Pharmacology, Biochemistry and Behavior 97 (2010) 156–162

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

journal homepage: www.elsevier.com/locate/pharmbiochembeh

Intra-accumbens baclofen, but not muscimol, mimics the effects of food withdrawal on feeding behaviour

K.G.T. Pulman [a], E.M. Somerville [b], P.G. Clifton [a,*]

[a] Schools of Psychology, University of Sussex, Brighton BN1 9QG, UK
[b] Life Sciences, University of Sussex, Brighton BN1 9QG, UK

ARTICLE INFO

Available online 4 June 2010

Keywords:
$GABA_A$ receptor
$GABA_B$ receptor
Accumbens
Behavioural satiety sequence
Muscimol
Baclofen
Feeding

ABSTRACT

Intra-accumbens stimulation of GABA receptors results in a robust increase in food intake. However the differential consequences of stimulating $GABA_A$ and $GABA_B$ receptors in the nucleus accumbens have not been extensively explored with respect to feeding behaviour. Here we compare the effects of the $GABA_B$ receptor agonist baclofen and $GABA_A$ receptor agonist muscimol, infused into the nucleus accumbens shell, on food intake and related behavior patterns. Baclofen (110–440 ρmol) dose dependently enhanced intake and delayed the onset of satiety within the test period as did the effects of 4–8 h food withdrawal. Muscimol (220–660 ρmol) enhanced intake but also disrupted the sequence of associated behaviours at every dose tested. We conclude that $GABA_B$ receptors in the nucleus accumbens shell may play a role in relation to feeding motivation whereas $GABA_A$ receptors may, as previously suggested, have a more restricted role in relation to the motor components of approach to food and ingestion.

1. Introduction

Stratford and Kelley (1997) reported that a robust feeding response is induced by intra-accumbens shell administration of the $GABA_A$ receptor agonist muscimol or of the $GABA_B$ receptor agonist baclofen. The GABA transaminase inhibitor γ-vinyl–GABA, which reduces the metabolism of GABA, also increases food intake, which would be consistent with a role for endogenous GABA in the modulation of feeding (Stratford and Kelley, 1997). These manipulations are thought to locally inhibit the activity of medium spiny neurons within the accumbens and thus to release downstream centres, particularly in the lateral hypothalamus, which could drive consummatory components of feeding behaviour without necessarily increasing motivation for food (Kelley et al., 2005). This hypothesis is consistent with the observation that the onset of consummatory responses to food is characterized by inhibition of a population of neurons within the nucleus accumbens (Taha and Fields, 2005) which could permissively gate goal directed sequences of behaviour (Taha and Fields, 2006).

Behavioural support for this interpretation comes from the observation that intra-accumbens administration of baclofen selectively increased intake of solid chow, but not generalized gnawing behaviour or drinking (Ward et al., 2000). In addition intra-accumbens shell administration of muscimol increased intake of caloric diets regardless of macronutrient content but did not increase intake of palatable non-caloric solutions (Basso and Kelley, 1999). Further evidence for this view, in the case of muscimol, is provided by studies of instrumental responding for food. Thus, muscimol failed to increase lever pressing for sucrose pellets in rats trained on a progressive ratio schedule (Zhang et al., 2003). In addition intra-accumbens muscimol failed to enhance the initial acquisition of lever pressing for sucrose pellets whereas food withdrawal was effective in this regard (Hanlon et al., 2004).

The effects of intra-accumbens infusions of muscimol and baclofen on *ad libitum* consumption of food have only previously been measured in terms of total intake. Standard paradigms used to explore drug effects on appetite and satiety have not been employed. One candidate paradigm is the Behavioural Satiety Sequence (BSS) which tracks the transition from feeding to post-prandial behaviours. Richter (1922) first described the predictable pattern of activity that follows feeding in rats. He observed a distinct temporal profile of behaviours following access to food characterized by an initial period of feeding followed by exploration, a period of grooming and, eventually, 'rest' or sleep. The BSS has been used to characterise the effects of a wide variety of drug and other manipulations (Halford et al., 1998). Here we use the method to characterise the early stages of feeding behaviour and its progression towards inactivity.

