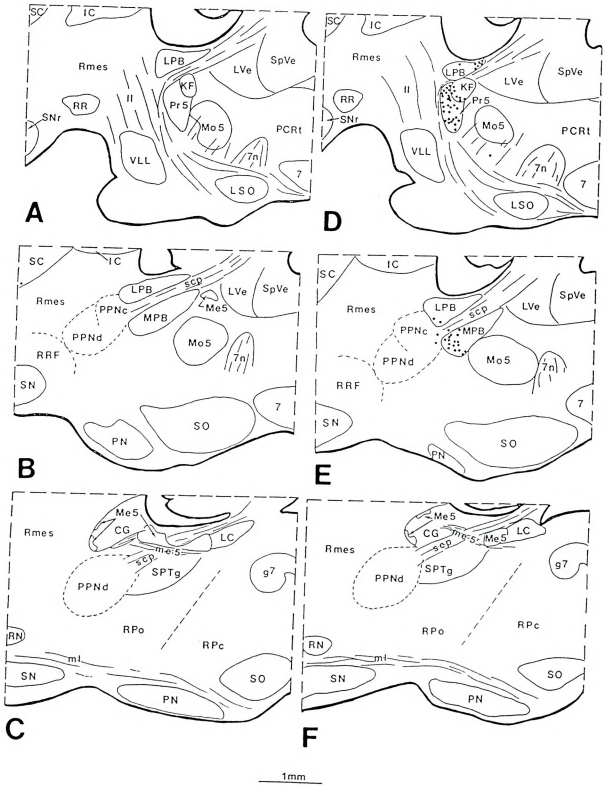

SC
IC
Rmes
LPB
LVe
SpVe
KF
II
Pr5
RR
SNr
Mo5
PCRt
VLL
7n
7
LSO
A
D
scp
MPB
PPNc
PPNd
RRF
SN
SO
PN
B
E
Me5
CG
LC
mes
SPTg
g7
RPo
RPc
RN
ml
C
F
1mm

Figure 10

Fig. 11: Photomicrographs of HRP Labeled Cells in the Ipsilateral Parabrachial Region in Case CN7 #17.

A&B: Show the position (A) and morphology (B) of retrogradely labeled neurons in the pontomesencephalic tegmentum lateral to the PPN. Labeled neurons in the ipsilateral KF (open arrows in B) exhibit round somata located ventral to the superior cerebellar peduncle while the smaller fusiform cells of the Pr5 (small arrows in B) lie more ventrally, immediately caudal to the lateral lemniscus. In addition, several larger multipolar neurons within the Pr5 (large arrowheads) also contain HRP granules.

C&D: Show HRP labeled cells in a more medial region of the pontomesencephalic tegmentum. Most of these cells lie well within the confines of the MPB (small arrows in D). Two neurons in a border zone between the MPB and PPN are indicated by open arrows. A few labeled cells are intermingled with the fibers of the scp (large arrows). Scale bar: 0.1mm

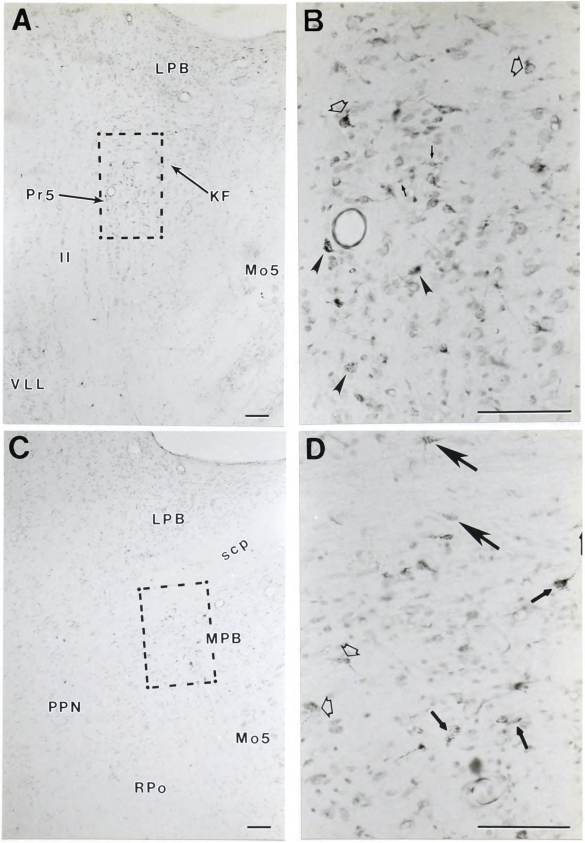


Figure 11

PPN nucleus was remarkably free of labeled cells.

Medial Facial Injections

In four animals, HRP-WGA injections were centered in the medial half of the facial nucleus (Fig. 12). In case CN7 #13, dense HRP-WGA reaction product was almost totally confined to the medial half of the facial nucleus. However, slight encroachment of the underlying fibers of the trapezoid body and faint HRP-WGA reaction product was also evident in a small region of the GiA medial to the facial nucleus (Fig. 9B). Results are presented in Table 2.

Similar to the observations following HRP-WGA injections in the lateral portions of the facial nucleus, there were no labeled cells well within the confines of the PPN. In case CN7 #13, only one PPN cell, located at the rostralmost boundary of the contralateral PPNd, was labeled (Fig. 13). Immediately rostral to the PPN, the contralateral RR was heavily labeled. This projection was exclusively contralateral. Labeled RR cells were located caudally, abutting the rostral pole of PPN and often occupying the border region between these two nuclei. In addition, a more moderate number of labeled neurons were observed in the ipsilateral MPB in case CN7 #13 (Fig. 14). Similar to the pattern observed following lateral HRP-WGA injections, retrogradely labeled MPB cells were found primarily along the rostral and dorsal borders of MPB in a zone bordering

Table 2: Retrogradely Labeled Cells Following Medial Facial HRP-WGA Injections

Case CN7 #	RR	PPN	Pr5	MPB	KF	LPB	Other
#13	0 (191)	0 (1)	11 (2)	38 (0)	9 (4)	3 (0)	I: 17 RPo, 10 CG, 7 Rmes, 2 RN C: 47 Rmes, 12 RRF, 3 RN, 2 RPo
#11	0 (21)	1 (0)	10 (0)	32 (0)	1 (0)	4 (0)	I: 8 Me5, 7 SN, 5 RPo, 5 SuVe C: 1 CG
#9	0 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	none
#4	0 (11)	0 (0)	0 (0)	2 (0)	0 (0)	0 (0)	I: 1 CG C: 1 RN, 1 CG

Table 2: Retrogradely labeled cells in the pontomesencephalic nuclei following HRP-WGA injections in the medial portions of the facial nucleus were counted from alternating 50 micron thick sections. (Cell counts from the contralateral nuclei are in parentheses.) Note the large numbers of labeled cells in the contralateral retrorubral nucleus (RR) as well as cells labeled ipsilaterally in the principal trigeminal (Pr5), medial parabrachial (MPB), Kolliker-Fuse (KF), and lateral parabrachial (LPB) nuclei.

Figure 12: Medial Facial HRP-WGA Injection Sites

Projection drawing of sagittal sections through the center of HRP-WGA injections involving the medial half of the facial nucleus in four representative cases described in the results. See legend to Figure 8 for further explanation.

