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Short communication

Intraperitoneal administration of baclofen increases consumption of both solid and liquid diets in rats

Ivor S. Ebenezer

Neuropharmacology Research Group, School of Pharmacy and Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, Hampshire, UK

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Abstract

It has previously been demonstrated that systemic administration of the $GABA_B$ receptor agonist baclofen increases food intake but decreases water intake in rats. In the present study, the effects of baclofen (2–4 mg/kg i.p.) were investigated on food intake in non-deprived rats given access to either pelleted food ($n = 8$) or a palatable liquid diet ($n = 8$). Baclofen (2–4 mg/kg i.p.) significantly increased the consumption of both the pelleted and the liquid foods. The increased intake of the liquid diet (i) argues against the involvement of non-specific gnawing in the increased consumption of the solid food by baclofen, and (ii) suggests that the inhibition of water intake produced by baclofen is not due to interference with the mechanical aspects of drinking, such as licking on a drinking spout, or the swallowing of liquid.

Keywords: Baclofen; $GABA_B$ receptor; Food intake; Water intake; Palatable liquid diet

1. Introduction

The recent demonstration that both central and systemic administration of the $GABA_B$ receptor agonist baclofen increases food intake in non-deprived rats, has led to the suggestion that a $GABA_B$ mediated mechanism may be involved in the control of food intake (Ebenezer, 1990; Ebenezer and Pringle, 1992; Liljequist, 1993). However, it has also been found that both systemic and central administration of baclofen inhibits water intake in response to water deprivation and the administration of a number of dipsogenic agents (Ebenezer et al., 1992; Houston et al., 1992, 1994; Ebenezer and Houston, unpublished results). The opposite effects of baclofen on these two aspects of ingestive behaviour raise questions about the specificity of the drug on one or both of these behaviours. For example, it is well known that GABAergic drugs can induce gnawing or chewing in rats (Klitenick and Wirtshafter, 1989), and it is possible that if baclofen produces such behaviour, it could be misinterpreted as increased feeding (see Ebenezer, 1992). On the other hand, it is possible that baclofen may inhibit the ability of the rat to drink by interfering with the mechanical aspects of drinking, such as licking on a drinking spout or the swallowing of liquid, rather than having a direct effect on the central mechanisms involved in the control of drinking. The experiments reported here were therefore undertaken to test these possibilities by examining the effects of systemically administered baclofen on the consumption of food pellets and a palatable liquid diet in non-deprived rats. It was argued that if baclofen increased consumption of a liquid diet in non-deprived rats then it would be unlikely that (a) the hyperphagic effect of the drug is due to gnawing or chewing, and (b) the inhibition of water intake produced by the drug is due to interference with the mechanical aspects of drinking.

2. Materials and methods

2.1. Experiment 1

Male Wistar rats ($n = 8$, body weight 300–390 g) were housed in cages in groups of 4, where they had access to food and water ad libitum. The animals were given 6 training sessions on separate days during which time they were placed singly in experimental cages measuring $32 \times 25 \times 19$ cm for 120 min where they were allowed free access to their normal laboratory

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pelleted food and water. The food was presented to the rats in a shallow cylindrical cup, as described previously (Ebenezer, 1990; Ebenezer and Pringle, 1992). During the experimental sessions that followed, each animal was injected i.p. with either physiological saline solution or baclofen (2 or 4 mg/kg) and placed individually in the experimental cage for 120 min. Food intake was measured 60 min and 120 min after drug administration. A repeated measures design was used with the rats receiving all treatments. Four days separated successive trials.

2.2. Experiment 2

Male Wistar rats ($n = 8$, body weight 290–390 g) were housed individually in suspended grid floor cages. They had free access to their normal laboratory rat food and water except during training and experimental sessions. They were given 10 training sessions lasting 120 min each during which time they were presented with drinking bottles containing a palatable liquid food (500 ml contained 250 ml Long-Life milk (Tesco, Cheshunt, UK), 40 g soluble malted food powder (Horlicks, SmithKlineBeecham, UK), 50 g sucrose, and tap water). During experimental sessions, the rats were injected i.p. with either physiological saline or baclofen (2 or 4 mg/kg) and 5 min later presented with the palatable liquid food in their home cages. The volume of liquid food consumed was measured 30, 60 and 120 min after presentation. A repeated measures design was used with each rat receiving all treatments. Two to three days separated successive drug trials.

2.3. Statistics

The data obtained for both experiments were analysed by one-way analysis of variance (ANOVA) with repeated measures, and post-hoc tests carried out using the Newman-Keuls test (Winer, 1971).

2.4. Drugs

(±)-Baclofen (Giba-Geigy) was dissolved in physiological saline solution (0.9% w/v) to give an injection volume of 0.1 ml/100 g body weight. Physiological saline solution was used in control experiments.

