Brain Research, 453 (1988) 89–102
Elsevier

BRE 13667

Nucleus cuneiformis and pain modulation: anatomy and behavioral pharmacology

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(Accepted 22 December 1987)

Key words: Analgesia; Nucleus cuneiformis; Pain modulation

The anatomical substrate and behavioral pharmacology of stimulation-produced analgesia resulting from electrical stimulation of the pontomesencephalic nucleus cuneiformis (NCF) was determined in the present study. Maximum increase in nociceptive tail-flick latencies following NCF stimulation occurred during the first 5 min post stimulation and decreased afterwards. The increased reflex latency could be attenuated by prior treatment with the narcotic antagonist, naloxone or the cholinergic antagonist, scopolamine. The anatomical projections of NCF were identified in autoradiographic and histochemical studies. Ipsilateral fibers coursed caudal from the NCF injection site through the ventral pontine reticular formation to innervate nucleus raphe magnus and the ipsilateral nucleus magnocellularis. At rostral medullary levels fibers coursed dorsolateral to innervate the ipsilateral nucleus reticularis parvocellularis. Descending contralateral fibers crossed through the decussation of the superior cerebellar peduncle, then coursed ventrolaterally projecting to the contralateral nucleus magnocellularis. Two primary groups of ascending fibers were observed. The dorsally located group ascended through the central tegmental tract projecting to the dorsal raphe, ipsilateral periaqueductal gray, nucleus parafascicularis and centromedianus, the intermediolateral and lateral thalamic nuclei. The ventral group coursed ventrolateral from the injection site projecting to the substantia nigra, zona compacta, ventral tegmental area of Tsai, zona incerta, Fields of Forel, lateral hypothalamic nucleus and nucleus reuniens. These anatomic and behavioral data suggest that NCF plays an important role in sensory/motor integration relevant to pain transmission.

INTRODUCTION

Spinal cord pain transmission is modulated by descending bulbospinal projections originating in the ventral medulla, nucleus raphe magnus (NRM) and the laterally adjacent nucleus magnocellularis (NMC). Anatomical studies have demonstrated that the major source of afferents to NRM/NMC arise from a continuous band of cells located within the periaqueductal gray (PAG) and the laterally adjacent nucleus cuneiformis[2–4]. Although the influence of the PAG on NRM/NMC modulation of spinal pain transmission has been extensively studied, recent data suggest that nucleus cuneiformis (NCF) may exert a more powerful influence on NRM/NMC neural activity. For example, electrical stimulation of NCF results in both mono- and polysynaptic effects on NRM/NMC neurons, and consistent with an NCF-mediated analgesia, 75% of responsive NRM/NMC units were excited by NCF stimulation[3]. In quantitative morphometric studies, we have recently reported that twice the number of NCF neurons per 100 μm coronal section are labeled following WGA–HRP injection to NRM/NMC compared to the PAG[3]. These anatomical data, indicating a stronger projection from NCF to NRM/NMC than from PAG to NRM/NMC, are consistent with behavioral studies which found that the stimulation current required to produce inhibition of the nociceptive jaw-opening reflex from NCF was about 1/8 that required to produce analgesia from the PAG[10].

Anatomical research focusing on NCF is limited.

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In a previous study[30] we identified the cytoarchitectural boundaries of NCF in the rat which were based on the definition of this nucleus developed by Taber[28] in the cat. In both species, NCF is a large midbrain reticular structure extending from the rostral pons to the pretectal thalamus, which may be subdivided into rostral and caudal portions on the basis of afferent and efferent projections. Rostral NCF, extending 2.0 mm in the rostrocaudal plane, does not project to NRM/NMC and has limited long afferent projections, while caudal NCF, which extends 2.5 mm in the rostrocaudal plane, receives more extensive afferent projections and is the major source of NRM/NMC afferents in the CNS[3,30]. Our previous recording studies indicated that caudal NCF sends a strong excitatory projection to NRM/NMC which is partially cholinergic[3]. The purpose of the present study was to: (1) define the ascending and descending anatomical projections of caudal NCF, (2) determine the behavioral affects of electrical stimulation of caudal NCF particularly with respect to stimulation-produced analgesia and (3) explore the pharmacology of NCF-induced analgesia.

MATERIALS AND METHODS

Stimulation studies

Thirty-one male Sprague–Dawley rats (250–300 g) were anesthetized with Equithesin, placed in a stereotaxic apparatus and a bipolar stimulation electrode (1 μm tip diameter) unilaterally implanted in caudal NCF (AP −5.0 to −5.8 mm; L 1.5–1.7 mm and D 5.5–6.5 mm with reference to bregma and the cortical surface). Two weeks after surgery, the effect of electrical stimulation on the animals behavioral response to noxious thermal stimulation was assessed employing the tail-flick test as previously described[32]. Tail-flick response latencies were determined prior to electrical stimulation in 3 tests conducted at 2-min intervals. Response latencies were determined 1, 3, 5 and 7 min following electrical stimulation (100–200 μA, 60 Hz, 200 ms pulse duration for 10 s). Tests were initially performed with a current intensity of 100 μA. The pre- and post-stimulation tests were repeated 1 h later with the current intensity increased 25 μA and the most effective current identified. One week later, response latencies were determined at the most effective current prior to and after i.p. administration of the cholinergic antagonist, scopolamine (50 mg/kg) or the narcotic antagonist naloxone (4 mg/kg). Stimulation site location was histologically determined. Animals were anesthetized with Equithesin, perfused with buffered formalin, the brain removed, stored in 30% sucrose/formalin, for 1 week, sectioned at 40 μm, stained with Neutral red and the location of the tip of the stimulating electrode charted.

Autoradiographic studies

Fourteen male Sprague–Dawley rats weighing 250–300 g were anesthetized with Equithesin and received stereotaxic injections of ^{3}H-amino acids to the NCF (n = 8) and nucleus subcuneiformis (n = 6). A solution of 1 part L-[2,3,4,5,-^{3}H]proline (spec. act. > 100 Ci/mmol) and 3 parts L-[3,4,5-^{3}H]leucine (spec. act. > 110 Ci/mmol, New England Nuclear) was desiccated and reconstituted with 0.01 N acetic acid to a concentration of 200 μCi/μl. Injections were made electrophoretically with micropipettes (internal diameter: 5–10 μm) to the caudal NCF (AP −5.0 to −5.8 mm; L 1.5–1.7 mm and D 5.5–6.5 mm with reference to bregma and the cortical surface) and the caudal nucleus subcuneiformis (similar AP and L coordinates; D 6.5–7.5 mm). Deposits were made by passing 700 nA +DC current for 7 min with the pipette left in place for an additional 30 min to minimize diffusion. After a 1-week survival, animals were anesthetized, transcardially perfused with saline and 10% formalin, the brain and spinal cord removed, blocked and placed in 30% sucrose formalin. The tissue was then processed for autoradiography employing Kodak NTB2 emulsion, D-19 developer and Rapid Fix. Two sets of slides were prepared for each animal. The first series had a 5-week and the second a 15-week exposure time. The 25-μm sections were counterstained with Cresyl violet and coverslipped.

