Available online at www.sciencedirect.com

SCIENCE DIRECT

Brain Research 1035 (2005) 154–167

BRAIN RESEARCH

www.elsevier.com/locate/brainres

Research report

Behavioral effects of 8-OH-DPAT injections into pontine and mesencephalic areas containing 5-HT-immunoreactive perikarya in the pigeon

Luciane P.N. Häckl, Graciela de Oliveira Richter, Moacir Serralvo Faria, Marta A. Paschoalini, José Marino-Neto*

Department of Physiological Sciences-CCB, Federal University of Santa Catarina, 88040-900 Florianópolis, SC, Brazil

Accepted 9 December 2004
Available online 2 February 2005

Abstract

This study examined the distribution of 5-HT-immunoreactive perikarya (5-HT-IRp) and the effects of local injections of 8-OH-DPAT into 5-HT-IRp-containing pontine and mesencephalic regions on feeding and drinking behaviors in free-feeding pigeons. When infused into the midline 5-HT-IRp-containing areas, 8-OH-DPAT (6.1 nmol) reliably elicited drinking and, to a lesser extent, feeding responses during the first hour after injection. These responses were significantly higher than the ingestive indexes observed (1) after vehicle (ascorbic acid 0.1%, 200 nl) injections at the same sites and (2) after 8-OH-DPAT injections into adjacent sites devoid of 5-HT-IRp. Increases in drinking were proportionally higher than those observed in feeding and a significant negative correlation was observed between water and food after midline 8-OH-DPAT injections. Similar dipsogenic responses were observed after injections of different 8-OH-DPAT doses (0.6, 2.0, and 6.1 nmol). Pretreatment with local injections of p-MPPI (an antagonist of 5-HT_{1A} receptors) attenuated the ingestive responses evoked by 8-OH-DPAT injections. Injections of 8-OH-DPAT into lateral 5-HT-IRp-containing sites evoked only inconsistent and weak ingestive responses. These results indicate that 5-HT_{1A} receptor-mediated circuits located in the midline superior raphe system of the pigeon may play an important role in mechanisms controlling water intake, similar to that observed in mammals.

Theme: Neural basis of behavior
Topic: Ingestive behaviors

Keywords: Food intake; Water intake; 5-HT 1A receptor; Avian; Raphe nuclei

Abbreviations: aq, aqueduct; Ann, nucleus annularis; AVT, area ventralis (Tsai); BCD, brachium conjunctivum descendens; Cb, cerebellum; CS, nucleus centralis superior; ep, ependyma; EW, Edinger–Westphal nucleus; FLM, fasciculus longitudinalis medialis; FRL, formatio reticularis lateralis mesencephali; FRM, formatio reticularis magnocellularis mesencephali; GCt, substantia grisea centralis; IO, nucleus isthmo-opticus; IP, nucleus interpeduncularis; LC, nucleus linearis caudalis; LoC, nucleus locus coeruleus (r = rostral, c = caudal part); MPv, nucleus mesencephalicus profundus, pars ventralis; nIII, nucleus nervi oculomotorii; NIII, oculomotor nerve; nIV, nucleus nervi trochlearis; nBOR, nucleus of the basal optic root; nDBC, nucleus decussationis brachiorum conjunctivorum; Pap, nucleus papillioformis; PM, nucleus pontis medialis; qf, tractus quintofrontalis; R, nucleus raphe superior, pars ventralis; RPgc, nucleus reticularis pontis caudalis, pars gigantocellularis; RPO, nucleus reticularis pontis oralis; Ru, nucleus ruber; SCd, nucleus subcoeruleus dorsalis; SCv, nucleus subcoeruleus ventralis; TPc, nucleus tegmenti pedunculo-pontinus, pars compacta; TV, nucleus tegmenti ventralis (Gudden); 4V, 4th ventricle; VT, nucleus ventrolateralis tegmenti (after Challet, 1996); zpFLM, zona peri fasciculus longitudinalis medialis; zpIP, zona peri nucleus interpeduncularis

* Corresponding author. Fax: +55 048 231 9672.
E-mail address: marino@ccb.ufsc.br (J. Marino-Neto).

0006-8993/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.brainres.2004.12.004

1. Introduction

Increases in the activity of central serotonin (5-HT) systems have been repeatedly shown to inhibit feeding behavior, while the decrease in firing rate of 5-HT neurons produced by the activation of somatodendritic 5-HT_{1A} receptors through systemic or intra-raphe injections of 8-hydroxy-2(di-*n*-propylamino)tetralin (8-OH-DPAT) increases food intake in free-feeding rats [3,11,13,20,21,22,28,35,45,54]. 5-HT circuits have also been shown to play an important role in hydrosaline homeostasis and in the regulation of angiotensin-mediated water intake in mammals by acting on both peripheral [55] and central mechanisms [7,10,36,38,39,40,49,44,58]. In line with these data, the mesencephalic raphe nuclei have been shown to exert an important role in the control of ingestive (of food, water and alcohol) behaviors through both serotonergic and non-serotonergic mechanisms (see Ref. [63], for a recent review).