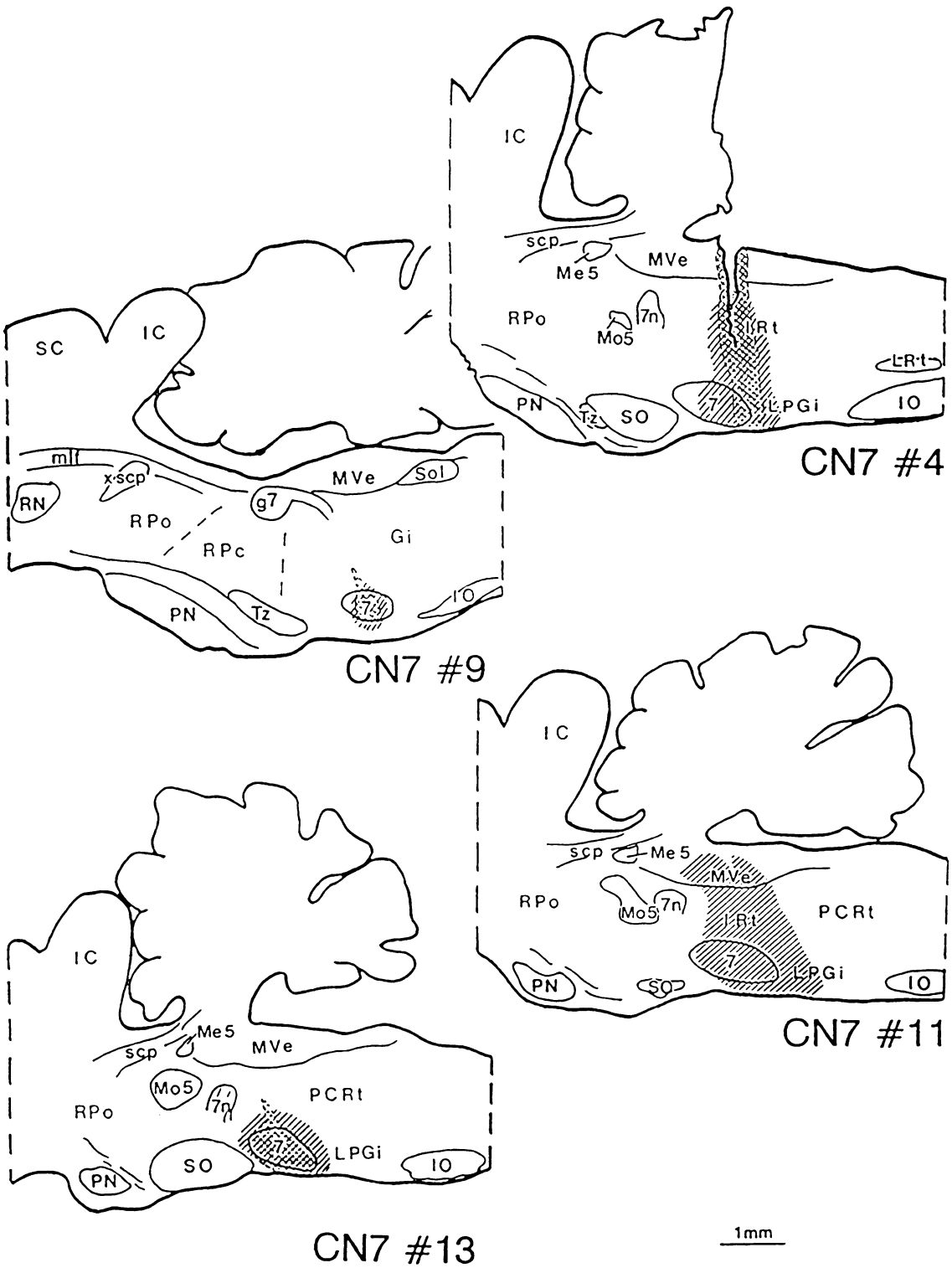

IC
scp
Me5
MVe
RPo
Mo5
7n
LRt
LRt
PN
Tz
SO
7
LPGi
IO
CN7 #4
SC
IC
mlf
x scp
MVe
Sol
RN
g7
RPo
RPc
Gi
PN
Tz
7
IO
CN7 #9
IC
scp
Me5
MVe
RPo
Mo5
7n
LRt
PCRt
7
LPGi
PN
SO
IO
CN7 #11
IC
Me5
scp
MVe
Mo5
7n
PCRt
RPo
7
LPGi
PN
SO
IO
CN7 #13
1mm

Figure 12

Figure 13: Photomicrographs of HRP Labeled Cells in the Contralateral Retrorubral Region in Case CN7 #13.

A&B: The location (A) and morphology (B) of retrogradely labeled cells in the contralateral RRF. Most of these cells lie well within the caudal half of the RRF (B). An arrow (B) indicates one labeled cell in the border zone between the PPNd (**) and the RRF. The PPNc is indicated by a single asterisk.

C&D: Show HRP reactive neurons in a more lateral region of the pontomesencephalic tegmentum. Labeled cells (arrows in D) are observed along the caudal border of the RR. Scale bar: 0.1mm

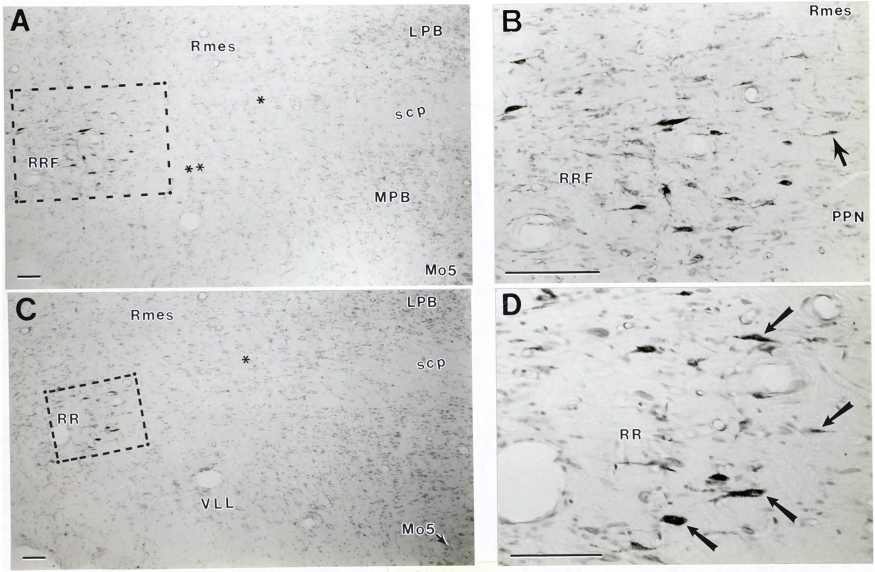

A
Rmes
LPB
scp
RRF
MPB
Mo5
B
Rmes
RRF
PPN
C
Rmes
LPB
scp
RR
VLL
Mo5
D
RR

Figure 13

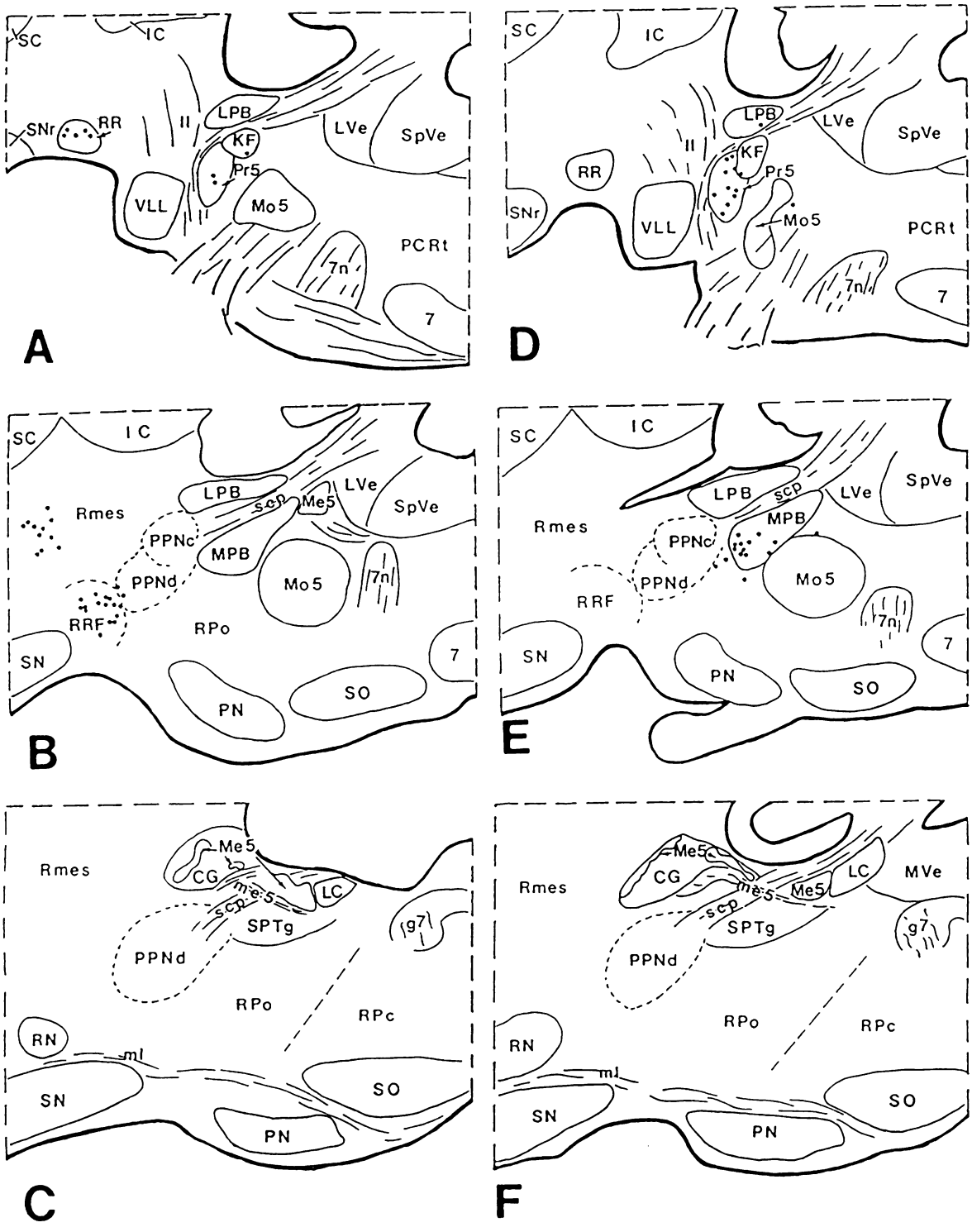
the caudal PPN. The other mesopontine nuclei exhibiting HRP-labeled neurons in case CN7 #13 included, in decreasing order: the bilateral Rmes (more contralaterally); bilateral RPo (more ipsilaterally); contralateral RRF; ipsilateral Pr5; ipsilateral CG (in clusters along the ventral border); bilateral KF; bilateral RN; and the ipsilateral LPB.