WGA-HRP studies

Five Sprague–Dawley rats (250–300 g) anesthetized with equithesin received injections of WGA-HRP (Sigma) to the ventral medulla (NRM/NMC) which was electrophysiologically located as previously described[31,32]. Pressure injections (7 p.s.i. for 3–8 min) were made with a glass micropipette (tip diameter 10–12 μm) filled with a 1% solution of WGA-HRP in buffered aqueous solution. After a 3-day sur-

vival time, animals were deeply anesthetized, transcardially perfused with aldehyde fixative, and the brain processed for TMB histochemistry as previously described[30].

RESULTS

Stimulation studies

Following electrical stimulation, maximal increase in tail-flick latency occurred during the 1-min and 3-min behavioral tests; by 5 min latencies began to return to prestimulation levels and by the 7-min test latencies had returned to baseline. Maximum increase in tail-flick latencies was observed at a mean current intensity of 187 ± 11 μA during the 3-min post-stimulation test (Fig. 1). During the 10-s period of electrical stimulation, ipsilateral circling behavior occurred followed by a period of muscle rigidity which dissipated within 20–30 s of stimulus cessation. Statistical analysis indicated that the increase in tail-flick latency observed 3 min after electrical stimulation (Fig. 1) was highly significant ($t = 8.79$, df = 30, $P < 0.0001$). Prior treatment with the cholinergic receptor blocker, scopolamine (50 mg/kg) blocked the effect of NCF stimulation on tail-flick latency (prestimulation versus post-stimulation latency comparison, $P > 0.10$) as did prior treatment with the narcotic antagonist, naloxone (4 mg/kg, $P > 0.10$).

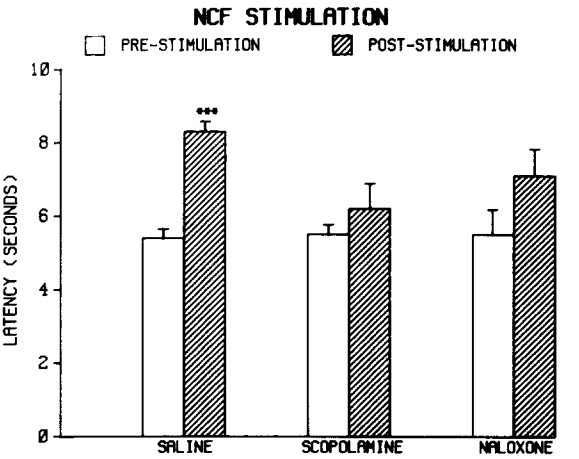

Fig. 1. The effect of NCF electrical stimulation on the nociceptive tail-flick reflex. A significant 50% increase in response latency was observed 3 min following NCF stimulation. No significant increase in latency was observed following NCF stimulation when animals were pretreated with scopolamine (50 mg/kg) or naloxone (4 mg/kg).

WGA-HRP experiments

Five moderate to large WGA-HRP injections to the NRM/NMC were made to identify the extent of the NCF projections to the ventral medulla. In all cases retrogradely labeled cells were observed in the same tegmental regions, however, the number of labeled cells per region appeared related to the size of the injection site. Case WGA-HRP 57 was chosen for illustration because it represented the largest injection site. Labeled cells were observed at the most caudal portion of NCF at rostral pontine levels immediately dorsal to the lateral parabrachial nucleus and the superior cerebellar peduncle (Fig. 2F). Few labeled cells in the PAG or the dorsal raphe were observed at this level. Rostrally, at the level of the maximal extent of the dorsal nucleus of the lateral lemniscus, a few labeled cells were observed immediately dorsal to the latter nucleus bilaterally with the density of labeled cells increasing medially (Fig. 2E). Also at this level labeled cells were observed in the dorsal raphe. The number of labeled cells increased rostrally as the decussation of the superior cerebellar peduncle became prominent with a mediolaterally distributed band of labeled cells occurring at this level similar to that observed caudally. These cells were located through NCF and laterally into the microcellular tegmental nucleus, which demonstrates substantial staining of acetyl cholinesterase[23]. Cells extended dorsally from the mediolaterally situated band of HRP cells with labeled cells observed throughout the deep layer of the ipsilateral superior colliculus. At more rostral levels, a similar pattern of labeled cells was observed, with the density of labeled cells increasing dramatically in NCF at the level of the troclear and oculomotor nuclei (Fig. 2A–C). Beyond the level of the oculomotor nucleus, labeled cells dissipated with no retrogradely labeled cells observed through the rostral 2 mm of NCF. Based on these data and other studies of the afferent connections of this most rostral portion of NCF[30], it appears likely that the rostral portion of NCF as defined by Taber[28] is actually a distinct reticular nucleus.

Autoradiographic studies

Eight iontophoretic ^{3}H-amino acid injections were

made into NCF at the level of the troclear and oculomotor nuclei. The pattern of orthograde labeling was similar across cases, therefore, typical results are illustrated from case ARG 159 (Fig. 3) which bore a relatively small (1.2 mm diameter) injection in NCF at the location identified in previous experiments from which electrical stimulation produced maximal analgesia and monosynaptic driving of single NRM units[3].

Several groups of labeled fibers coursed from the injection site centered in NCF (Fig. 3H). At the level of the injection, fibers coursed medially with terminal fields observed throughout the ipsilateral PAG. Fibers projected ventrolaterally from the injection site, through nucleus linearis with a substantial number turning dorsally to innervate the nucleus of the dorsal raphe and the remainder continuing ventral to the MLF and sweeping dorsally to innervate the contralateral NCF. Additional fibers coursed dorsally from the injection site around the annular ring giving off fibers of passage to the deep nucleus of the superior colliculus, ipsilaterally. These fibers crossed the midline dorsal to the PAG then moved ventrally, projecting to the more dorsal aspects of the contralateral NCF.

