BRAIN RESEARCH 1358 (2010) 123–139

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BRAIN RESEARCH

Research Report

Projections from the hypothalamic paraventricular nucleus and the nucleus of the solitary tract to prechoroidal neurons in the superior salivatory nucleus: Pathways controlling rodent choroidal blood flow ☆

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ARTICLE INFO

Article history:
Accepted 20 August 2010
Available online 27 August 2010

Keywords:
Biotinylated dextran amine (BDA)
Pseudorabies virus (PRV)
Fluorogold (FG)

ABSTRACT

Using intrachoroidal injection of the transneuronal retrograde tracer pseudorabies virus (PRV) in rats, we previously localized preganglionic neurons in the superior salivatory nucleus (SSN) that regulate choroidal blood flow (ChBF) via projections to the pterygopalatine ganglion (PPG). In the present study, we used higher-order transneuronal retrograde labeling following intrachoroidal PRV injection to identify central neuronal cell groups involved in parasympathetic regulation of ChBF via input to the SSN. These prominently included the hypothalamic paraventricular nucleus (PVN) and the nucleus of the solitary tract (NTS), both of which are responsive to systemic BP and are involved in systemic sympathetic vasoconstriction. Conventional pathway tracing methods were then used to determine if the PVN and/or NTS project directly to the choroidal subdivision of the SSN. Following retrograde tracer injection into SSN (biotinylated dextran amine 3K or Fluorogold), labeled perikarya were found in PVN and NTS. Injection of the anterograde tracer, biotinylated dextran amine 10K (BDA10K), into PVN or NTS resulted in densely packed BDA10K+ terminals in prechoroidal SSN (as defined by its enrichment in nitric oxide synthase-containing perikarya). Double-label studies showed these inputs ended directly on prechoroidal nitric oxide synthase-containing neurons of SSN. Our study thus establishes that PVN and NTS project directly to the part of SSN involved in parasympathetic vasodilatory control of the choroid via the PPG. These results suggest that control of ChBF may be linked to systemic blood pressure and central control of the systemic vasculature.

0006-8993/$ – see front matter. Published by Elsevier B.V.
doi:10.1016/j.brainres.2010.08.065

☆ Supported by the University of Tennessee Neuroscience Institute (CL), Department of Ophthalmology unrestricted grant from Research to Prevent Blindness (MECF), Benign Essential Blepharospasm Research Foundation Inc. (ML), NIH-EY-12232 (ML), NIH-EY-05298 (AR), and NIH/NEI-5P30EY013080 (D. Johnson).

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Abbreviations: 6, abducens nucleus; 10, dorsal motor nucleus of vagus; 12, hypoglossal nucleus; 3V, third ventricle; 7n, facial nerve; 8cn, cochlear root of 8n; 8n, vestibulocochlear nerve; 8vn, vestibular root of 8n; A5, A5 noradrenaline cells; Acs7, accessory facial nucleus; AD, anterodorsal thalamic nucleus; AH, anterior hypothalamus; Amb, ambiguus nucleus; AP, area postrema; Arc, arcuate nucleus; AV, anteroventral thalamic nucleus; AVPe, anteroventral periventricular nucleus; BAOT, bed nucleus of accessory olfactory tract; BDA, biotinylated dextran amine; BDA3K, biotinylated dextran amine 3000 kDa MW; BDA10K, biotinylated dextran amine 10,000 kDa MW; BLA, anterior part of basolateral amygdaloid nucleus; BMA, anterior part of basomedial amygdaloid nucleus; BP, blood pressure; BST, bed nucleus of stria terminalis; C3, C3 adrenaline cells; CA3, field CA3 of hippocampus; cc, corpus callosum; Ce, central amygdaloid nucleus; cg, cingulum; ChAT, choline acetyltransferase; ChBF, choroidal blood flow; CLSM, confocal laser scanning microscope; CM, central medial thalamic nucleus; CPu, caudate putamen; CxA, cortex–amygdala transition zone; cu, cuneate fasciculus; Cu, cuneate nucleus; DAB, diaminobenzidine tetrahydrochloride; das, dorsal acoustic stria; DC, dorsal cochlear nucleus; DH, dorsomedial hypothalamus; DV, dorsoventrally; ec, external capsule; ECu, external cuneate nucleus; En, endopiriform cortex; f, fornix; FG, Fluorogold; fi, fimbria of hippocampus; g7, genu of facial nerve; Gi, gigantocellular reticular nucleus; GiA, alpha part of gigantocellular reticular nucleus; Gr, gracile nucleus; HDB, nucleus of horizontal limb of diagonal band; IAM, interanteromedial thalamic nucleus; ic, internal capsule; icp, inferior cerebellar peduncle; IM, intercalated nucleus of amygdala; IO, inferior olive; ISN, inferior salivatory nucleus; IRt, intermediate reticular nucleus; LA, lateroanterior hypothalamus; LC, locus coeruleus; LD, laterodorsal thalamic nucleus; LGP, lateral globus pallidus; LH, lateral hypothalamus; LPGi, lateral paragigantocellular nucleus; LPO, lateral preoptic area; LRt, lateral reticular nucleus; LSO, lateral superior olive; m7, facial nucleus; MD, mediodorsal thalamic nucleus; Me, medial amygdaloid nucleus; ml, medial lemniscus; mlf, medial longitudinal fasciculus; MPO, medial preoptic nucleus; mt, mammillothalamic tract; MVe, medial vestibular nucleus; NO, nitric oxide; NOS, nitric oxide synthase; NTS, nucleus of solitary tract; opt, optic tract; ox, optic chiasm; P5, peritrigeminal zone; Pa6, para-abducens nucleus; Pr5, principal trigeminal nucleus; PAG, periaqueductal central gray; PAP, peroxidase–antiperoxidase; PBL, lateral parabrachial nucleus; pd, predorsal bundle; PDTg, posterodorsal tegmental nucleus; Pir, piriform cortex; PK15, porcine kidney cells; PMn, paramedian raphe nucleus; PnC, caudal pontine reticular nucleus; PnV, ventral pontine reticular nucleus; PPG, pterygopalatine ganglion; PPy, parapyramidal nucleus; Pr, prepositus nucleus; PRV, pseudorabies virus; PT, paratenial thalamic nucleus; PVA, anterior part of paraventricular thalamic nucleus; PVA, paraventricular thalamic nucleus; PVN, paraventricular nucleus; py, pyramid; RAmb, retroambiguus nucleus; Re, reunions; Rh, rhomboid thalamic nucleus; RMg, raphe magnus; unc, uncinate fasciculus; ROb, raphe obscurus nucleus; RPa, raphe pallidus nucleus; rs, rubrospinal tract; Rt, reticular thalamic nucleus; RVLM, rostroventral lateral medulla; SCG, superior cervical ganglion; SCN, suprachiasmatic nucleus; scp, superior cerebellar peduncle; SD, Sprague-Dawley; sm, stria medullaris of thalamus; sol, solitary tract; SO, superior olive; SON, supraoptic nucleus; sox, supraoptic decussation; Sp5, spinal trigeminal nucleus; sp5, spinal trigeminal tract; SPO, superior paraolivary nucleus; SSN, superior salivatory nucleus; st, stria terminalis; Sub, submedius thalamic nucleus; ts, tectospinal tract; VA, ventral anterior thalamic nucleus; VDB, nucleus of vertical limb of diagonal band; VeCb, vestibulocerebellar nucleus; VeL, lateral vestibular nucleus; VeM, medial vestibular nucleus; VeS, superior vestibular nucleus; VIP, vasoactive intestinal polypeptide; VL, ventrolateral thalamic nucleus; VM, ventromedial thalamic nucleus; VMH, ventromedial hypothalamic nucleus; VPL, ventral posterolateral thalamic nucleus; VPO, ventral paraolivary nucleus; vsc, ventral spinocerebellar tract; ZI, zona incerta