In the other three animals with injections in medial portions of the facial nucleus, moderately dense HRP-WGA reaction product was observed in neighboring regions of the adjacent reticular nuclei. GiA was labeled medial to the facial nucleus in cases CN7 #11, CN7 #4, and CN7 #9, while the reticular formation caudodorsal to the facial nucleus was labeled only in cases CN7 #11, and CN7 #4.

Results from these animals confirmed those of animal CN7 #13. There were essentially no labeled cells in the PPN following HRP-WGA injections into medial portions of the facial nucleus. Diffusely labeled neurons were observed in nuclei surrounding (but not including) the ipsilateral PPN, particularly the MPB and Pr5. Distinct labeling in the contralateral RR was present in all medial cases, even in one case (CN7 #9) with an extremely small injection site.

Figure 14: Distribution of HRP Labeled Cells in Case CN7 #13

Projections drawings of sagittal sections illustrating the distribution of HRP labeled cells in the contralateral (A-C) and ipsilateral (D-F) pedunculopontine region following HRP-WGA injection involving the medial part of the facial nucleus in case CN7 #13. Each dot represents one labeled cell.


SC
IC
SNr
RR
II
LPB
KF
Pr5
LVe
SpVe
VLL
Mo5
PCRt
7n
7
A
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scp
Me5
PPNc
MPB
PPNd
RRF
RPo
SN
PN
SO
B
E
CG
LC
SPTg
g7
RPc
RN
ml
MVe
C
F
1mm

Figure 14

Summary of Results

In summary, results of unilateral PHA-L injections centered in the PPN showed anterograde labeling primarily in the ventromedial pontomedullary reticular nuclei, but also in several nuclei of the cranial nerves. Labeled fibers were most dense in the facial nucleus, and relatively sparse in the caudal cranial nerve nuclei (12, Sol, 10, and Am). PHA-L projections to the facial nucleus exhibited two distinct patterns: 1) a diffuse ipsilateral projection present in all cases, and 2) a punctate contralateral projection to the rostromedial two thirds of the facial nucleus in two cases.

The HRP-WGA experiments which were designed to clarify the organization of this PPN-facial pathway failed to confirm the existence of such projections. Retrograde labeling of cells located well within the PPN was not observed after injections of HRP-WGA in either the lateral or medial portions of the facial nucleus. The exception was case CN7 #14, in which HRP-WGA was also deposited in the reticular formation caudal to the facial nucleus. Similarly, retrograde labeling in the PPN (136 cells ipsilaterally, 54 contralaterally) was observed in one additional case (CN7 #18) in which the core area of the HRP-WGA injection included the entire extent of the facial nucleus and substantial portions of the surrounding reticular nuclei.

In contrast to the absence of labeled cells in PPN, retrograde experiments showed labeling of several nuclei

surrounding the PPN. HRP-WGA injections into the medial facial nucleus resulted in distinct labeling of cells in the contralateral RR. Furthermore, both medial and lateral facial injections resulted in a primarily ipsilateral pattern of HRP-labeled neurons in the MPB, KF, LPB, and Pr5. These nuclei were labeled most distinctly in lateral facial injections.

DISCUSSION

PPN Projections to the Facial Nucleus

The anterograde and retrograde labeling experiments yielded contradictory results. While PHA-L injections in the PPN clearly demonstrated two distribution patterns of labeled fibers in the facial nucleus, the HRP-WGA experiments failed to retrogradely label cells located in the core of the PPN. Particularly significant was a complete absence of retrogradely labeled cells in the medial two thirds of the PPNd which appear to receive the bulk of nigral afferents (Spann & Grofova '88). It may be argued that the negative results obtained from the HRP experiments were due to technical failure. However, this seems unlikely since retrogradely labeled cells were consistently present in the areas surrounding the PPN. Furthermore, the PPN cells did exhibit distinct labeling in one of the experimental animals in which the HRP-WGA injection involved mostly the ventral part of the reticular formation adjacent to the medial aspect of the facial nucleus. Taken together, these observations indicate that the PPN does not give rise to the facial projections demonstrated in the experiments utilizing anterograde transport of PHA-L. Although there exist occasional reports (Cliffer & Giesler '88, Schofield '89) that the PHA-L can be taken up by fibers passing through the injection site, most authors agree with the original

observations of Gerfen & Sawchenko ('84) that PHA-L does not appear to be taken up and transported effectively by fibers of passage. Our own observations fully support the latter notion. The PPN is traversed by several prominent fiber systems including the superior cerebellar peduncle and the central tegmental tract which were unavoidably involved in all PHA-L injections. However, there was no evidence of PHA-L uptake and transport by these fiber systems. In fact, the fiber bundles of the scp traversing the center of PHA-L deposits were clearly discernable by the absence of reaction product (Fig.2), and no labeled fibers could be traced to the red nucleus. Thus labeling of fibers "en passage" does not provide a reasonable explanation of the results of the anterograde tracing experiments.

Most likely, the labeled fibers in the facial nucleus originated from scattered PHA-L labeled cells located within the nuclei surrounding the lateral aspect of the PPN. This conclusion is substantiated by careful comparisons between the distributions of HRP labeled cells following medial and/or lateral facial injections, and the distribution of single PHA-L labeled cells surrounding the dense center of PHA-L deposit. The HRP-WGA injections into the medial groups of facial motor neurons resulted in labeling of a discrete group of cells in the contralateral RR and lateral RRF. Correspondingly, single Golgi-like labeled cells were seen in these regions in the two PHA-L experiments (#25 and #31) which demonstrated a

contralateral projection to the medial portion of the facial nucleus. On the other hand, retrogradely labeled neurons were most numerous in the ipsilateral MPB, KF, LPB and Pr5 following HRP-WGA injections centered laterally in the facial nucleus, and uptake of PHA-L by isolated cells within these regions was more prominent in cases PHA-L #28, #27 and #24 which demonstrated a diffuse projection terminating predominantly ipsilaterally in the lateral division of the facial nucleus.