Two groups of descending fibers were observed. One group coursed dorsolaterally from the injection site crossing the midline through nucleus linearis which was innervated, and more caudally through the decussation of the superior cerebellar peduncle. Fibers moved ventral to join the ventral tegmental bundle with projections to the pontine reticulotegmental nucleus, nucleus reticularis pontis caudalis (RPOC; Fig. 3I), nucleus reticularis gigantocellularis (Fig. 3J), nucleus reticularis magnocellularis (Fig. 3J,K) and raphe magnus. This contralateral projection could not be traced beyond the level of the rostral medulla. Ipsilateral to the injection, labeled fibers coursed caudally to innervate caudal levels of NCF while moving ventrally through the superior cerebellar peduncle and nucleus subcoeruleus to occupy a position in the ventral aspect of RPOC which was innervated (Fig. 3I). At the level of the caudal pons, fibers cut in cross-section were observed coursing dorsolaterally from the main group of fibers. These fibers gave rise to a strong terminal field throughout the parvocellular reticular formation in the rostral medulla (Figs. 3I–L, 4B). The main group of descending ipsilateral fibers continued through the ventral medulla providing a substantial innervation to NMC and to a lesser extent NRM.

Ascending fibers coursed in a tight bundle through NCF and the immediately adjacent portion of the PAG (Fig. 3E,F) projecting to the ipsilateral PAG (Fig. 4A), the nucleus of Darkschewitsch, the Edinger-Westphal nucleus, and to a lesser extent the contralateral PAG. Fibers coursed ventrolaterally from the main group of fibers and projected to the substantia nigra, zona compacta and lateralis as well as the mesencephalic reticular formation medial to lateralis. This ventrolaterally coursing fiber group crossed the midline in the ventral tegmental decussation, moved laterally around the medial lemniscus to innervate the mesencephalic reticular formation medial to the substantia nigra. At rostral levels of the red nucleus, the ventral group of ascending fibers coursed through the ventral tegmental area of Tsai to innervate the zona inserta. Additional fibers from this group coursed dorsolaterally (Fig. 3D) to join the optic tract to project to the dorsolateral geniculate (Fig. 3C).

Rostral to the red nucleus the main group of ascending fibers occupied a position dorsal to the medial lemniscus (Fig. 3D). A subgroup of these fibers coursed ventrally around the medial lemniscus to innervate the Fields of Forel (Fig. 3C), the lateral hypothalamic nucleus and the lateral aspect of the anterior hypothalamic nucleus ipsilaterally and nucleus reuniens (Fig. 3B). The remaining ascending fibers coursed medially as part of the central tegmental tract to innervate nucleus parafascicularis (Fig. 3C), nucleus centromedianus, the intermediolateral thalamic nucleus (Fig. 3B), and the lateral thalamic nucleus (Fig. 3A,B).

Subcuneiformis. Six injections were made 1.0–2.0 mm ventral to the NCF in nucleus subcuneiformis; as the course of labeled fibers was similar in these 6 cases a typical case is illustrated in Fig. 5. The injection site was approximately 1 mm in diameter and located in caudal subcuneiformis at the level of the red nucleus. Labeled ipsilateral descending fibers moved as a group ventrally to occupy a position medial to the ventral nucleus of the lateral lemniscus at rostral pontine levels with fibers given off to the ventrolateral aspect of nucleus reticularis pontis oralis (Fig. 5H,I). Fibers could not be traced to caudal pontine levels.

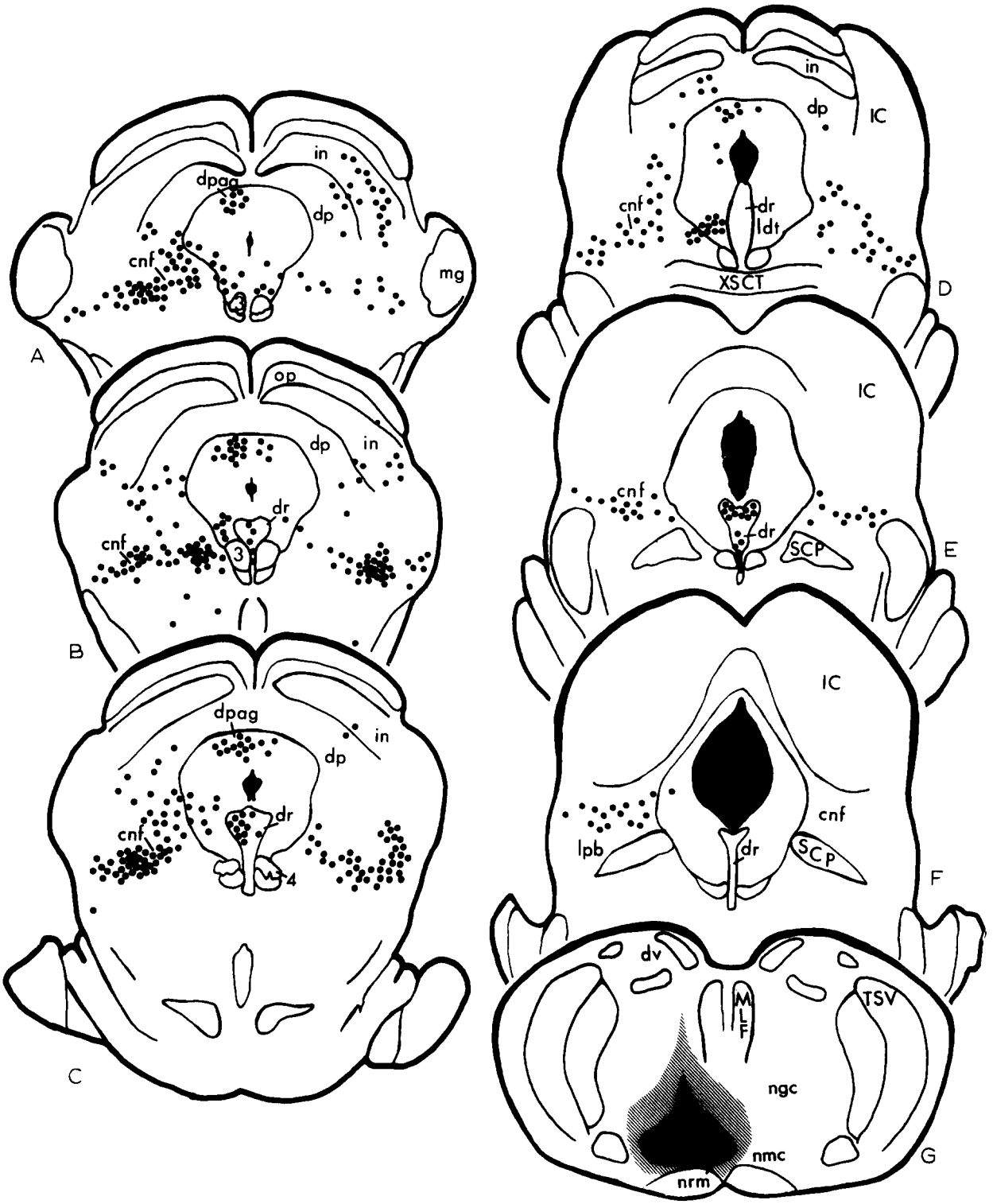

Fig. 2. The distribution of retrogradely labeled cells in the mesencephalon and pons following WGA-HRP microinjection to the ventral medulla.