The data from experiments 1 and 2 characterise the BSS elicited by intra-accumbens administration of baclofen or muscimol in pre-fed animals. The hypothesis suggested by Stratford and Kelley (1997)

* Corresponding author. Tel.: +44 1273 678396; fax: +44 1273 678058.
E-mail address: pete@sussex.ac.uk (P.G. Clifton).

0091-3057/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2010.05.028

predicts that an increase in motor behaviours specifically directed at food consumption would limit and disrupt the expression of the rest of BSS behavioural repertoire. This is supported by their observation that temporary inactivation of excitatory inputs to the accumbens also reduces "exploratory-like motor responses" (Kelley et al., 2005). The third experiment provides a reference profile for a 'natural' manipulation of the BSS under the same conditions as the previous experiments. Animals were systematically exposed to short but varied periods of food withdrawal prior to a free-feeding test period. The effects of hunger and presatiation have been demonstrated using a mash meal (Ishii et al., 2003a) and it was anticipated that the same general effects would be observed here although the timings of the transition from feeding to inactive behaviour might be different because of the use of solid chow. This food type was chosen to be in line with previous studies investigating the effects of baclofen and muscimol on feeding (Stratford and Kelley, 1997; Ward et al., 2000).

2. Methods

2.1. Animals

Male Lister hooded rats (Harlan, UK), weighing 250–275 g at the start of each experiment were initially housed in groups of 3. Separate groups of animals were used in each experiment. In Experiments 1 and 2, at least 7 days prior to surgery, and, in Experiment 3, 7 days prior to testing, they were habituated to single housing. All animals were maintained on an *ad libitum* diet of chow (SDS expanded diet) and water. The animals were held in rooms with controlled temperature (20–22°) and humidity (40–60%RH) on a 12:12 h light cycle (lights on: 07.00 h). In Experiment 2 the animals were trained on an instrumental schedule prior to surgery and were then tested on this schedule (data not reported here) prior to the BSS test. These animals were habituated to the BSS test procedure prior to and post instrumental testing and no difference in intake was observed. In Experiments 1 and 2, using centrally administered drugs, test sessions ran between 10.00–16.00 h and in Experiment 3 at 15.30 h for fasted animals.

All experimental protocols were in accordance with the Home Office Animals (Scientific Procedures) Act 1986, and were also approved by the University of Sussex Local Ethical Review Committee.

2.2. Surgery

Anaesthesia was induced with 4% isoflurane in 0.5 L/min N_2O and 0.5 L/min O_2, and then maintained by adjusting the isoflurane concentration to 1.5–2.5%. Thin wall 26ga, 16 mm stainless steel cannulae (Coopers Needleworks, UK) were implanted bilaterally aimed 2.2 mm dorsal to the target site in the accumbens shell using the coordinates anteroposterior (AP), +1.2 mm, mediolateral (ML), ±1.5 mm relative to bregma (β) and dorsoventral (DV),−5.8 mm relative to the flat skull surface (Paxinos and Watson, 1998). The cannulae were secured with three small screws, Geristore dental resin and finished with a cap of Simplex dental acrylic. Cannula patency was maintained by 33 g wire obdurators. The incision was treated with Cicatrin (GlaxoSmithKline) and the animals were administered an antibiotic (oxytetracycline 10 mg/kg) and a non-steroidal analgesic (meloxicam 2 mg/kg) immediately, and then at 24 and 48 h after surgery. These drugs were mixed into a small pot of palatable wet mash, to which the animals had been accustomed prior to surgery.

2.3. Histological verification

Brains were sectioned coronally at 60 μm on a freezing microtome. Relevant sections were mounted on gelatinized slides and, following alcohol dehydration, run through a standard Nissl staining procedure using Thionin. The location of infusion sites was determined from Paxinos and Watson (1998).