PPN Projections to Medullary Cranial Nerve Nuclei

While retrograde experiments were not carried out to clarify our findings of labeled fibers in the caudal cranial nerve nuclei (12, 10, Sol, and Am) following PHA-L injections centered in PPN, the literature supports the impression that these projections may also originate in nuclei surrounding the PPN. Several authors have shown retrogradely labeled KF, and to a lesser extent MPB and LPB neurons following HRP-WGA injections in several regions of the Sol in the rat (Herbert et.al. '90, Fulwiler & Saper '84, Rye et.al. '88). The largest proportion of these cells have been reported in the KF, with the remaining retrogradely labeled cells surrounding the ventrolateral scp in the MPB and LPB nuclei. Rye and colleagues ('88) have additionally shown that while many cells were retrogradely labeled in the parabrachial nuclei following injections of HRP-WGA in the ventrolateral Sol region, only

a few cells in the PPN were so labeled. In the present experiment, PHA-L injections sites did not include cells in the KF but did include several cells of the rostral and middle regions of the LPB and MPB. This may explain the sparse distribution of PHA-L labeled fibers to Sol in our results.

Parabrachial projections to the ventrolateral medulla (including Am) and the hypoglossal nucleus have also been reported in the rat (Rye, et.al. '88; Saper & Loewy, '80; Fulwiler & Saper, '84; Herbert, et.al '90) and in the pigeon (Wild, et.al. '90). The ventrolateral medulla is widely thought to be involved in respiratory control (Ellenberger et.al. '90, Feldman & Grillner '83), and it has been suggested that the ventrolateral portion of the Sol also contributes to the control of respiration (Herbert et.al., '90). Moreover, the muscles controlling the patency of the upper airway are innervated by the hypoglossal (Krammer, et.al. '79; Lewis, et.al. '71; Odutola, '76) and dorsal motor vagus (Lewis, et.al. '70) nuclei and receive parabrachial input (Saper & Loewy '80). On the basis of their connections with these respiratory and oral motor nuclei, it has been proposed that the parabrachial nuclei (particularly the KF) may contribute to the control of respiration (Herbert, et.al. '90) and vocalization (Wild, et.al. '90). While it seems unlikely that the PPN contributes directly to these functions, the present study can not rule out this possibility.

Mesopontine Efferents to the Facial Nucleus:

1) Parabrachial Nuclei

An ipsilateral projection from the KF, MPB, and LPB to intermediate and lateral portions of the facial nucleus has been reported previously in the rat (Isokawa-Akesson & Komisaruk '87, Hinrichsen & Watson '83, Travers & Norgren '83, Saper & Loewy '80), cat (Fort et.al. '89, Holstege et.al. '86, Takeuchi et.al. '80), and opossum (Panneton & Martin '83). Our findings confirm these results. In many species, the lateral facial subnuclei contain motoneurons innervating the buccolabial musculature (Watson et.al. '82, Komiyama et.al. '84, Dom et.al. '73). Our data implicates the MPB to a greater degree than other parabrachial nuclei in projecting to lateral portions of the ipsilateral facial nucleus, and these results are supported in the literature by autoradiographic studies (Saper & Loewy '80). The MPB has been identified as having gustatory functions (Saper & Lowey '80, Hill '87, Herbert et.al. '90) and, as was previously discussed, the ventrolateral parabrachial region has been associated with respiratory function. It follows that projections from parabrachial nuclei to the lateral facial subnuclei may contribute to the control of oral musculature in respiratory and feeding behaviors.

2) Retrorubral Nucleus

In addition to parabrachial facial afferents, our data confirm a contralateral projection from RR to medial subdivisions of the facial nucleus which was first reported in the rat by Isokawa-Akesson & Komisaruk ('87). The rat RR is a compact group of small to medium sized cells located rostral to the ventral nucleus of the lateral lemniscus and rostromedial to the fibers of the lateral lemniscus (Paxinos & Watson '86). In other retrograde tracing studies in the rat, the contralateral "midbrain reticular formation" (Hinrichsen & Watson '83) or the "paralemniscal zone" (Travers & Norgren '83) have been identified as sources of afferents to the medial groups of facial motoneurons. Similar observations have also been reported in the cat (May et.al. '89, Fort et.al. '89, Takeuchi et.al. '79, Henkel & Edwards '78) and opossum (Panneton & Martin '83). Since all these regions are rather vaguely defined, it is possible that the discrepancies are more semantic than factual.

The cat "paralemniscal zone" has been described in coronal sections as a narrow, vertical region consisting of darkly staining clusters of medium-sized, densely packed neurons extending from the nuclei of the lateral lemniscus to the caudal pole of the RR (Henkel & Edwards '78). The cat retrorubral nucleus represents a distinct entity which is characterized by the presence of catecholaminergic cells projecting to the striatum (Vandermaelen et.al. '78) and

having similar morphological and functional properties as the nigral cells in the pars compacta (Preston et.al. '81). No similar information is available for the rat RR delineated by Paxinos and Watson ('86). In fact, the cytoarchitectural features of the rat RR resemble more those described for the cat paralemniscal zone. This zone appears to receive projections from the superior colliculus and other structures known to be involved in visual and auditory orienting responses (Henkel '81), and it has been suggested that the connection from this zone to the medial facial motoneurons may play a role in the pinnae orienting response. Although no such function has been previously proposed for the rodent RR, it is interesting that the projection from the rat RR to the contralateral facial nucleus is restricted only to medial facial motoneurons which innervate the pinnae (Watson et.al. '82). Thus, the rodent RR is clearly in a position to affect pinnae movements during the orienting response. It would be of interest to further explore the functional connectivity of the rat RR, particularly with regard to its involvement in the orienting reflexes.

3) Red Nucleus

Our experiments confirm a crossed rubro-facial pathway terminating in the lateral and intermediate facial subnuclei as described in the literature (Travers & Norgren '83, Hinrichsen & Watson '83, Isokawa-Akesson & Komisaruk '87,

Edwards '72, Dom et.al. '73, Panneton & Martin '83). Our data shows this to be a sparse projection. The large number of RN cells labeled in case CN7 #14 is very likely due to uptake of HRP-WGA by damaged fibers of the rubrospinal tract passing caudolateral to the facial nucleus.

4) Principal Sensory Trigeminal Nucleus

Finally, we have demonstrated a rather substantial projection from Pr5 to the lateral and intermediate facial subnuclei. Many neurons located just caudal to the ventral spinocerebellar tract (rostrolateral to Mo5) were labeled following HRP-WGA injections in both the medial and lateral portions of the facial nucleus. These were more numerous after lateral facial injections. Physiological studies demonstrating disynaptic responses of facial motoneurons to stimulation of the trigeminal nerve seem to support these findings (Tanaka et.al., '71). In contrast to our results, previous investigators have described Pr5 innervation of the facial nucleus to be rather sparse in the rat (Travers & Norgren '83, Erzurumlu & Killackey '79) and opossum (Panneton & Martin '83).

The discrepancy with respect to the abundance of facial-projecting Pr5 cells may be due to the difficulties in the delineation of the Pr5 from the KF. In the sagittal plane, the KF and Pr5 nuclei intermix and the exact borders are difficult to distinguish. We defined KF cells as round or

pyramidal, darkly staining cells with a distinct nucleolus and a cell diameter exceeding 16μm (Fulwiler & Saper '84). Pr5 cells were smaller and more lightly stained than KF cells (Fukushima & Kerr '79). It is also possible that some of the retrogradely labeled cells in this transitional region represent neurons of the catecholaminergic A7 cell group. A7 cells are dispersed throughout the subcoeruleus, KF, and Pr5 nuclei and are known to project to the facial nucleus in the rat (Grzanna et.al. '87) and cat (Fort, et.al. '89). Cells labeled in the ipsilateral Pr5 may have also resulted from uptake of HRP-WGA in reticular regions lateral to the targeted facial nucleus. However, this can not entirely explain our results since several Pr5 cells were also labeled ipsilaterally with injections of HRP-WGA in the medial portions of the facial nucleus which completely avoided this reticular region.

Since the Pr5 receives primary facial sensory input, a projection from Pr5 to the lateral subdivisions of the facial nucleus may provide a pathway mediating the tactual guidance of oromotor behavior.