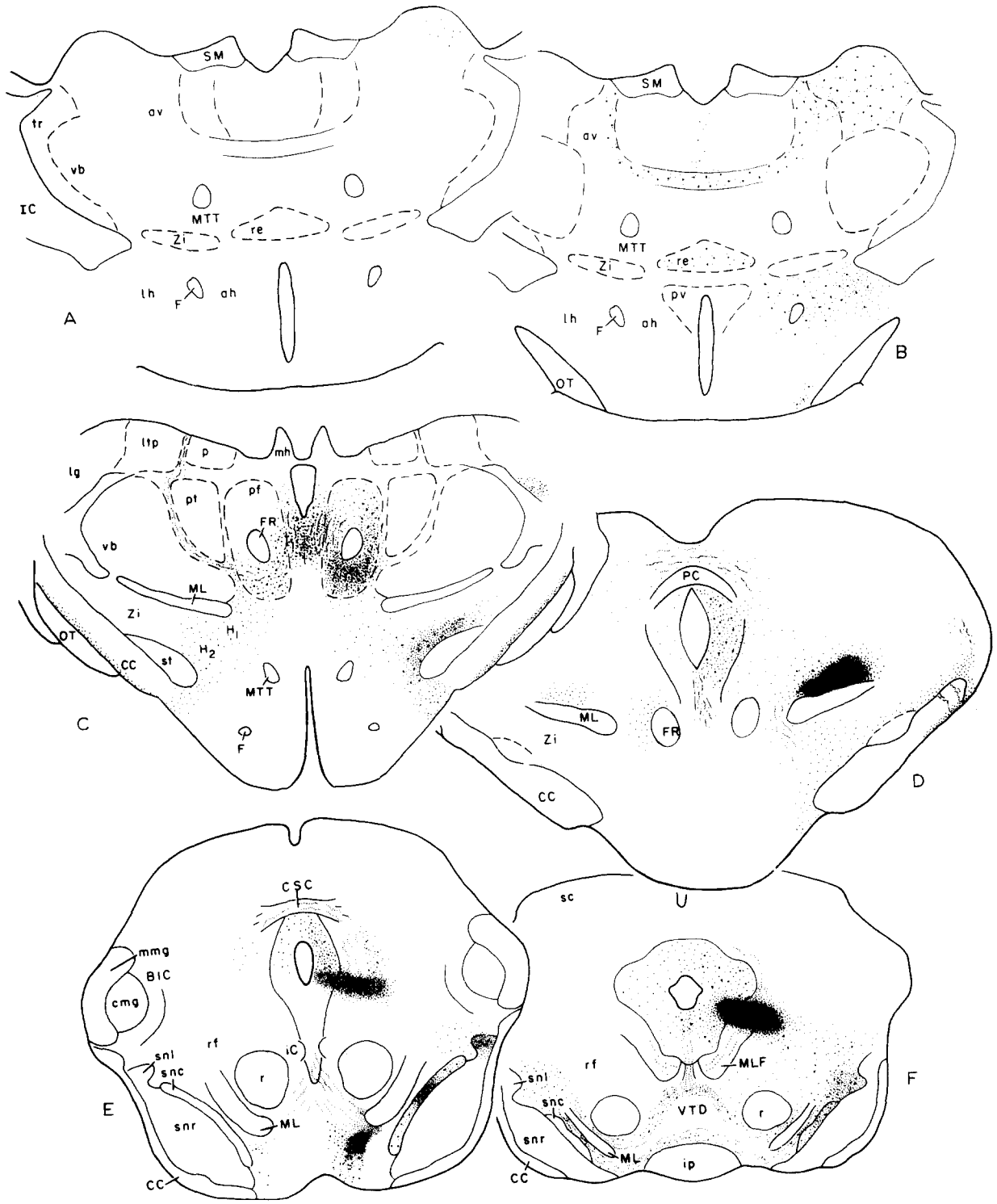

Fig. 3. A-L: the distribution of labeled fibers after ^{3}H-amino acid injections into NCF illustrated in H.