2.4. Drugs and drug administration

Baclofen (Sigma, UK) was dissolved in 0.9% sterile saline and the pH of the solution adjusted to around 7.5 using 1 M sodium hydroxide and administered in doses of 110, 220, and 440 ρmol per μl. This dose range was chosen to avoid motor side effects that were observed in pilot experiments at higher doses, including 880 ρmoles per side, the most effective dose, in terms of intake, used by Stratford and Kelley (1997). Muscimol (Sigma, UK) was dissolved in 0.9% sterile saline, which gave a solution with a pH of 7.5 without further adjustment and administered at doses of 220, 440 and 660 ρmol per μl. Baclofen increases intake across a lower dose range than muscimol and a total infusion of 176 ρmol muscimol has been shown to have no effect on total intake of chow during a 2 h test session (Stratford and Kelley, 1997) so a dose of 110 ρmol muscimol was not used.

On test days bilateral infusions of drug or vehicle were made simultaneously into the accumbens shell at a rate of 0.5 μl per side over 30 s (1 μl of drug solution infused in total). Injectors were left in for a further minute to allow diffusion of drug away from the tip. The infusions were given using 31 g stainless steel infusors which extended 2.2 mm beyond the tip of the guide cannulae to reach the target structure. These injectors were connected via number 10 PPE tubing to 10 μl Hamilton syringes. A microinfusion syringe pump model 802 (Univentor, Malta) which held two syringes allowed bilateral infusions to be made simultaneously. Behavioural testing followed immediately after the infusions were completed.

2.5. Behavioural testing

The method was based on procedures previously described (Clifton et al., 1989; Vickers et al., 1996). 1 h prior to daily test sessions food was removed from the home cage and replaced with 5 g of fresh chow pellets to which the rats had access for 30 min. Pre-fed animals were then transferred to the test cage for a 30 min acclimation period. Finally, they were presented with a pre-weighed pot of chow for a 30 min test session. As expected, consumption was initially low and habituation continued until there was no significant difference in the mean meal size over four consecutive days. The average habituation period was 7 days. Water was available throughout.

During the subsequent test sessions in Experiments 1 and 2 infusions were made following the 30 min acclimation period in the test cage and in all 3 experiments chow was then presented and the BSS was recorded using the method described by Vickers et al. (1996). The behavioural categories were: *Ingest*: retrieval of food with mouth or paws, holding chewing and ingesting food; *Active:* moving around cage, rearing, sniffing, standing alert and any other behaviour not already defined; *Groom:* grooming, biting or licking of head, body or tail using mouth or limbs; *Inactive:* absence of movement in a resting posture (head and / or body lowered) with, or without, eye closure. Test sessions were separated by at least 48 h. In Experiments 1 and 2 animals were tested in pairs (5 s inter-observation interval) following infusions. In Experiment 3 animals were tested as a single cohort of 12 (30 s inter-observation interval) following i.p. injections of saline to provide a degree of handling stress equivalent to infusing. A 30 min test session for Experiments 1 and 2 was chosen to minimise time of day effects.

2.6. Statistics

Food intake was expressed as mean (±SEM) intake of chow (g) and analysed using repeated measures ANOVA with dose or food withdrawal as the repeated measure factor. Each of the four mutually

exclusive behaviour patterns associated with the BSS were treated separately. They were summed into five minute bins, plotted as proportions and analysed using repeated measures ANOVA with time and drug treatments(s) or food withdrawal duration(s) as the repeated measures factors. Subsequent paired comparisons between control and experimental groups were made using Dunnett's test. Statistical analysis was carried out using the Genstat computer statistical package.

3. Results

3.1. Experiment 1

10 (of N = 12) animals were found to have placements that fell between 1.2 and 1.6 mm anterior to bregma and clearly located in shell or on the border of shell and core.

Baclofen infused into the accumbens shell of pre-fed animals resulted in a dose dependent increase in chow intake relative to intake with vehicle [Fig. 1: $F(3,27) = 15.48$, $p<0.001$], which was significant at 110 ρmols ($p<0.05$), 220 and 440 ρmols ($p<0.001$).

