Available online at www.sciencedirect.com
ScienceDirect
European Journal of Pharmacology 559 (2007) 184–188
www.elsevier.com/locate/ejphar

Short communication

The effects of 8-hydroxy-2-(di-*n*-propylamino)-tetralin (8-OH-DPAT) on food intake in non-deprived C57BL6 mice

Ivor S. Ebenezer [a,b,*], Ashya Surujbally [a]

[a] *Neuropharmacology Research Group, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK*
[b] *Institute of Biomedical and Biomolecular Sciences, University of Portsmouth, Portsmouth, PO1 2DZ, UK*

Received 17 August 2006; received in revised form 27 December 2006; accepted 8 January 2007
Available online 19 January 2007

Abstract

The effects of the $5HT_{1A}$ agonist 8-hydroxy-2-(di-*n*-propylamino)-tetralin (8-OH-DPAT) were investigated on food intake in non-deprived mice. 8-OH-DPAT (50–200 mg/kg) administered subcutaneously (s.c.) 5 min prior to presentation of food, produced a dose-related increase in cumulative food intake in C57BC6 mice. The hyperphagic effect of 8-OH-DPAT (100 mg/kg, s.c.) was abolished by concurrent treatment with the $5HT_{1A}$ receptor antagonist *N*-[2-(4-2-methoxyphenyl)-1-piperazinyl]-*N*-(2-pyridyl) cyclohexanecarboxamide (WAY100635; 0.3 mg/kg, s.c.). These data show that 8-OH-DPAT produces an increase in food consumption in non-deprived mice by a $5\text{-}HT_{1A}$ receptor-mediated mechanism of action.
© 2007 Published by Elsevier B.V.

Keywords: $5\text{-}HT_{1A}$ receptors; Food intake; 8-OH-DPAT; WAY100635; (Mouse)

1. Introduction

Research carried out over the past 30 years has suggested that brain 5-hydroxytryptamine (5-HT; serotonin) plays an important role in the control of feeding behaviour (Blundell, 1977, 1984; Simansky, 1996). 5-HT acts at a number of different receptor subtypes (Hoyer et al., 2002), and it has been generally found that drugs that are agonists at these multiple 5-HT receptors decrease food intake (Blundell, 1984). By contrast, however, it was demonstrated that the $5\text{-}HT_{1A}$ receptor agonist 8-hydroxy-2(di-*n*-proylamino)tetralin (8-OH-DPAT) produces hyperphagia in non-food-deprived rats (Dourish et al., 1985) in a behaviourally specific manner (Ebenezer, 1992). Subsequently, similar effects on food intake were obtained for other $5\text{-}HT_{1A}$ receptor agonists, such as buspirone and gepirone (Gilbert and Dourish, 1987; Fletcher and Davis, 1990; Ebenezer, 1993). The mechanism by which these $5\text{-}HT_{1A}$ receptor agonists increase feeding has been the subject of much research, and converging evidence from electrophysiological, neurochemical, and behavioural studies have suggested that these drugs act at $5\text{-}HT_{1A}$ somatodendritic autoreceptors in the raphe nucleus to decrease 5-HT function in the central nervous system (CNS) (Bendotti and Samanin, 1986; Sprouse and Aghajanian, 1987; Hjorth and Magnusson, 1988; Sharp and Hjorth, 1990). Thus, their mechanism of action remains consistent with the putative inhibitory role of 5-HT in the control of ingestive behaviour.

Most of the research on $5\text{-}HT_{1A}$ agonists and feeding behaviour has been carried out in the rat and very little work has been undertaken to see if these drugs have similar effects in other species. Recently, it has been demonstrated that 8-OH-DPAT also increases food intake in non-deprived pig (Ebenezer et al., 2001) and chicken (Saadoun and Cabrera, 2002). However, there has been a marked paucity of research on the effects of $5\text{-}HT_{1A}$ agonists and food intake in the mouse. Shepherd and Rogers (1990) demonstrated that s.c. administration of 8-OH-DPAT to free-feeding mice produced significant increases in the duration spent feeding compared with control mice. In this study, the authors administered 8-OH-DPAT 20 min prior to assessing time spent feeding for 5 min. Food intake was not measured and, as 8-OH-DPAT can induce

* Corresponding author. Neuropharmacology Research Group, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK. Tel.: +44 23 92 842661; fax: +44 23 92 843565.
E-mail address: ivor.ebenezer@port.ac.uk (I.S. Ebenezer).