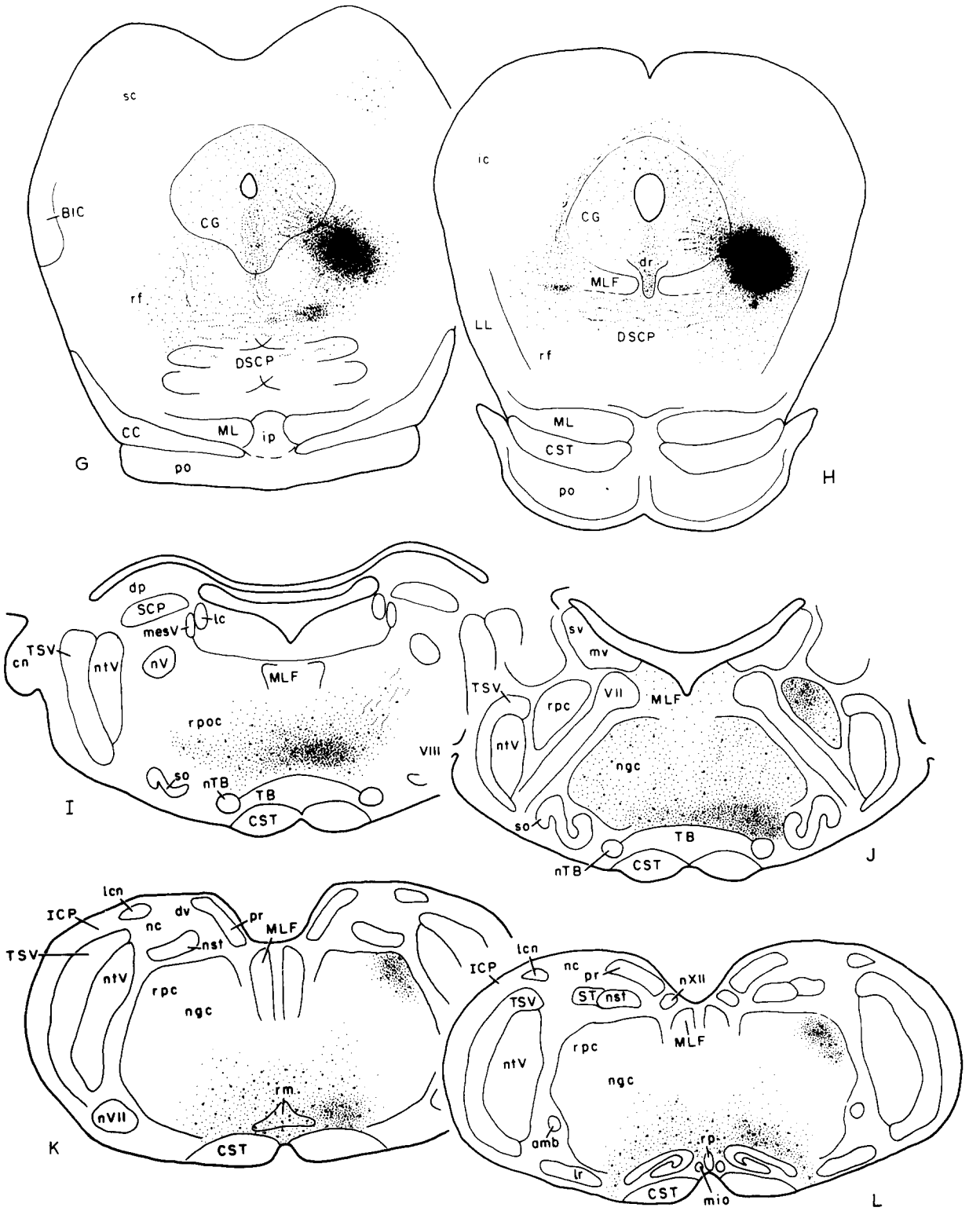

Fig. 3 (continued).

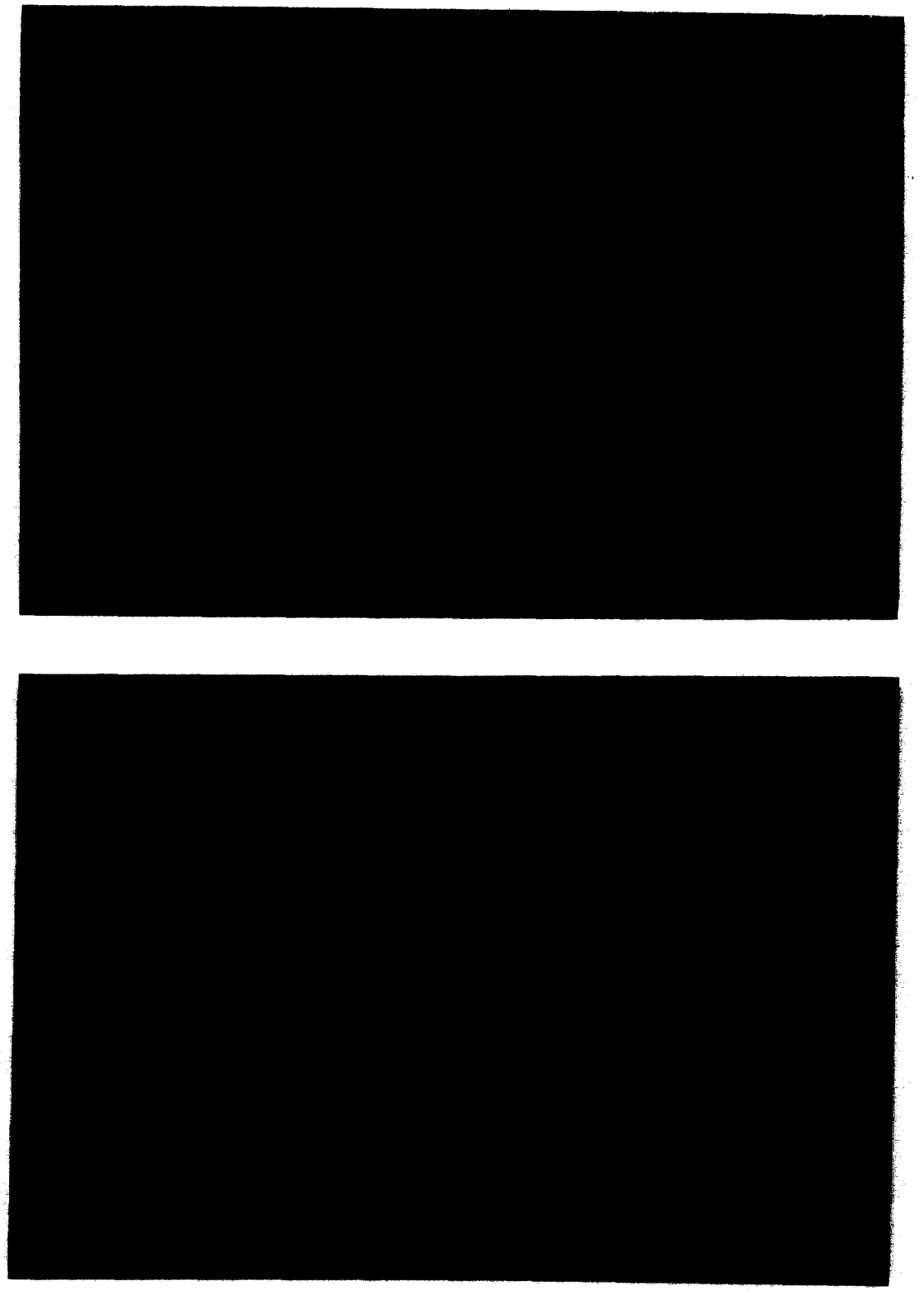

Fig. 4. A: ipsilateral labeling of the rostral PAG following ^{3}H-amino acid injection to NCF. Cerebral aqueduct is located at center with posterior commissure located immediately above. Photomicrograph corresponds with Fig. 3D. B: descending projection to the parvocellular reticular formation following NCF injection.