Descending PPN Efferents

Our data suggests there does not exist a direct projection from the PPN to the cranial nerve nuclei, but descending PPN efferents clearly project to the ventromedial pontomedullary reticular nuclei. The majority of PPN

efferents to the reticular formation are concentrated ventromedially in the RPc, GiA, and Giv (Grofova et.al. in press, Nakamura et.al. '89, Mitani et.al. '88, Rye et.al. '88, Jackson & Crossman '83, Moon-Edley & Graybiel '83), and these nuclei have been shown to project to somatic and autonomic motor columns in the medulla and spinal cord (Vertes et.al. '86, Jones & Yang '85, Travers & Norgren '83, Zemlan et.al. '82, Holstege & Kuypers '82, Martin et.al. '81, Peterson '80), thus establishing a potential pathway by which PPN may affect motor behavior. The existence of a PPN-reticulo-spinal pathway has been proposed by Garcia-Rill & Skinner ('87) on the basis of electrophysiological experiments. Extracellular recordings of single medioventral medullary neurons in the cat showed short latency orthodromic responses following stimulation of the mesencephalic locomotor region (MLR) coexistent with the ability to antidromically activate these same neurons from stimulation of the spinal cord. Since the reticular nuclei receiving input from the PPN project not only to the spinal cord but also to several motor and autonomic nuclei of the cranial nerves, it is possible that the PPN may influence both the spinal and cranial motor systems indirectly, through a relay in the brainstem reticular formation. Clinical syndromes associated with neuronal loss in the PPN in humans seem to support this suggestion since they invariably include disorders related to dysfunctions of the cranial nerves.

In progressive supranuclear palsy (PSP), symptoms include unsteady gait, dysarthric or dysphonic speech, and impaired ocular movements, particularly in the vertical plane (Jellinger '88, Maher & Lees '86). Another syndrome associated with PPN cell loss is Meige syndrome, a rare disorder involving involuntary head turning, blepharospasm, and grimacing movements of the orofacial musculature (Tolosa & Marti '88, Zweig et.al. '88).

Functional Considerations

The PPN has been implicated in motor control by virtue of its abundant connections with the basal ganglia and spinal cord projecting reticular nuclei, and by its co-localization within the physiologically identified mesencephalic locomotor region. However, it became increasingly obvious that it would be an oversimplification to consider PPN functions only in terms of locomotion or motor control in general. In the light of various lines of evidence, it is tempting to speculate that the PPN may represent a part of a complex substrate underlying orienting reflexes.

While the precise pathways involved in the orienting reflex are far from clear, several contributing nuclei have been identified (Fig. 15). In particular, the deep layers of the SC are necessary to elicit orienting behaviors (Peterson '80). It is possible that the orienting reflex, characterized by turning of the head, pinnae and eyes toward a novel

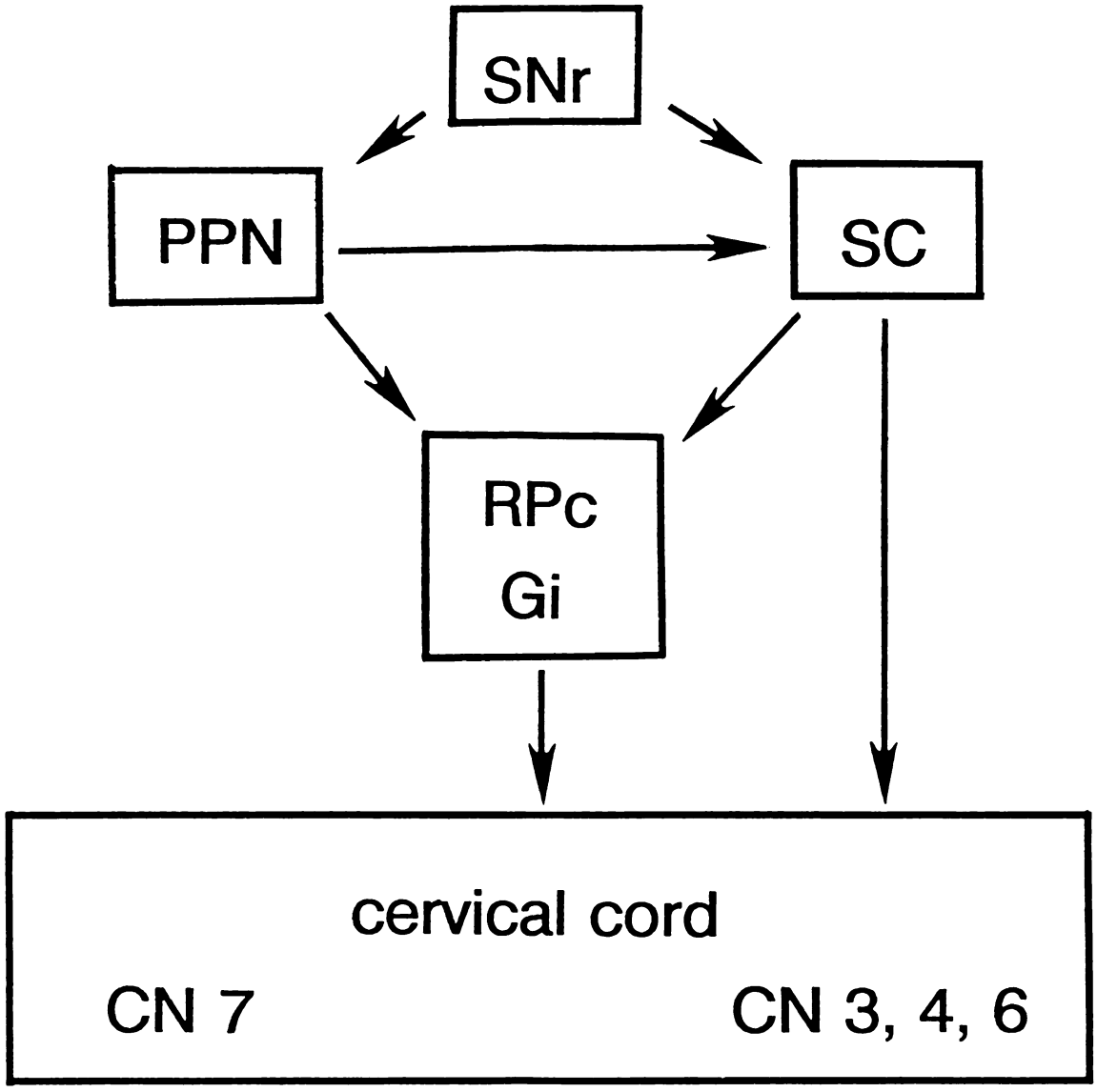

Figure 15: Circuit Diagram - Orienting Reflex

Circuit diagram illustrates the connections of some of the structures thought to be involved in the orienting reflex. Abbreviations: intermediate and deep layers of the superior colliculus (SC), substantia nigra pars reticulata (SNr), pedunculopontine nucleus (PPN), nucleus reticularis pontis caudalis (RPc), nucleus gigantocellularis (Gi), cranial nerves (CN) 3, 4, 6, and 7.

stimulus, may be executed via deep tectal efferents projecting directly to appropriate motor structures.

Intermediate and deep layers of the SC project to the upper cervical segments, innervating axial musculature required for head turning (Huerta & Harting '82), to the cranial motor nuclei involved in extraocular and pinnae movements (Vidal et.al. '88, Keller '79, Graham '77) and to the pontomedullary reticular formation projecting to these cranial motor nuclei (Vertes et.al. '86, Kawamura & Hashikawa '78, Edwards '80, Isokawa-Akesson & Komisaruk '87, Panneton & Martin '83, Takeuchi et.al. '79, Fort et.al. '89). Since the PPN sends descending projections to these same reticular nuclei (i.e. the medioventral RPc, GiA, and Giv) (Grofova et.al. in press, Mitani et.al. '88, Rye et.al. '88, Moon-Edley & Graybiel '83, Jackson & Crossman '83, Zemlan '84) it is well situated to modulate neural activity occurring during the orienting response.

On the other hand, the SNr is in a position to influence these two structures (i.e. the SC and PPN) which both project either directly or indirectly to the motor nuclei required for execution of the orienting response. The SNr projects substantially to the ipsilateral deep layers of the SC (Grofova et.al. in press, Williams & Faull '88, Beckstead & Frankfurter '82, Gerfen et.al. '82) as well as extensively to the ipsilateral PPN (Spann & Grofova '88, Noda & Oka '84, Garcia-Rill et.al. '83, Gerfen et.al. '82, Beckstead et.al.

