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Research report

Afferents of vocalization-controlling periaqueductal regions in the squirrel monkey

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Abbreviations: A1, primary auditory cortex; ab, ambigual nucleus; ac, nucleus accumbens; aca, claustro-amygdaloid region; adh, dorsal hypothalamic region; ALD, "Aldi" (name of experimental animal); alh, lateral hypothalamic region; amh, medial hypothalamic region; ann, annular nucleus; ap, preoptic region; aph, posterior hypothalamic region; apl, lateral preoptic region; apm, medial preoptic region; apr, prerubral area; apt, pretectal region; ARN, "Arnold" (name of experimental animal); atv, ventral tegmental area; av, anterior ventral thalamic nucleus; ba, basal amygdala; baa, accessory basal amygdala; bal, accessory basolateral amygdala; bam, accessory basomedial amygdala; bc, brachium conjunctivum; BER, "Berry" (name of experimental animal); bla, basolateral amygdala; bma, basomedial amygdala; bp, brachium pontis; c, cochlear nucleus; cb, cerebellum; cc, corpus callosum; Cca 24, anterior cingulate cortex; Ccp 23, posterior cingulate cortex; cd, caudate nucleus; cea, central amygdala; cei, central inferior thalamic nucleus; cel, central lateral thalamic nucleus; Cet 28, entorhinal cortex; Cfa 6, frontal agranular cortex; Cfg 9, frontal granular cortex; Cfi 8, frontal intermediate cortex; Cfo 44, frontal opercular (ventrolateral) cortex; Cgp 4, giant pyramidal cortex; cho, optic chiasm; CIs, insular cortex; cl, claustrum; cm, centromedian thalamic nucleus; cn, cuneate nucleus; Co, 18 occipital cortex; coa, amygdaloid body; coi, inferior colliculus; coiC, inferior colliculus, central nucleus; coiD, inferior colliculus, dorsal nucleus; coiX, inferior colliculus, external nucleus; Cop 19, preoccipital cortex; cos, superior colliculus; cosI, superior colliculus, intermediate layer; cosP, superior colliculus, profound layer; cosS, superior colliculus, superficial layer; Cp 5/7, parietal cortex; Cpc 1/2, postcentral parietal cortex; Cpe 35, perirhinal cortex; Cpf 10, frontopolar cortex; Cpm 32, medial prefrontal cortex; Cpo 11, posterior orbital cortex; Crs 29/30, retrosplenial cortex; Csb 27, subiculum; Cst 17, striate cortex; Cti 20, inferior temporal cortex; Ctm 21, middle temporal cortex; Ctp 38, polar temporal cortex; Cts 22, superior temporal cortex; dg, dorsal tegmental nucleus of Gudden; dh, dorsal hypothalamic nucleus; dmh, dorsomedial hypothalamic nucleus; dr, dorsal raphe nucleus; dv, dorsal nucleus of the vagal nerve; ep, epiphysis; FA 8, frontal eye-field; fc, cuneate funiculus; FLI, "Flizi" (name of experimental animal); frm, medullary reticular formation; frpc, caudal pontine reticular formation; frpo, rostral pontine reticular formation; frtm, mesencephalic reticular formation; fx, fornix; g, nucleus gracilis; gcd, dorsal central gray; gcv, ventral central gray; gl lateral, geniculate body; gm, medial geniculate body; gp, globus pallidus; gph, periventricular hypothalamus; gpm, mesencephalic periventricular gray; gpr, pregeniculate gray; Gr 12, rectal gyrus; Gsc 25, subcallosal cortex; hip, hippocampus; hl, lateral habenula; Ia, agranular insula; Id, dysgranular insula; Ig, granular insula; i.m., intramuscularly; ip, interpeduncular nucleus; isc, interstitial nucleus of Cajal; KOL, "Kolja" (name of experimental animal); la, lateral amygdala; lc, locus coeruleus; lcb, lingula cerebelli; ld, laterodorsal thalamic nucleus; lim, nucleus limitans; lld, dorsal nucleus of the lateral lemniscus; llv, ventral nucleus of the lateral lemniscus; lm, medial lemniscus; lp, lateral posterior thalamic nucleus; ma, medial amygdala; md, mediodorsal thalamic nucleus; ml, lateral mammillary nucleus; mm, mammillary body; MT, middle temporal field; MUL, "Müller-Lüdenscheidt" (name of experimental animal); nap, nucleus of the ansa peduncularis; ncp, nucleus of the posterior commissure; ncs, central tegmental superior nucleus; nct, trapezoid nucleus; nfdb, nucleus of the diagonal band of Broca; nIII, oculomotor nucleus; nIV, nucleus of the trochlear nerve; nmv, mesencephalic trigeminal nucleus; nr, red nucleus; nst, nucleus of the stria terminalis; nsV, spinal trigeminal nucleus; nts, nucleus of the solitary tract; nVI, nucleus of the abducent nerve; nVII, nucleus of the facial nerve; oi, inferior olivary complex; os, superior olivary complex; p, posterior thalamic nucleus; Pa, postauditory field; pag, periaqueductal gray; pbl, lateral parabrachial nucleus; pbm, medial parabrachial nucleus; pc, paracentral thalamic nucleus; PC, cerebral peduncle; pd, peripeduncular nucleus; pg, parabigeminal nucleus; ph, periventricular hypothalamic nucleus; Pi, parainsular cortex; plld, dorsal paralemniscal zone; pllv, ventral paralemniscal zone; pm, medial preoptic nucleus; po, pons; pp, nucleus praepositus; pre-SMA, presupplementary motor area; ptc, pretectal nucleus; pu, pulvinar complex; puo, oral pulvinar nucleus; put, putamen; pv, periventricular thalamic nucleus; pvc, caudal periventricular thalamic nucleus; py, pyramidal tract; r, reticular thalamic nucleus; rab, retroambigual nucleus; reu, nucleus reuniens; Ri, retroinsular cortex; rl, lateral reticular nucleus; rtp, pontine tegmental reticular nucleus; s, septal area; SC, sulcus cinguli; s.c., subcutaneous; sg, medullary gray substance; sgD, dorsal medullary gray substance; sgV, ventral medullary gray substance; si, substantia innominata; SII, secondary somatosensory cortex; smh, supramammillary nucleus; sn, substantia nigra; snc, substantia nigra, pars compacta; snd, substantia nigra, pars diffusa; st, stria terminalis/subthalamic nucleus; T1, superior temporal cortex; T2, middle temporal cortex; T3, inferior temporal cortex; to, olfactory tract; TP, temporoparietal cortex; trs, triangular septal nucleus; vIII, third ventricle; va, ventral anterior thalamic nucleus; ves, vestibular nuclei; vesI, inferior vestibular nucleus; vesL, lateral vestibular nucleus; vesM, medial vestibular nucleus; vesS, superior vestibular nucleus; vl, ventrolateral thalamic nucleus; vmh, ventromedial hypothalamic nucleus; vp, ventral posterior thalamic nucleus; vr, ventral raphe nucleus; zi, zona incerta.