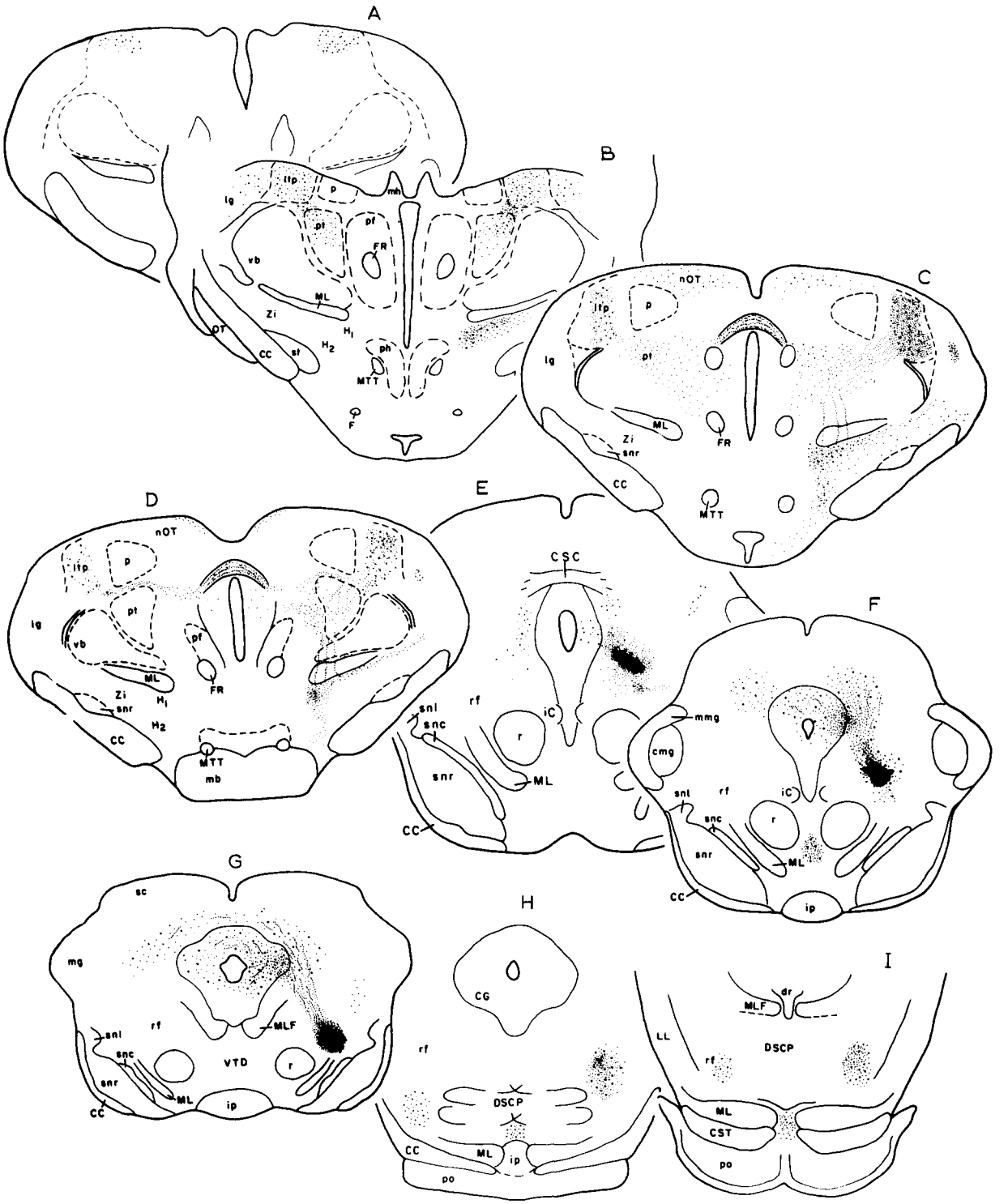

Fig. 5. A-I: distribution of labeled fibers following ^{3}H-amino acid injection into nucleus subcuneiformis which is illustrated in F.