'82). Physiological experiments have also confirmed a SNr-PPN-reticular pathway (Kelland & Asdourian '89, Nakamura et.al. '89, Garcia-Rill & Skinner '87), and monosynaptic input from SNr to tectospinal neurons has been described (Williams & Faull '88). There seem to be considerable interconnections within this circuitry. In this regard, it is of interest to note that the PPN also sends input to the SC (Hall et.al. '89, Woolf & Butcher '86, Beninato & Spencer '86). Thus, nigral efferents may assist in coordinating the influence of the SC and PPN on the medial RPc, GiA, and Giv reticular nuclei.

Physiological observations of directionally specific behavioral abnormalities following unilateral lesions of the rat PPN (Kilpatrick & Starr '81) also support a possible role of the PPN in the orienting reflex. Because of the multiplicity of nuclei involved in control of the orienting response, and the complexity of interconnections among them, further detailed studies will be required to elucidate the role of the PPN in the orienting reflex as well as other functions.

BIBLIOGRAPHY

BIBLIOGRAPHY

Basbaum, A.A. & Fields, H.L. (1980) Pain Control: A New Role for the Medullary Reticular Formation. In THE RETICULAR FORMATION REVISITED, edited by J.A. Hobson & M.A.B. Brazier, Raven Press, New York, pp. 329-348.

Beckstead, R.M. & Frankfurter, A. (1982) The Distribution and Some Morphological Features of Substantia Nigra Neurons That Project to the Thalamus, Superior Colliculus and Pedunculopontine Nucleus in the Monkey. NEUROSCIENCE 7(10): 2377-2388.

Beckstead, R.M., Domesick, V.B., & Nauta, W. (1979) Efferent Connections of the Substantia Nigra and Ventral Tegmental Area in the Rat. BRAIN RES 175: 191-217.

Beninato, M. & Spencer, R.F. (1986) A Cholinergic Projection to the Rat Superior Colliculus Demonstrated by Retrograde Transport of Horseradish Peroxidase and Choline Acetyltransferase Immunohistochemistry. J COMP NEUROL 253: 525-538.

Carstens, E., Klump, D. & Zimmerman, M. (1980) Differential Inhibitory Effects of Medial and Lateral Midbrain Stimulation on Spinal Neuronal Discharges to Noxious Skin Heating in the Rat. J NEUROPHYSIOL 43: 332-342.

Carter, D.A. & Fibiger, H.C. (1978) The Projections of the Entopeduncular Nucleus and Globus Pallidus in Rat as Demonstrated by Autoradiography and Horseradish Peroxidase Histochemistry. J COMP NEUROL 177: 113-124.

Cliffer, K.D. & Giesler, G.J. (1988) PHA-L Can Be Transported Anterogradely Through Fibers of Passage. BRAIN RES 458: 185-191.

DeVito, J.L. & Anderson, M.E. (1982) An Autoradiographic Study of Efferent Connections of the Globus Pallidus in Macaca Mulatta. EXP BRAIN RES 46: 107-117.

Dom, R., Falls, W., & Martin, G. F. (1973) The Motor Nucleus of the Facial Nerve. In the Opossum (Didelphis marsupialis virginiana). Its Organizations and Connections. J COMP NEUROL 152: 373-402.

Edwards, S.B. (1980) The Deep Cell Layers of the Superior Colliculus in THE RETICULAR FORMATION REVISITED, edited by J.A. Hobson & M. Brazier. Raven Press, New York, pp. 193-209.

Edwards, S.B. (1972) The Ascending and Descending Projections of the Red Nucleus in the Cat: An Experimental Study Using an Autoradiographic Tracing Method. BRAIN RES 48: 45-63.

Ellenberger, H.H., Feldman, J.L. & Zhan, W.Z. (1990) Subnuclear Organization of the Lateral Tegmental Field of the Rat. II: Catecholamine Neurons and Ventral Respiratory Group. J COMP NEUROL 294: 212-222.

Erzurumlu, R.S. & Killackey, H.P. (1979) Efferent Connections of the Brainstem Trigeminal Complex with the Facial Nucleus of the Rat. J COMP NEUROL 188: 75-86.

Feldman, J.L & Grillner, S. (1983) Control of Vertebrate Respiration and Locomotion: A Brief Account. PHYSIOL 26: 310-316.

Fort, P., Sakai, K., Luppi, P., Salvert, D. & Jouvet, M. (1989) Monoaminergic, Peptidergic, and Cholinergic Afferents to the Cat Facial Nucleus as Evidenced by a Double Immunostaining Method with Unconjugated Cholera Toxin as a Retrograde Tracer. J COMP NEUROL 283: 285-302.

Fukushima, T. & Kerr, F.L. (1979) Organization of Trigeminothalamic Tracts and Other Thalamic Afferent Systems of the Brainstem in the Rat. J COMP NEUROL 183: 169-184.

Fulwiler, C.E. & Saper, C.B. (1984) Subnuclear Organization of the Efferent Connections of the Parabrachial Nucleus in the Rat. BRAIN RES REV 7: 229-259.

Garcia-Rill, E., Skinner, R.D., Jackson, M.B. & Smith, M.M. (1983) Connections of the Mesencephalic Locomotor Region (MLR): I. Substantia Nigra Afferents. BRAIN RES BULLETIN 10: 57-62.

Garcia-Rill, E., Skinner, R.D., Gilmore, S.A. & Owings, R. (1983) Connections of the Mesencephalic Locomotor Region (MLR): II. Afferents and Efferents. BRAIN RES BULLETIN 10: 63-71.

Garcia-Rill, E. (1983) Connections of the Mesencephalic Locomotor Region (MLR): III. Intracellular Recordings. BRAIN RES BULLETIN 10: 73-81.

Garcia-Rill, E. (1986) The Basal Ganglia and the Locomotor Regions. BRAIN RES REV 11: 47-63.

Garcia-Rill, E., Houser, C.R., Skinner, R.D., Smith, W., & Woodward, D.J. (1987) Locomotion-Inducing Sites in the Vicinity of the Pedunculopontine Nucleus. BRAIN RES BULLETIN 18: 731-738.

Garcia-Rill, E. & Skinner, R.D. (1987) The Mesencephalic Locomotor Region. II. Projections to Reticulospinal Neurons. BRAIN RES 411: 13-20.

Garcia-Rill, E. & Skinner, R.D. (1988) Modulation of Rhythmic Function in the Posterior Midbrain. NEUROSCIENCE 27(2): 639-654.

Gerfen, C.R. & Sawchenko, P.E. (1984) An Anterograde Neuroanatomical Tracing Method that Shows the Detailed Morphology of Neurons, Their Axons and Terminals: Immunohistochemical Localization of an Axonally Transported Plant Lectin, Phaseolus vulgaris Leucoagglutinin (PHA-L). BRAIN RES 290: 219-238.

Gerfen, C.R., Staines, W.A., Arbuthnott, G.W., & Fibiger, H.C. (1982) Crossed Connections of the Substantia Nigra in the Rat. J COMP NEUROL 207: 283-303.

Goldsmith, M. & Vanderkooy, D. (1988) Separate Non-Cholinergic Descending Projections and Cholinergic Ascending Projections from the Nucleus Tegmenti Pedunculopontinus. BRAIN RES 445: 386-391.

Gonya-Magee, T. & Anderson, M.E. (1983) An Electrophysiological Characterization of Projections from the Pedunculopontine Area to Entopeduncular Nucleus and Globus Pallidus in the Cat. EXP BRAIN RES 49: 269-279.

Graham, J. (1977) An Autoradiographic Study of the Efferent Connections of the Superior Colliculus in the Cat. J COMP NEUROL 173: 629-654.

Granata, A.R. & Kitai, S.T. (1989) Intracellular Analysis of Excitatory Subthalamic Inputs to the Pedunculopontine Neurons. BRAIN RES 488: 57-72.