1. Introduction

The choroid contains the blood supply to the outer retina. The choroid and blood vessels supplying the choroid are innervated by parasympathetic, sympathetic, and sensory nerve fibers that adaptively regulate choroidal blood flow (ChBF) according to retinal need (Bill, 1984; Bill, 1985; Bill, 1991; Cuthbertson et al., 1996; Cuthbertson et al., 1997; Fitzgerald et al., 1990a; Fitzgerald et al., 1990b; Fitzgerald et al., 1996; Guglielmone and Cantino, 1982; Kirby et al., 1978; Stone et al., 1987). Such adaptive control may be important for maintaining the health of retinal photoreceptors and maintaining normal visual function (Fitzgerald et al., 1990a; Fitzgerald et al., 1990b; Fitzgerald et al., 2001; Hodos et al., 1998; Potts, 1966; Reiner et al., 1983; Shih et al., 1993; Shih et al., 1994). The pterygopalatine ganglion (PPG) is the major source of parasympathetic input to the choroid and orbital vessels, and this input utilizes two vasodilators: vasoactive intestinal polypeptide (VIP) and nitric oxide (NO) (Alm et al., 1995; Bill, 1984; Bill, 1985; Bill, 1991; Ruskell, 1971a; Stone, 1986; Stone et al., 1987; Uddman et al., 1980a; Yamamoto et al., 1993). These fibers also appear to be cholinergic (Johansson and Lundberg, 1981; Lundberg et al., 1981; Lundberg et al., 1982; Suzuki et al., 1990).

The PPG receives its preganglionic input from the superior salivatory nucleus (SSN) of the hindbrain via the greater petrosal branch of the facial nerve (Contreras et al., 1980; Ng et al., 1994; Nicholson and Severin, 1981; Schrödl et al., 2006; Spencer et al., 1990; Tóth et al., 1999). The SSN itself is located dorsolateral to the rostral part of the facial motor nucleus. The SSN neurons, which are somewhat intermingled with noradrenergic neurons of the more rostrally situated A5 cell group, are cholinergic. In rats, rabbits and humans, a subset has been reported to contain nitric oxide synthase (NOS), as well (Cuthbertson et al., 2003; Gai and Blessing, 1996; Zhu et al., 1996; Zhu et al., 1997). The SSN also provides preganglionic input via the corda tympani nerve to the submandibular ganglion (Contreras et al., 1980; Jansen et al., 1992; Ng et al., 1994; Nicholson and Severin, 1981), which sends postganglionic fibers to the submandibular and sublingual glands, and thereby regulates blood flow and salivary secretion within these glands (Izumi and Karita, 1994). The PPG, in addition to its innervation of choroidal and orbital blood vessels, also innervates the Meibomian glands, the lacrimal gland, the Harderian gland, blood vessels of the nasal mucosa and palate, and cerebral blood vessels (LeDoux et al., 2001; Nakai et al., 1993; Ruskell, 1965; Ruskell, 1971b; Ten Tusscher et al., 1990;