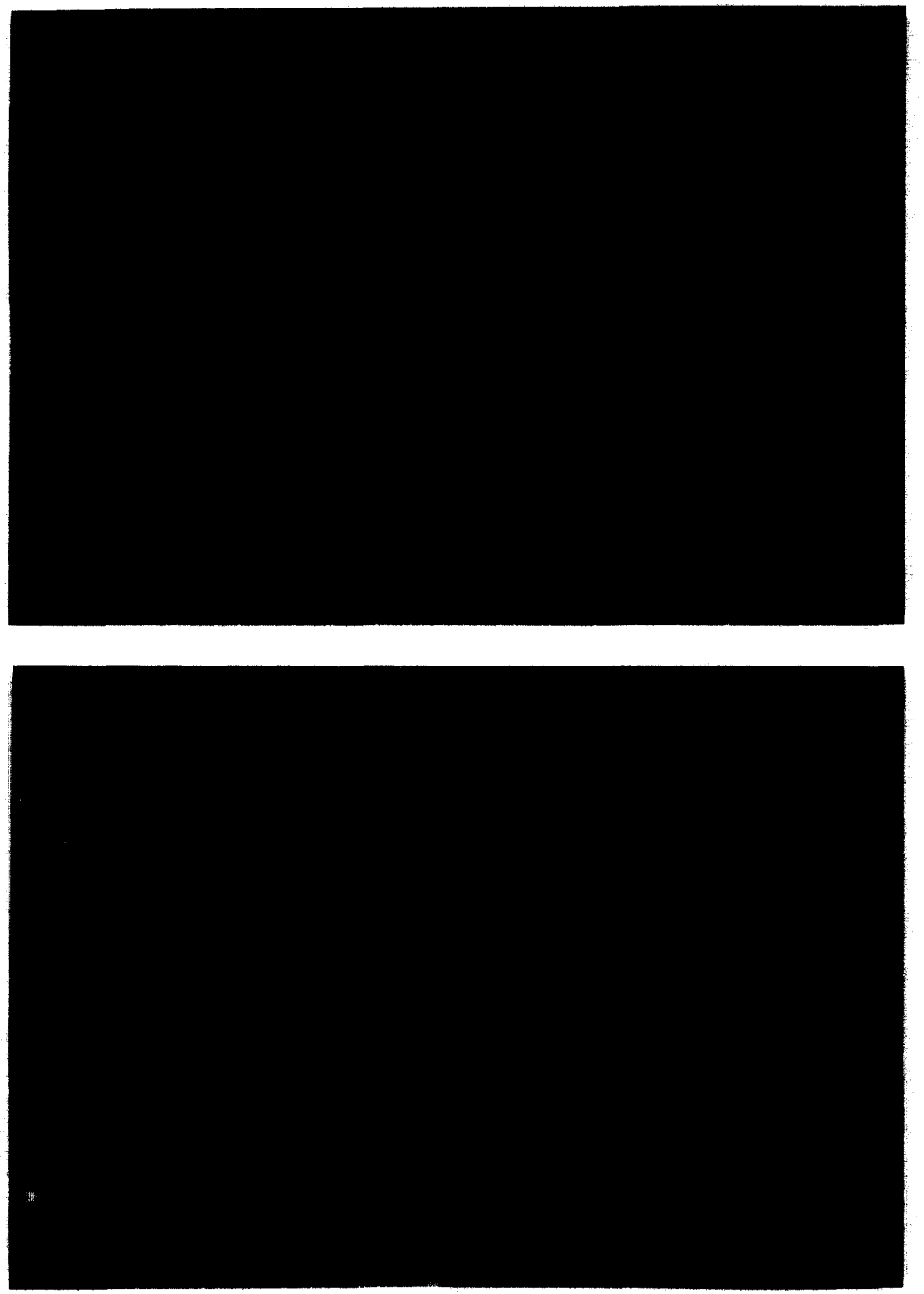

Fig. 6. A: fiber bundle ascending in the ipsilateral central tegmental tract following ^{3}H-amino acid injection of nucleus subcuneiformis. Photomicrograph corresponds to Fig. 5H. Medial is to the left of the illustration and ventral is at the bottom. B: rostral to Fig. 6A labeled fibers turned medial from the main group of ascending fibers in the central tegmental tract, decussated through the posterior commissure which is illustrated in this photomicrograph and projected to the lateral thalamic nucleus as shown in Fig. 5A–D.

Contralaterally, fibers coursed medially from the injection site, crossed through the caudal portion of the ventral tegmental decussation; then turned caudally to course near the fibers of the rubrospinal tract. Projections were given off to the ventrolateral aspect of nucleus reticularis pontis oralis. Labeled fibers could not be traced beyond the rostral pons.

Rostral to the injection site fibers moved as a group dorsomedially to join the central tegmental tract (Fig. 5F,G). Fibers coursed dorsally from the main group to innervate the PAG and adjacent deep layers of the superior colliculus, with the strongest projection to the ipsilateral side. Through the diencephalon, labeled fibers coursed ventral to the medial lemniscus giving off projections to ventrally located regions including the Fields of Forel, the Zona Incerta and the lateral hypothalamic nucleus (Fig. 6A). Additional fibers coursed dorsally to innervate the pretectal nucleus, lateral thalamic nucleus and a restricted portion of the dorsal lateral geniculate (Fig. 5A–D) with fibers reaching the contralateral pretectal and lateral thalamic nuclei by coursing through the posterior commissure (Fig. 6B).

DISCUSSION

The present behavioral studies indicate that electrical stimulation of caudal NCF results in a significant increase in nociceptive reflex latency, an effect which was both scopolamine and naloxone reversible. The reported autoradiographic and histochemical studies indicate that NCF projects to several anatomical regions which have been implicated in the modulation of pain transmission and sensory/motor integration.

Anatomical studies

The purpose of the present anatomical studies was to define the afferent projections of the pontomesencephalic region which when stimulated produces analgesia and activates the descending analgesia system in the ventral medulla (NRM/NMC). In a previous study, we demonstrated that caudal NCF stimulation was most effective in producing short-latency excitation of NRM neurons[3]. In the present study, electrical stimulation of the same region inhibited the nociceptive tail-flick reflex while the present HRP data indicate that the major afferent input to the ventral medulla arises from caudal NCF (Figs. 1 and 2). Consistent with these HRP data, the present autoradiographic study demonstrated a strong projection from caudal NCF to the ventral medulla (Fig. 3). The only other autoradiographic study of the pontomesencephalic reticular formation in the rat found no descending projections to any region of the pons or medulla[29]. This difference in projections can be explained by the more lateral and rostral location of the injection sites in this study in comparison to the earlier study which is discussed below[29]. In the cat, a strong projection from NCF to the ventral medulla[12] and from the pontopeduncular/cuneiformis region to the ventral medulla[11] has been reported in autoradiographic studies.

Two major cholinergic cell groups, not associated with motoneurones, have been identified in the pontomesencephalic reticular formation[21,23,27]. These choline acetyltransferase- and acetylcholine esterase-positive cells occur throughout caudal NCF with the largest concentration of cells located medial to NCF in the lateral tegmental nucleus and ventrolateral to NCF in the pedunculopontine nucleus. Although from these immunohistochemical studies it is known that these cells provide about 80% of the cholinergic input to the thalamus[21]; their descending projections have not been anatomically determined. In this regard, we have demonstrated that the majority of NRM neurons responding to electrical stimulation of NCF also respond to iontophoretic application of acetylcholine and that the effect of NCF stimulation on NRM units can be attenuated or blocked in the majority of cases by iontophoretic application of the cholinergic antagonist, scopolamine[3]. These data are consistent with the hypothesis that a major cholinergic projection exists between NCF and the ventral medulla. In the present study, the ability of scopolamine to block the effect of NCF stimulation on nociceptive reflex activity (Fig. 1) suggests that the ascending and descending cholinergic projections from the NCF region play an important role in sensory/motor integration.

In the present study, substantial numbers of labeled cells were observed throughout the deep layer of the superior colliculus (Fig. 1A–D) and the ventral aspect of the intermediate layer of the superior colliculus (Fig. 2A,B) which has previously been reported in the rat[4], cat[2] and monkey[8]. This observa-

tion lends support to the suggestion of Edwards[13] that based on cell morphology and projection the deep layers of the superior colliculus are reticular in nature and not intimately associated with the superior colliculus. Further, these data indicate that, as the large cells characteristic of the intermediate layers of the superior colliculus are located dorsally, the more ventral aspect of the intermediate layer appears to be a transition zone between the reticular formation and the more specific sensory portion of the colliculus.

Comparison of the ascending projections from the caudal NCF region identified in the present study with other studies in the rat and cat suggest that this area may be clearly demarcated from adjacent structures on the basis of afferent and efferent projections and histochemical criteria. As suggested by Paxinos and Watson[24], nucleus cuneiformis refers to the caudal portion of the region defined by Taber[28] as nucleus cuneiformis, while the more rostral portion of Taber's nucleus cuneiformis is named the deep mesencephalic nucleus. Employing this nosology, nucleus cuneiformis extends rostrally to the level of the oculomotor nucleus which is the rostral extent of NCF neurons projecting to the ventral medulla (Fig. 2A). At this level NCF is bordered ventrally by the A8 dopamine cell group, medially by the PAG, laterally by the brachium of the inferior colliculus and merges dorsally with the deep layers of the superior colliculus with which it has many cytoarchitectural[13] and anatomical similarities[4]. At the level of the trochlear nucleus, NCF is ventrally demarcated by the decussation of the superior cerebellar peduncle and the pedunculopontine nucleus which is functionally associated with the extrapyramidal motor system. In the present study, not projections to motor structures such as the entopeduncular nucleus, globus pallidus or motor cortex were observed from NCF, while other autoradiographic studies in which the injection sites included the pedunculopontine nucleus identified extensive projections to pyramidal or extrapyramidal motor areas[11,26,29]. At this level, the microcellular tegmental nucleus appears at the lateral boundary of NCF[22]. The microcellular nucleus can be distinguished from NCF by the high density of small diameter cells (mean diameter 10.5 μm) in the former which are strongly AChE reactive[23]. At caudal levels NCF is bordered dorsally by the external cortex of the inferior colliculus, laterally by the dorsal nucleus of the lateral lemniscus and ventrally by the superior cerebellar peduncle and the microcellular nucleus. At the transition to the caudal pons, NCF dissipates to be replaced by the choline acetyl transferase- and calcium gene-related peptide-positive cells of the lateral parabrachial nucleus[19,27].