Graybiel, A.M. & Devor, M. (1974) A Micro-electrophoretic Delivery Technique for Use with Horseradish Peroxidase. BRAIN RES 68: 167-173.

Grofova, I., Spann, B.M., & Bruce, K. (in press) Involvement of the Nucleus Tegmenti Pedunculopontinus in the Descending Pathways of the Basal Ganglia in the Rat. In BASAL GANGLIA III: PROCEEDINGS OF THE INTERNATIONAL BASAL GANGLIA SOCIETY'S THIRD TRIENNIAL MEETING, edited by G. Bernardi, Plenum Press, New York.

Grzanna, R., Chee, W.K. & Akeyson, E.W. (1987) Noradrenergic projections to Brainstem Nuclei: Evidence for Differential Projections From Noradrenergic Subgroups. J COMP NEUROL 263: 76-91.

Hall, W.C., Fitzpatrick, D., Klatt, L.L & Raczkowski, D. (1989) Cholinergic Innervation of the Superior Colliculus in the Cat. J COMP NEUROL 287: 495-514.

Henkel, C.K. & Edwards, S.B. (1978) The Superior Colliculus Control of Pinna Movements in the Cat: Possible Anatomical Connections. J COMP NEUROL 182: 763-776.

Henkel, C. (1981) Afferent Sources of a Lateral Midbrain Tegmental Zone Associated with the Pinnae in the Cat as Mapped by Retrograde Transport of Horseradish Peroxidase. J COMP NEUROL 203: 213-226.

Herbert, H., Moga, M.M., & Saper, C.B. (1990) Connections of the Parabrachial Nucleus with the Nucleus of the Solitary Tract and the Medullary Reticular Formation in the Rat. J COMP NEUROL 293: 540-580.

Hill, D.L. (1987) Development of Taste Responses in the Rat Parabrachial Nucleus. J NEUROPHYSIOL 57(2):481.

Hinrichsen, C.F.L. & Watson, C.D. (1983) Brain Stem Projections to the Facial Nucleus of the Rat. BRAIN BEHAV EVOL 22: 153-163.

Holstege, G., Van Ham, J., Joeptan (1986) Afferent Projections to the Orbicularis Oculi Motoneuronal Cell Group. An Autoradiographical Tracing Study in the Cat. BRAIN RES 374: 306-320.

Holstege, J.C. & Kuypers, H.G.J.M. (1982) Brain Stem Projections to Spinal Motoneuronal Cell Groups in Rat Studied by Means of Electron Microscopy Autoradiography. In PROG BRAIN RES vol. 57, DESCENDING PATHWAYS TO THE SPINAL CORD, edited by H. Kuypers & G.F. Martin, Elsevier, New York, pp. 177-183.

Huerta, F.M. & Harting, J.K (1982) Tectal Control of Spinal Cord Activity: Neuroanatomical Demonstration of Pathways Connecting the Superior Colliculus with the Spinal Cord Grey. PROG BRAIN RES 57: 293-328.

Hylden, J.K., Hayashi, H., Bennett, G.J., & Dubner, R. (1985) Spinal Lamina I Neurons Projecting to the Parabrachial Area of the Cat Midbrain. BRAIN RES 336: 195-198.

Isokawa-Akesson, M. & Komisaruk, B.R. (1987) Difference in Projections to the Lateral and Medial Facial Nucleus: Anatomically Separate Pathways for Rhythmical Vibrissa Movements in Rats. EXP BRAIN RES 65: 385-398.

Jackson, A. & Crossman, A.R. (1983) Nucleus Tegmenti Pedunculopontinus: Efferent Connections with Special Reference to the Basal Ganglia, Studied in the Rat by Anterograde and Retrograde Transport of Horseradish Peroxidase. NEUROSCIENCE 10(3): 725-765.

Jellinger, K. (1988) The Pedunculopontine Nucleus in Parkinson's Disease, Progressive Supranuclear Palsy and Alzheimer's Disease. J NEUROL NEUROSURG PSYCHIATRY 51:540-543.

Jones, B.E. & Yang T-Z (1985) The Efferent Projections From the Reticular Formation and the Locus Coeruleus Studied by Anterograde and Retrograde Axonal Transport in the Rat. J COMP NEUROL 242: 56-92.

Katayama, Y., DeWitt, D.S., Becker, D.P., & Hayes, R.L. (1984) Behavioral Evidence for a Cholinoceptive Pontine Inhibitory Area: Descending Control of Spinal Motor Output and Sensory Input. BRAIN RES 269: 241-262.

Kawamura, K. & Hashikawa, T. (1978) Cell Bodies of Origin of Reticular Projections from the Superior Colliculus in the Cat: An Experimental Study with the Use of Horseradish Peroxidase as a Tracer. J COMP NEUROL 182: 1-16.

Kelland, M.D. & Asdourian, D. (1989) Pedunculopontine Tegmental Nucleus-induced Inhibition of Muscle Activity in the Rat. BEH BRAIN RES 34: 213-234.

Keller, E.L. (1979) Colliculoreticular Organization in the Oculomotor System. PROG BRAIN RES 50: 725-734.

Kilpatrick, I.C. & Starr, M.S. (1981) The Nucleus Tegmenti Pedunculopontinus and Circling Behavior in the Rat. NEUROSCI LETTR 26: 11-16.

Kim, R., Nakano, K., Jayaraman, A., & Carpenter, M.B. (1976) Projections of the Globus Pallidus and Adjacent Structures: An Autoradiographic Study in the Monkey. J COMP NEUROL 169: 263-290.

Komiyama, M., Shibata, H., & Takashi, S. (1984) Somatotopic Representation of Facial Muscles within the Facial Nucleus of the Mouse. BR BEHAV EVOL 24: 144-151.

Krammer, E.B., Rath, T., & Lischka, M.F. (1979) Somatotopic Organization of the Hypoglossal Nucleus: a HRP Study in the Rat. BRAIN RES 170: 533-537.

Larsen, K.D. & McBride, R.L. (1979) The Organization of Feline Entopeduncular Nucleus Projections. J COMP NEUROL 184: 293-308.

Lewis, P.R., Flumerfelt, B.A., & Shute, C.C.D. (1971) The Use of Cholinesterase Techniques to Study Topographical Localization in the Hypoglossal Nucleus of the Rat. J ANAT 110(2): 203-213.

Lewis, P.R., Scott, J.A. & Navaratnam V. (1970) Localization in the Dorsal Motor Nucleus of the Vagus in the Rat. J ANAT 107: 197-208.

Maher, E.R. & Lees, A.J. (1986) The Clinical Features and a Natural History of the Steele-Richardson-Olszewski syndrome (Progressive Supranuclear Palsy). NEUROLOGY 36: 1005-1008.

Martin, G.F., Cabana, T., Humbertson, A.O., Laxson, L.C., & Panneton, W.M. (1981) Spinal Projections from the Medullary Reticular Formation of the North American Opossum: Evidence for Connectional Heterogeneity. J COMP NEUROL 196: 663-682.

May, P.J., Vidal, P-P, & Baker, R. (1989) Synaptic Organization of the Tecto-Facial Pathways in the Cat: II. Synaptic Potentials Following Midbrain Tegmentum Stimulation. J NEUROPHYSIOL (submitted).

Mesulam, M. (1982) TRACING NEURAL CONNECTIONS WITH HORSERADISH PEROXIDASE. Wiley & Sons, New York.

Mitani, A., Ito, K., Hallanger, A.E., Wainer, B.H., Kataoka, K. & McCarley, R.W. (1988) Cholinergic Projections from the Laterodorsal and Pedunculopontine Tegmental Nuclei to the Pontine Gigantocellular Tegmental Field in the Cat. BRAIN RES 451: 397-402.

Moon Edley, S. & Graybiel, A. (1983) The Afferent and Efferent Connections of the Feline Nucleus Tegmenti Pedunculopontinus, Pars Compacta. J COMP NEUROL 217: 187-215.

Mori, S., Nishimura, H., & Aoki, M. (1980) Brain Stem Activation of the Spinal Stepping Generator. In THE RETICULAR FORMATION REVISITED, edited by J.A. Hobson & M. Brazier. Raven Press, New York, pp.171-192.