0014-2999/$ - see front matter © 2007 Published by Elsevier B.V.
doi:10.1016/j.ejphar.2007.01.010

chewing (see Ebenezer, 1992), it is not clear whether there was increased food consumption. More recently, Swiergiel and Dunn (2000) reported that 8-OH-DPAT reduces consumption of a sweetened condensed milk in mice, whereas the partial 5-HT_{1A} receptor agonist ipsapirone had no effect on sweetened condensed milk intake. However, Dourish et al. (1988) have reported that non-deprived rats do not generally display hyperphagia following administration of 8-OH-DPAT when presented with sweetened condensed milk and display hypophagia at high doses of the drug. We have also shown that 5-HT_{1A} receptor agonists decrease palatable food consumption in non-deprived rats (Ebenezer and Tite, 2003; Tite and Ebenezer, 2004). The lack of an increase in food consumption following the administration of 8-OH-DPAT or ipsapirone in the mouse (Swiergiel and Dunn, 2000) may therefore be due to the fact that the animals were presented with palatable food. The present study was therefore undertaken to investigate the effects of 8-OH-DPAT on food intake in non-deprived mice given access to their normal diet so that comparisons could be made with the effects of the 5-HT_{1A} receptor agonist in other species where hyperphagic responses has been reported (see above).

2. Methods and materials

The protocols used in this study were approved by the Ethical Review Committee at the University of Portsmouth.

2.1. Experiment 1. Effects of subcutaneous administration of 8-OH-DPAT on food intake in C57BL6 mice

Male C57BL6 mice (body weight: 29–32 g, $n=14$) were divided into two equal groups, designated the Control Group and the Treatment Group. The animals were housed in groups of 7 according to their designated group in home cages with free access to food and water. The animals were kept on a 12 h light–dark cycle; lights on at 8.00 h. and lights off at 20.00 h. All training and test sessions (see below) were undertaken during the light cycle starting at 14.00 h. The ambient temperature of the room was maintained at between 22 and 23 °C during the experiments. The mice were handled regularly for 14 days on a daily basis. This took several forms including daily gentle stroking of their heads and back, removal from their home cages and being placed in another cage and habituating them to having their weights measured on a balance. The mice were given 4 training sessions when they were allowed free access to food and water in experimental cages measuring 30×25×20 cm for 120 min. The food was similar to that consumed by the animals in their home cages and was presented as a single pellet with an average weight of 5.2 g. The nutrient composition of the food was as follows: protein 20%, oil 4.5%, fibre 5%, ash 7%+traces of vitamins and metals. The animals were also given 2 s.c. injections of physiological saline solution prior to the 2nd and 4th training session to acclimatise them to the injection procedure. During the experimental sessions that followed, the mice in the Control Group were injected subcutaneously (s.c.) with physiological saline, and those in the Treatment Group were injected s.c. with 8-OH-DPAT (50–200 μg/kg). Food was presented 5 min after injection. The amount of food consumed was measured in mg at 30 min intervals over the 120 min experimental period, as described previously (Ebenezer, 1990). The mice in the Treatment Group received all doses of 8-OH-DPAT in an ascending order of 50, 100 and 200 μg/kg, while the mice in the Control Group received saline injections during each trial. A dry-out period of 7 days separated successive trials.

2.2. Experiment 2. Effects of N-[2-(4-2-methoxyphenyl)-1-piperazinyl]-N-(2-pyridyl) cyclohexanecarboxamide (WAY 100635) and 8-OH-DPAT on food intake in C57BL6 mice

Male C57BL6 (body weight: 30–32 g, $n=16$) were divided into two equal groups and housed in groups of 8. The mice were handled and trained to eat in the experimental cages as described for Experiment 1. During the experimental trials, the mice in Group 1 were injected s.c. with saline or with 8-OH-DPAT (200 μg/kg). The mice in the Group 2 were injected s.c. with a solution containing WAY 100635 (300 μg/kg) or WAY 100635 (300 μg/kg)+OH-DPAT (200 μg/kg). Food was presented 5 min after the injection. The amount of food consumed was measured 30 min after presentation. The mice in each group received both treatments designated to that group in a cross-over design. A dry-out period of 4 days separated successive trials.

2.3. Drugs

8-Hydroxy-2-(di-*n*-propylamino)-tetralin and WAY 100635 were purchased from Sigma Biochemicals, Dorset, UK. The drugs were dissolved in physiological saline solution (0.9% $^{w}/_{v}$ NaCl) and administered s.c. in a volume of 10 ml/kg. Physiological saline solution was used in control experiments.

2.4. Statistical analysis

Two way analysis of variance (ANOVA) with repeated measures was performed on the cumulative intake data at each measurement time point for Experiment 1 to determine effects of treatment (saline vs. 8-OH-DPAT) and experimental trials on food consumption. The Neuman Keul test was used for *post-hoc* comparisons. The data from Experiment 2 was analysed by two way analysis of variance with repeated measures on trials within groups and *post-hoc t*-tests (Winer, 1971).

3. Results

3.1. Experiment 1. Effects of subcutaneous administration of 8-OH-DPAT on food intake in C57BL6 mice

The effects of s.c. administration of 8-OH-DPAT (50–200 μg/kg) on food intake measured over 120 min in non-deprived C57BL6 mice are shown in Fig. 1. For illustrative clarity, Fig. 1A shows the cumulative effects of saline and 8-OH-DPAT (50 μg/kg) on food intake measured during the first experimental trial, Fig 1B shows the cumulative effects of saline and 8-OH-DPAT (100 μg/kg) measured during the second

Download English Version:

https://daneshyari.com/en/article/2536369

Download Persian Version:

https://daneshyari.com/article/2536369

Daneshyari.com