The BSS was also affected in a dose dependent manner (Fig. 2). Over all there was a highly significant interaction between drug and time manifested as an increase across the early part of session for feeding ('Ingest') [$F(15,135) = 1.87$, $p = 0.032$]. The significant drug × time interaction for active behaviour [$F(15,135) = 3.78$, $p<0.001$] reflected both a decrease and consequent increase. Inactive behaviour was reduced by drug treatment, especially in later time bins [$F(15,135) = 8.64$, $p<0.001$]. There was no effect of drug treatment on grooming.

Planned post-hoc analysis using Dunnett's test indicated that the increase in feeding behaviour was only significant 5–10 min into the session at the lowest dose of 110 ρmols ($p<0.05$), between 0–15 min at 220 ρmols (0–5 min, $p<0.05$; 5–15 min, $p<0.01$) and throughout the last 25 min of the session at the highest dose of 440 ρmols (5–15 min, $p<0.01$; 15–20 min, $p<0.05$; 20–25, $p<0.01$; 25–30 min, $p<0.05$). Active behaviour was significantly lower during the first 0–15 min at doses of 220 ρmols (0–10 min $p<0.01$ and 10–15 min, $p<0.05$) and 440 ρmols (0–15 min, $p<0.01$) of baclofen. It was also lower during this period at 110 ρmols but only significantly so between 5–10 min ($p<0.05$).

There was no significant difference in activity at any dose between 15–25 min but it was significantly higher in the last 5 min at 220 ρmols ($p<0.05$). In the last 10 min inactive behaviour was significantly lower than with vehicle at all doses of baclofen (20–30 min, $p<0.01$). In fact this behaviour was almost completely absent over the 30 min test period at all three doses. Observations over a longer period (for which the BSS was not recorded) revealed that at least some of the animals given baclofen become inactive within 1 h of infusions (data not published here).

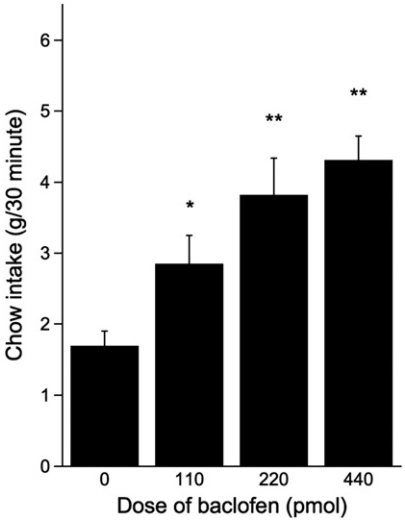

Fig. 1. The effect of intra-accumbens shell infusion of baclofen (0, 110, 220, 440 ρmol) on intake of chow.

3.2. Experiment 2

8 (of N = 12) animals were found to have placements that fell between 1.2 and 1.7 mm anterior to bregma and clearly located in shell or on the border of shell and core. It was not possible to collect data from one animal after infusion with 660 ρmol muscimol.

Muscimol infused into the accumbens shell of pre-fed animals increased chow intake relative to intake with vehicle [Fig. 3: $F(3,20) = 17.3$, $p<0.001$], significantly so at all doses ($p<0.001$) but there was no difference in the total amount of chow consumed between doses.

The BSS was significantly different from vehicle with all drug treatments but, as with intake, there was no apparent dose dependent effect (Fig. 4). Over all there was a highly significant interaction between drug and time manifested as an increase in the category 'Ingest' [$F(15,100) = 2.01$, $p = 0.021$], across the session. The interaction for the 'Active' category [$F(15,100) = 3.09$, $p<0.001$] reflected a decrease as it did for the category 'Inactive' [$F(15,100) = 4.32$, $p<0.001$]. There was an effect of drug on grooming [$F(3,20) = 15.2$, $p<0.001$] but there was no interaction between drug and time.

Planned post-hoc analysis using Dunnett's test indicated that the increase in feeding was significant at all doses across all time bins ($p<0.01$). Active behaviour was significantly lower at all doses for the first 20 min (0–20 min, $p<0.01$ at all doses). There was no significant difference in activity at any dose during the last 10 min. Inactive behaviour was significantly lower than with vehicle at all doses of muscimol in the final 10 min ($p<0.05$). The lack of interaction between drug and time for grooming behaviour reflects a proportional decrease across every time bin with all three doses of muscimol.