Behavioral studies

In the present study, electrical stimulation of NCF in the awake rat produced a significant increase in tail-flick latency during the 5 min following stimulation. Similarly, electrical stimulation of NCF during behavioral testing or as a conditioning volley resulted in increased tail-flick latencies and suppression of the nociceptive jaw-opening reflex in the anesthetized rat and cat[10,25]. Several lines of evidence suggest that this increase in nociceptive reflex latency may result from impaired motor function following electrical stimulation. In the present study, during the period of electrical stimulation ipsilateral circling behavior occurred. This behavioral observation is consistent with the present autoradiographic data indicating a strong projection from NCF to the substantia nigra, zona compacta which when electrically stimulated results in ipsilateral circling behavior[9]. Similarly, electrical stimulation of the PAG in the awake rat and cat produces an increased threshold to noxious stimulation which is routinely associated with motor effects (rotation, tremor, gnawing)[14].

Several observations suggest that the increase in tail-flick latency seen in the present study was not due exclusively to motor inhibition, but rather was a direct effect on central processing of sensory information reflecting a stimulation-produced analgesia. First, no evidence of motor impairment was noted during the 1- to 7-min post-stimulation testing period. Second, reported latencies (Fig. 1) are from the 3-min post-stimulation test session. All animals demonstrated the behavioral response, of normal magnitude, during the preceding 1-min post-stimulation test indicating that they were capable of performing the required motor activity. Third, the effect of NCF stimulation of tail-flick latency was reversed by the narcotic antagonist, naloxone (Fig. 1). As the effect of naloxone is mediated by stereoselective high affinity binding to opiate receptors associated with CNS analgesia systems[17], the naloxone reversibility of the NCF stimulation effect is consistent with other

types of stimulation-produced analgesia. For example, electrical or chemical stimulation of the PAG which is medially adjacent to NCF results in behaviorally observed analgesia that is naloxone reversible[1,18,20]. Further, interpretation of the behavioral effects of NCF stimulation as either exclusively sensory or exclusively motor may be a false dicotomy. In the present study, NCF was found to project to anatomical areas usually associated with modulation of sensory systems (NRM/NMC, midline thalamic areas) and motor systems (substantia nigra). Similarly, NCF stimulation inhibits the response of dorsal horn nociceptive neurons to noxious stimulation[6,7,15,16] and inhibits the magnitude (EMG) of the flexor reflex[5]. Therefore, the function of NCF may be related to the modulation of both sensory and motor systems.

ACKNOWLEDGEMENTS

We wish to thank Greta Harris for technical assistance with the study and Karen Parker for manuscript preparation.

ABBREVIATIONS

3	oculomotor nucleus
4	trochlear nucleus
ah	anterior hypothalamic nucleus
amb	nucleus ambiguus
av	anterior ventral hypothalamic nucleus
BIC	brachium of the inferior colliculus
CC	crus cerebri
CG	central gray matter
cmg	central nucleus of the medial geniculate body
cn	cochlear nucleus
cnf	nucleus cuneiformis
csc	commissure of the superior colliculus
CST	corticospinal tract
dp	dorsal parabrachial nucleus
dpag	dorsal nucleus of the periaqueductal gray matter
dr	dosal raphe
DSCP	decussation of the superior cerebellar peduncle
dv	descending vestibular nucleus
F	fornix
FR	fasciculus retroflexus
H_1,H_2	fields of Forel
iC	interstitial nucleus of Cajal
IC	internal capsule
ICP	inferior cerebellar peduncle
in	intercalated nucleus of the medulla
ip	interpeduncular nucleus
ldt	lateral dorsal tegmental nucleus
lc	locus coeruleus
lcn	lateral cuneate nucleus
lh	lateral hypothalamic nucleus
LL	lateral lemniscus
lpb	lateral parabrachial nucleus
lr	lateral reticular nucleus
ltp	lateral thalamic nucleus, posterior portion
mb	mammillary body
mesV	mesencephalic nucleus of the trigeminal nerve
mg	medial geniculate body
mh	medial habenular nucleus
mio	medial inferior olive
ML	medial lemniscus
MLF	medial longitudinal fasciculus
mmg	marginal nucleus of the medial geniculate body
MTT	mammillothalamic tract
mv	medial vestibular nucleus
nc	cuneate nucleus
ngc	nucleus reticularis gigantocellularis
nmc	nucleus reticularis magnocellularis
nOT	nucleus of the optic tract
nrm	nucleus raphe magnus
nst	nucleus of the solitary tract
nTB	nucleus of the trapezoid body
ntV	nucleus of the spinal trigeminal tract
nV	motor nucleus of the trigeminal nerve
nVII	nucleus of the facial nerve
nXII	nucleus of the hypoglossal nerve
op	optic nerve layer of the superior colliculus
OT	optic tract
p	pretectal nucleus
PC	posterior commissure
pf	nucleus parafascicularis
ph	posterior hypothalamic nucleus
po	pontine nuclei
pr	nucleus prepositus
pt	posterior thalamic nucleus
pv	paraventricular nucleus
r	red nucleus
re	nucleus reuniens
rf	reticular formation
rm	nucleus raphe magnus
rp	nucleus raphe pallidus
rpc	nucleus reticularis parvocellularis
rpoc	nucleus reticularis pontis caudalis
sc	superior colliculus
SCP	superior cerebellar peduncle
SM	stria medullaris
snc	substantia nigra, zona compacta
snl	substantia nigra, lateral portion
snr	substantia nigra, reticular portion
so	superior olive
st	subthalamic nucleus
ST	solitary tract
sv	superior vestibular nucleus
TB	trapezoid body
tr	reticular thalamic nucleus
TSV	tract of spinal V
vb	ventrobasal complex
VTD	ventral tegmental decussation
XSCT	decussation of the superior cerebellar tract
Zi	zona incerta

Numerals on brain sections refer to cranial nerves:

VII	facial nerve
VIII	vestibular nerve

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