Central serotonergic mechanisms appear to have important roles in the control of ingestive behavior also in avian species. The ingestive effects of central injections of 5-HT in chickens and turkeys appear to depend on the lineage examined [17–19], while in the pigeon, a species that was not artificially selected for a particular feeding or growth phenotype, intracerebroventricular (ICV) 5-HT injections provoke hypophagic responses as well as a marked, angiotensin II-dependent, increase in water intake [6,57]. The hypophagic responses, but not increased water intake, were observed in pigeons after ICV injections of the 5-HT-2A/2C agonist DOI [57]. Dipsogenic responses were not observed after ICV injections of 5-HT in other avian species [17–19]. On the other hand, ICV injections of 8-OH-DPAT in 24-h food-deprived [57] or in free-feeding pigeons [16] have been shown to produce a strong dipsogenic effect and a mild potentiation of the deprivation-induced increase in the duration of feeding behavior, but had no effect on food intake 1 h after treatment. In contrast to these data, systemic injections of 8-OH-DPAT in layer chickens [52] evoked late (60 min after injections) increases in food intake in fed animals (without significant effects on water intake), reduced food intake (without changes in water intake) in 16-h food-deprived animals, and potentiated the water intake increase after 16 h of water deprivation (with a late increase in food intake). These data suggest that the ingestive effects of this drug are not only dependent on the nutritional state (as observed in mammals, see Refs. [21,23]) but are also species-dependent.

While substantial data indicate the existence of serotonergic systems in the avian brain (chicken: [27,41,65,66]; quail: [12]), the distribution of 5-HT-immunoreactive perikarya (5-HT-IRp) in the pigeon's brainstem has been extensively described in only one report [9]. These studies revealed that, in parallel to mammalian species, 5-HT-IR somata in the pigeon's brain are mainly found in a number of midline (raphe) brainstem nuclei located at rostral pontine and mesencephalic levels (the raphe superior), at caudal pontine and medullary levels (the raphe inferior), as well as in the dorsolateral pontine tegmentum (the lateral group). As indicated by a number of studies confined to selected brain areas examining the distribution of 5-HT-IR fibers in the pigeon [4,27,42,50,53,61], these areas originate extensive ascending and descending fiber systems extending from the spinal cord to the rostral telencephalon. In addition, 5-HT-IR, CSF-contacting cell bodies are also found in a circumventricular organ (the paraventricular organ) of the posterior third ventricle of birds, which appears to represent a distinctive attribute of non-mammalian vertebrates. While the brainstem 5-HT-IRp-containing areas of avian species have been collectively compared to the mammalian raphe nuclei with regard to neurochemical and anatomical aspects, the behavioral effects of direct experimental manipulations of serotonergic neurotransmission in these areas have not been investigated in birds.

It is interesting that, in contrast to results obtained in rats, the pigeon has been found to be a very sensitive model to probe for anxiolytic effects of 5-HT-1A receptor agonists (such as 8-OH-DPAT and buspirone) when tested in conflict procedures that manipulate ingestive behaviors. Systemic injections of these drugs increase operant (key-pecking) feeding responses in trials during which this response is punished by an electrical shock, but do not change response levels during non-punished trials (e.g., [2,32–34]). It is thus apparent that data regarding the effects of these drugs on drinking, feeding, and other spontaneous behaviors in pigeons may also be relevant to understanding of the mechanisms associated with the special sensitivity of this species to behavioral effects of 5-HT-1A agonists. To date, however, the behavioral effects of direct experimental manipulations in these distinct brainstem serotonergic areas have not been investigated in birds.

In the present study, we examined the effects of 8-OH-DPAT injections into 5-HT-IRp-containing areas in the rostral brainstem on feeding, drinking, and sleep-like behaviors in free-feeding (FF) pigeons, as well as the effects of the pretreatment with 4-Iodo-*N*-[2-[4-methoxyphenyl)-1-piperaziny]ethyl]-*N*-2pyridinyl-benzamide hydrochloride (p-MPPI, a selective 5-HT_{1A} receptor antagonist, see Refs. [37,59]) on 8-OH-DPAT-induced behaviors. Serial sections of the pigeon's brainstem, oriented according to stereotaxically relevant coordinates, were immunohistochemically processed to reveal 5-HT-containing perikarya and fibers, and were used to further examine and describe the distribution of these elements and to estimate the position of the injection cannula as located in or out of the 5-HT-IRp-containing pontine and mesencephalic areas.

2. Materials and methods

2.1. Animals

All the experimental procedures described below were conducted in strict adherence to the recommendations found