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Abstract

In order to determine the input of vocalization-controlling regions of the midbrain periaqueductal gray (PAG), wheat germ agglutinin-horseradish peroxidase was injected in six squirrel monkeys (*Saimiri sciureus*) at PAG sites yielding vocalization when injected with the glutamate agonist homocysteic acid. Brains were scanned for retrogradely labeled areas common to all six animals. The results show that the vocalization-eliciting sites receive a widespread input, with the heaviest projections coming from the surrounding PAG, dorsomedial and ventromedial hypothalamus, medial preoptic region, substantia nigra pars diffusa, zona incerta and reticular formation of the mesencephalon, pons, and medulla. The heaviest cortical input reaches the PAG from the mediofrontal cortex. Moderate to weak projections come from the insula, lateral prefrontal, and premotor cortex as well as the superior and middle temporal cortex. Subcortical moderate to weak projections reach the PAG from the central and medial amygdala, nucleus of the stria terminalis, septum, nucleus accumbens, lateral preoptic region, lateral and posterior hypothalamus, globus pallidus, pretectal area, deep layers of the superior colliculus, the pericentral inferior colliculus, mesencephalic trigeminal nucleus, locus coeruleus, substantia nigra pars compacta, dorsal and ventral raphe, vestibular nuclei, spinal trigeminal nucleus, solitary tract nucleus, and nucleus gracilis. The input of the periaqueductal vocalization-eliciting regions thus is dominated by limbic, motivation-controlling afferents; input, however, also comes from sensory, motor, arousal-controlling, and cognitive brain areas.