Whilst recording the BSS it was noted that animals treated with muscimol were in contact with the food much of the time although not necessarily eating. Additionally animals forced so much food into their mouths that they would often chew and gag for long periods before collecting the next pellet. Animals under the influence of muscimol but not baclofen also appeared to be less responsive to cues that were not in their immediate vicinity e.g. movement in adjacent cages.

3.3. Experiment 3

Food withdrawal significantly increased intake [Fig. 5: $F(2,22) = 57.93$, $p = <0.001$) and this increase was significant at both 4 and 8 h ($p<0.01$). There was no significant difference between the amount consumed at 4 and 8 h.

The non-deprived animals in this experiment and the vehicle treated animals in Experiments 1 and 2 showed essentially identical patterns of behaviour despite the use of different inter-observation intervals. There was a significant effect of length of food withdrawal on the BSS expressed (Fig. 6). Food withdrawal significantly increased the proportion of behaviour in the category 'Ingest' [$F(2,22) = 19.23$, $p<0.001$] and the proportion changed over time [$F = 7,77 = 39.25$, $p<0.001$]. There was no interaction between the period of food withdrawal and time. There was a significant interaction between the period of food withdrawal and time for the category 'Active' [$F(14,154) = 2.94$, $p<0.001$] which both decreased and subsequently increased across the session. The 'Groom' and 'Inactive' categories were unaffected by withdrawal of food.

Planned post-hoc analyses indicated that both periods of food withdrawal increased the time spent feeding during the first 20 min ($p<0.001$). Significantly less time was spent in active behaviour in the