Nakamura, Y., Tokuno, H., Moriizumi, T., Kitao, Y., & Kudo, M. (1989) Monosynaptic Nigral Inputs to the Pedunculopontine Tegmental Nucleus Neurons Which Send Their Axons to the Medial Reticular Formation in the Medulla Oblongata. An Electron Microscopic Study in the Cat. NEUROSCI LETTR 103: 145-150.

Nauta, H.J.W. & Cole, M. (1978) Efferent Projections of the Subthalamic Nucleus: An Autoradiographic Study in Monkey and Cat. J COMP NEUROL 180: 1-16.

Nauta, H.J.W. & Mehler, W.R. (1966) Projections of the Lentiform Nucleus in the Monkey. BRAIN RES 1: 3-42.

Noda, T. & Oka, H. (1986) Distribution and Morphology of Tegmental Neurons Receiving Nigral Inhibitory Inputs in the Cat: An Intracellular HRP Study. J COMP NEUROL 244: 254-266.

Odutola, A.B. (1976) Cell Grouping and Golgi Architecture of the Hypoglossal Nucleus of the Rat. EXP NEUROL 52: 356-371.

Olucha, F., Martinez-Garcia, F. & Lopez-Garcia, C. (1985) A New Stabilizing Agent for the Tetramethyl Benzidine (TMB) Reaction Product in the Histochemical Detection of Horseradish Peroxidase (HRP). J NEUROSCI METHODS 13: 131-138.

Olszewski, J. & Baxter, D. (1954) CYTOARCHITECTURE OF THE HUMAN BRAIN STEM. J.P. Lippincott & Co., Philadelphia.

Panneton, W. M. & Martin, G. F. (1983) Brainstem Projections to the Facial Nucleus of the Opossum: A Study Using Axonal Transport Techniques. BRAIN RESEARCH 267: 19-33.

Parent, A. & DeBellefeuille, L. (1982) Organization of Efferent Projections from the Internal Segment of Globus Pallidus in Primate as Revealed by Fluorescent Retrograde Labeling Method. BRAIN RES 245: 201-213.

Paxinos, G. & Watson, C. (1986) THE RAT BRAIN IN STEREOTAXIC COORDINATES, SECOND EDITION. Academic Press, New York.

Peterson, B.W. (1980) Participation of Pontomedullary Reticular Neurons in Specific Motor Activity in THE RETICULAR FORMATION REVISITED, edited by J.A. Hobson & M. Brazier. Raven Press, New York, pp.171-192.

Preston, R.J., McCrea, R.A., Chang, H.T., & Kitai, S.T. (1981) Anatomy and Physiology of Substantia Nigra and Retrorubral Neurons Studied by Extra- and Intracellular Recording and by Horseradish Peroxidase Labeling. NEUROSCIENCE 6(3): 331-344.

Rye, D.B., Lee, H.J., Saper, C.B., & Wainer, B.H. (1988) Medullary and Spinal Efferents of the Pedunculopontine Tegmental Nucleus and Adjacent Mesopontine Tegmentum in the Rat. J COMP NEUROL 269: 315-341.

Saper, C.B. & Loewy, A.D. (1982) Projections of the Pedunculopontine Tegmental Nucleus in the Rat: Evidence for Additional Extrapyramidal Circuitry. BRAIN RES 252: 367-372.

Saper, C.B. & Loewy, A.D. (1980) Efferent Connections of the Parabrachial Nucleus in the Rat. BRAIN RES 197: 291-317.

Schofield, P.R. (1989) Labeling of Axons of Passage by Phaseolus Vulgaris Leucoagglutinin (PHA-L). NEUROSCI ABSTR 15: 306.

Spann, B.M. & Grofova, I. (1988) Substantia Nigra Afferents of the Nucleus Tegmenti Pedunculopontinus. NEUROSCI ABSTR 14: 1027.

Spann, B.M. & Grofova, I. (1989) The Origin of Ascending and Spinal Pathways from the Nucleus Tegmenti Pedunculopontinus in the Rat. J COMP NEUROL 283: 13-27

Takeuchi, Y., Uemura, M., Matsuda, K., Matsushima, R. & Mizuno, N. (1980) Parabrachial Nucleus Neurons Projecting to the Lower Brain Stem and the Spinal Cord. A Study in the Cat by the Fink-Heimer and the Horseradish Peroxidase Methods. EXP NEUROL 70: 403-413.

Tanaka, T., Yu, H., & Kitai, S.T. (1971) Trigeminal and Spinal Inputs to the Facial Nucleus. BRAIN RES 33: 504-508.

Tolosa, E. & Marti, M.J. (1988) Blepharospasm-Oromandibular Dystonia Syndrome (Meige's Syndrome): Clinical Aspects. In ADVANCES IN NEUROLOGY vol.49: FACIAL DYSKINESIAS, edited by J. Jankovic & E. Tolosa, Raven Press, New York, pp. 73-84.

Travers, J.B. & Norgren, R. (1983) Afferent Projections to the Oral Motor Nuclei in the Rat. J COMP NEUROL 220: 280-298.

VanDerKooy, D. & Carter, D.A. (1981) The Organization of the Efferent Projections and Striatal Afferents of the Entopeduncular Nucleus and Adjacent Areas in the Rat. BRAIN RES 211: 15-36.

Vandermaelen, C.P., Kocsis, J.D., & Kitai, S.T. (1978) Caudate Afferents From the Retrorubral Nucleus and Other Midbrain Areas in the Cat. BRAIN RES BULLETIN 3: 639-644.

Vertes, R.P., Martin, G.F., & Waltzer, R. (1986) An Autoradiographic Analysis of Ascending Projections from the Medullary Reticular Formation in the Rat. NEUROSCIENCE 19(3): 873-898.

Vidal, P-P, May, P.J., & Baker, R. (1988) Synaptic Organization of the Tecto-Facial Pathways in the Cat: I. Synaptic Potentials Following Collicular Stimulation. J NEUROPHYSIOL 60 (2): 769-797.

Watson, C.R.R., Sakai, S., Armstrong, W. (1982) Organization of the Facial Nucleus in the Rat. BRAIN BEHAV EVOL 20: 19-28.

Wild, J.M., Arends, J., & Zeigler, H.P. (1990) Projections of the Parabrachial Nucleus in the Pigeon. J COMP NEUROL 292: 499-523.

Williams, M.N. & Faull, R.L.M. (1988) The Nigrotectal Projections and Tectospinal Neurons in the Rat: A Light and Electron Microscopic Study Demonstrating a Monosynaptic Nigral Input to Identified Tectospinal Neurons. NEUROSCIENCE 25(2): 533-562.

Woolf, N.J. & Butcher, L.L. (1986) Cholinergic Systems in the Rat Brain: III. Projections from the Pontomesencephalic Tegmentum to the Thalamus, Tectum, Basal Ganglia, and Basal Forebrain. BRAIN RES BULL 16(5): 603-37.

Zemlan, F.P., Behbehani, M.M., & Beckstead, R.M. (1984) Ascending and Descending Projections from Nucleus Reticularis Magnocellularis and Nucleus Reticularis Gigantocellularis: An Autoradiographic and Horseradish Peroxidase Study in the Rat. BRAIN RES 292: 207-220.

Zweig, R.M., Jankel, W.R., Hedreen, J.C., Mayeux, R., & Price, D.L. (1989) The Pedunculopontine Nucleus in Parkinson's Disease. ANN NEUROL 26: 41-46.

Zweig, R.M., Whitehouse, P.J., Casanova, M.F., Walker, L.C., Jankel, W.R., & Price, D.L. (1985) Loss of Putative Cholinergic Neurons of the Pedunculopontine Nucleus in Progressive Supranuclear Palsy. ANN NEUROL 18(1): 144.

Zweig, R.M., Hedreen, J.C., Jankel, W.R., Casanova, M.F., Whitehouse, P.J., & Price, D.L. (1988) Pathology in Brainstem Regions of Individuals with Primary Dystonia. NEUROLOGY 38: 702-706.

Zweig, R.M., Whitehouse, P.J., Casanova, M.F., Walker, L.C., Jankel, W.R., & Price, D.L. (1987) Loss of Pedunculopontine Neurons in Progressive Supranuclear Palsy. ANN NEUROL 22: 18-25.