Theme: Neural basis of behavior
Topic: Neuroethology

Keywords: Vocalization; *Saimiri sciureus*; Periaqueductal gray; Brain stimulation; Horseradish peroxidase

1. Introduction

The midbrain periaqueductal gray (PAG) is assumed to play an essential role in the vocal expression of emotional states. Various findings suggest that it represents a crucial relay station of the limbic vocalization pathway. Localized electrical stimulation of the PAG has been shown to produce species-specific vocalization in numerous species (for review, see Ref. [45]). Vocalization can also be obtained by injection of glutamate agonists and GABA antagonists (cat: [6]; squirrel monkey: [48]), suggesting that the PAG does not only contain fibers of passage, but also synapses of the vocalization pathway. Single-unit recording studies have revealed vocalization-correlated activity in the PAG [27,58]. Lesion studies have reported mutism after bilateral destruction of the PAG and bordering tegmentum in various experimental animals, as well as in human patients (rat: [19]; cat: [51,83,94]; dog: [93]; squirrel monkey: [47]; humans: [15,30]). Partial destruction of the PAG does not affect the acoustical structure of vocalization in general, but abolishes discrete vocal reactions, while leaving others intact [47,51,94]. After inactivation of the PAG by injections of the GABA agonist muscimol, naturally sounding vocalization is still elicitable in regions of the caudal midbrain and rostral pons [91]. This suggests that the PAG serves gating functions rather than vocal pattern generation. In other words, its function probably is to trigger vocal output on the basis of motivational and sensory input. Neuroanatomical studies have revealed a major input from various limbic regions to the PAG [11,16,20,24,32,38,39,57,64,66,67,78]. Besides limbic afferents, projections from sensory structures have been also described [8,13,50,60,65]. Apart from the Kyuhou and Gemba study [57], however, none of these studies has investigated the input into functionally verified vocalization-controlling regions of the PAG. The present study will fill this gap.

2. Materials and methods

The experiments were carried out in six adult male squirrel monkeys (*Saimiri sciureus*), weighing 790–1060 g. Under general anesthesia (40 mg pentobarbital sodium per kg body weight), a dental acrylic platform (35 × 20 mm) containing numerous stainless steel guiding tubes (outer diameter 0.8 mm) was mounted on the animal's skull in a stereotaxic surgery according to the procedure described by MacLean [62]. The head was fixed in a stereotaxic apparatus (David Kopf Instruments, Tujunga, USA), the skin was incised with a midsagittal cut, and stainless steel screws were anchored in the skull by the help of nuts and dental cement (Paladur®, Kulzer GmbH, Germany). The platform was positioned above the skull with a stereotaxic carrier in such a way that the guiding tubes were just above the PAG (according to the anterior/posterior and medial/lateral coordinates taken from the stereotaxic atlas of Gergen and MacLean [34]). The platform then was fixed to the screws with dental cement, and the stereotaxic platform height was measured for determination of the length of the electrode to be implanted. Stereotaxic target positions of the guiding tubes for reaching the PAG were AP4 to AP-1 and L0.5 to 1.5. All experimental animals received prophylactically antibiotic treatment, the first time immediately after surgery and a second time 3 days later (0.3 ml/kg i.m. penicillin-streptomycin combination, Tardomyocel III Compositum®, Bayer, Germany). Analgesic treatment was applied if required (0.1 ml/kg s.c. flunixine-meglumine, Finadyne® 1%, Essex Pharma, Germany).