3. Results

3.1. Experiment 1

Table 1 shows the effects of baclofen on the consumption of food pellets in non-deprived rats. Baclofen (2 and 4 mg/kg) produced significant increases in the cumulative food intake of the rats measured over the 120 min recording period ($F(2,14) = 24.920$, $P < 0.0001$). Further analysis of the data showed that both doses of baclofen produced significant increases in food intake during the first 60 min after administration

Table 1
Effect of baclofen (2 and 4 mg/kg i.p.) on consumption of food pellets in non-deprived rats

Treatments	Mean food intake (g) ± S.E.		
	0–60 min after i.p. injection	60–120 min after i.p. injection	0–120 min after i.p. injection
Saline	2.2 ± 0.3	1.1 ± 0.3	3.3 ± 0.3
Baclofen (2 mg/kg)	3.8 ± 0.3 [b]	1.6 ± 0.3	5.4 ± 0.3 [b]
Baclofen (4 mg/kg)	3.5 ± 0.3 [b]	2.4 ± 0.3 [a]	5.9 ± 0.3 [b]

Statistical analysis of the data (ANOVA with repeated measures) showed significant main effects of drug treatment ($F(2,14) = 24.920$, $P < 0.0001$) and time ($F(1,7) = 16.0172$, $P < 0.01$). The interaction between drug treatment and time was not significant ($F(2,14) = 2.1064$). Post-hoc comparisons between saline and baclofen treatments were carried out using the Newman-Keuls test.
[a] $P < 0.05$, [b] $P < 0.001$. $n = 8$ rats.

Table 2
Effect of baclofen (2 and 4 mg/kg i.p.) on consumption of a palatable liquid food diet in non-deprived rats

Treatment	Mean food intake (ml) ± S.E.			
	0–30 min after i.p. injection	30–60 min after i.p. injection	60–120 min after i.p. injection	0–120 min after i.p. injection
Saline	19.2 ± 0.6	0.4 ± 0.4	0.8 ± 0.8	20.3 ± 0.8
Baclofen (2 mg/kg)	25.6 ± 1.8 [a]	1.4 ± 1.4	2.3 ± 1.5	29.3 ± 1.8 [b]
Baclofen (4 mg/kg)	27.0 ± 2.7 [a]	3.0 ± 2.7	2.4 ± 1.6	32.4 ± 2.2 [c]

Statistical analysis of the data (ANOVA with repeated measures) showed significant main effects of drug treatment ($F(2,14) = 13.3240$, $P < 0.001$) and time ($F(2,14) = 87.6886$, $P < 0.001$). The interaction between drug treatment and time was not significant ($F(4,28) = 1.1413$). Post-hoc comparisons between saline and baclofen treatments were carried out using the Newman-Keuls test.
[a] $P < 0.05$, [b] $P < 0.01$, [c] $P < 0.001$. $n = 8$ rats.

($P < 0.001$ in each case), but that only the 4 mg/kg dose significantly increased feeding during the 60–120 min measurement period ($P < 0.05$) (see Table 1). Thus, the main hyperphagic effects of i.p. administered baclofen on solid food consumption in rats seems to occur during the first 60 min after administration. The 4 mg/kg dose produced mild ataxia in some of the rats during the first 10 min after injection, but this did not prevent the animals from eating.

3.2. Experiment 2

The effects of baclofen (2 and 4 mg/kg) on the consumption of a palatable liquid diet in non-deprived rats are shown in Table 2. Although the rats were not food deprived, the control intake was high (see Table 2) presumably because of the palatable nature of the food. Interestingly, however, baclofen (2 and 4 mg/kg) caused a dose-related increase in the cumulative consumption of the liquid diet measured over the 120 min recording period ($F(2,14) = 13.3240$, $P < 0.001$). Further analysis of the data revealed that both doses of baclofen caused significant increases in the consumption of the liquid food during the first 30 min after drug administration (see Table 2). Thereafter (i.e. during the 30–60 min and 60–120 min measurements periods) there were no significant effects on food intake. Nevertheless, both doses of baclofen caused small but non-significant increases in consumption of the liquid food during these intervals (Table 2).

4. Discussion

The results obtained in this study show that i.p. administration of baclofen increases both solid and liquid food consumption in non-deprived rats. These data confirm and extend previous findings which showed that subcutaneous administration of baclofen increases solid food consumption in non-deprived rats (Ebenezer and Pringle, 1992). The mechanism by which systemic administration of baclofen increases food intake is not known, but it is likely to involve central $GABA_B$ mechanisms (Ebenezer, 1990; Ebenezer and Pringle, 1992), as baclofen can cross the blood-brain barrier (Faigle and Keberle, 1972).

The present results have important implications. Firstly, the observation that baclofen increases the consumption of a palatable liquid diet suggests that the hyperphagic response is not due to non-specific effects such as chewing or gnawing. Secondly, the finding that baclofen increased consumption of a liquid meal, argues against the suggestion that the inhibitory effect of the drug on water intake (Ebenezer et al., 1992; Houston et al., 1992, 1994) may be due to inhibition of the mechanical aspects of drinking, such as licking on a drinking spout, or swallowing of liquid. Thus, the results of this study support the view that the effects of baclofen on food and water intake are behaviourally specific.

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