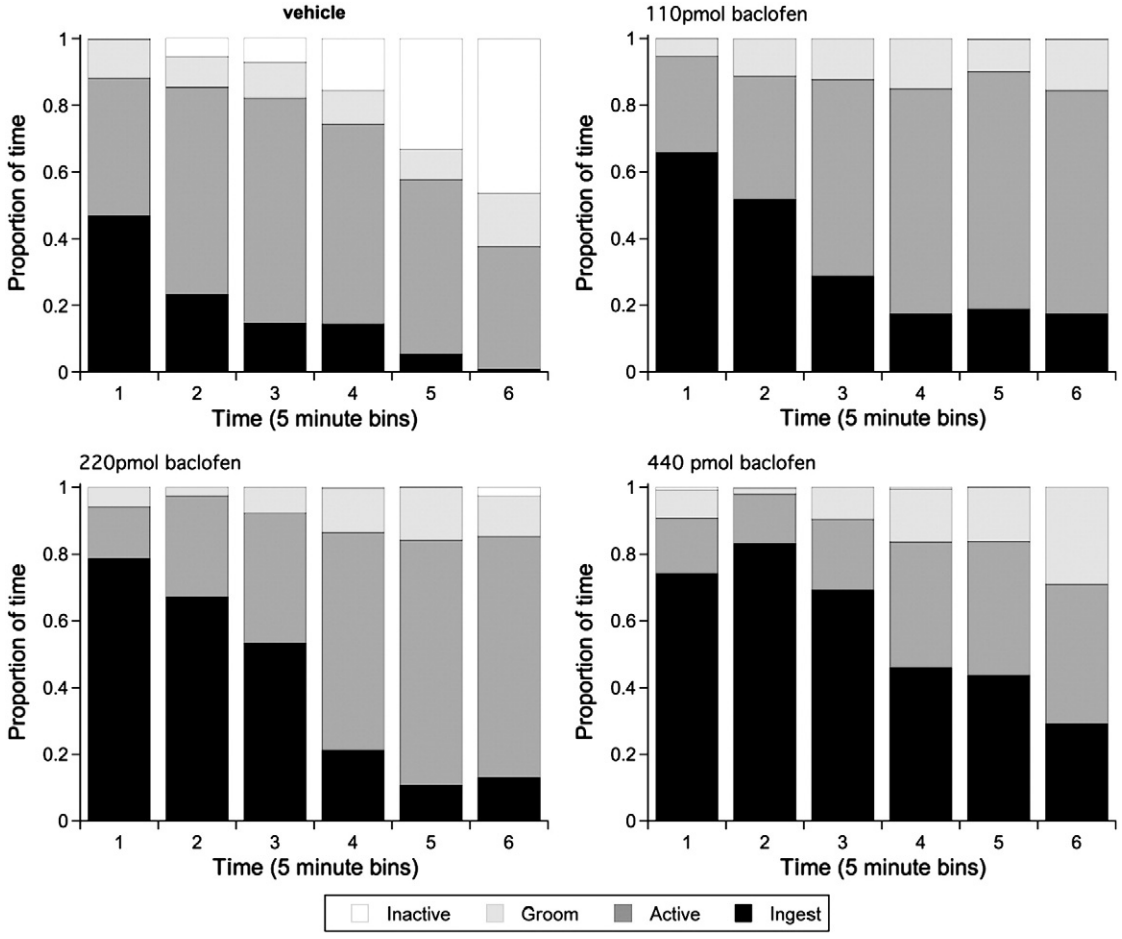

Fig. 2. The effect of intra-accumbens shell infusion of baclofen (0, 110, 220, 440 ρmol) on the components of feeding related behaviour.

first 15 min with a 4 or 8 h fast (0–10 min, $p<0.05$ for both; 10–15 min, $p<0.01$ for both). Grooming and inactive behaviour were unaffected by food withdrawal.

4. Discussion

As expected, intra-accumbens infusions of either baclofen or muscimol, as well as short periods of food withdrawal, led to increases in food intake during a subsequent 30 min test session. In the case of baclofen (110–440 ρmol) the effect was dose related. The observed behavioural sequence following food withdrawal was clearly shifted to the right over the period observed, indicating a delay in the onset of satiety. The same pattern of rightward shift was evident in the behavioural sequences recorded following administration of baclofen, although inactive behaviour was suppressed, especially at higher doses. However, as reported above, at least some of the animals did rest within an hour of starting the meal. With both baclofen and food withdrawal the increase in intake was most evident at the onset of the meal. Muscimol (220–660 ρmol), by contrast, increased feeding behaviour and decreased active behaviour throughout the observation period and at all doses, with an almost complete loss of both grooming and inactive behaviour. The apparent lack of a transition from feeding to rest may be due to the short test period relative to the extended increase in intake. The additional observation reported here that animals under the influence of intra-accumbens muscimol appear less responsive or less vigilant to external cues than those under the influence of baclofen supports the assertion that the two agonists differ in their behavioural effects.

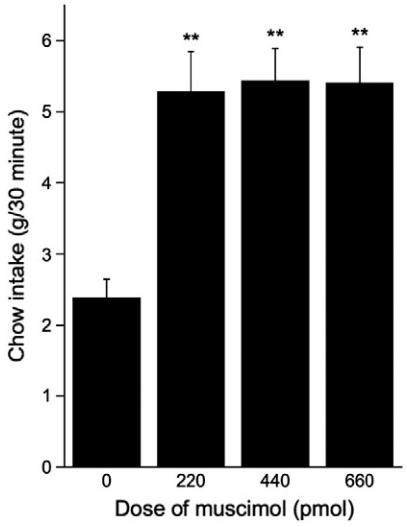

Fig. 3. The effect of intra-accumbens shell infusion of muscimol (0, 220, 440, 660 ρmol) on intake of chow.

The doses of baclofen and muscimol used here were chosen, in part, on the basis of those used in previous studies (e.g. Ward et al., 2000). The lowest doses of muscimol and baclofen used were within the range of the minimally effective doses reported by Stratford and Kelley (1997).

Food withdrawal influences many aspects of feeding behaviour. In addition to increasing short term food intake, it also increases the incentive salience and the hedonic value of food and food related cues and consequently enhances several aspects of the performance of food motivated instrumental tasks. Ishii et al. (2003a) examined the effects

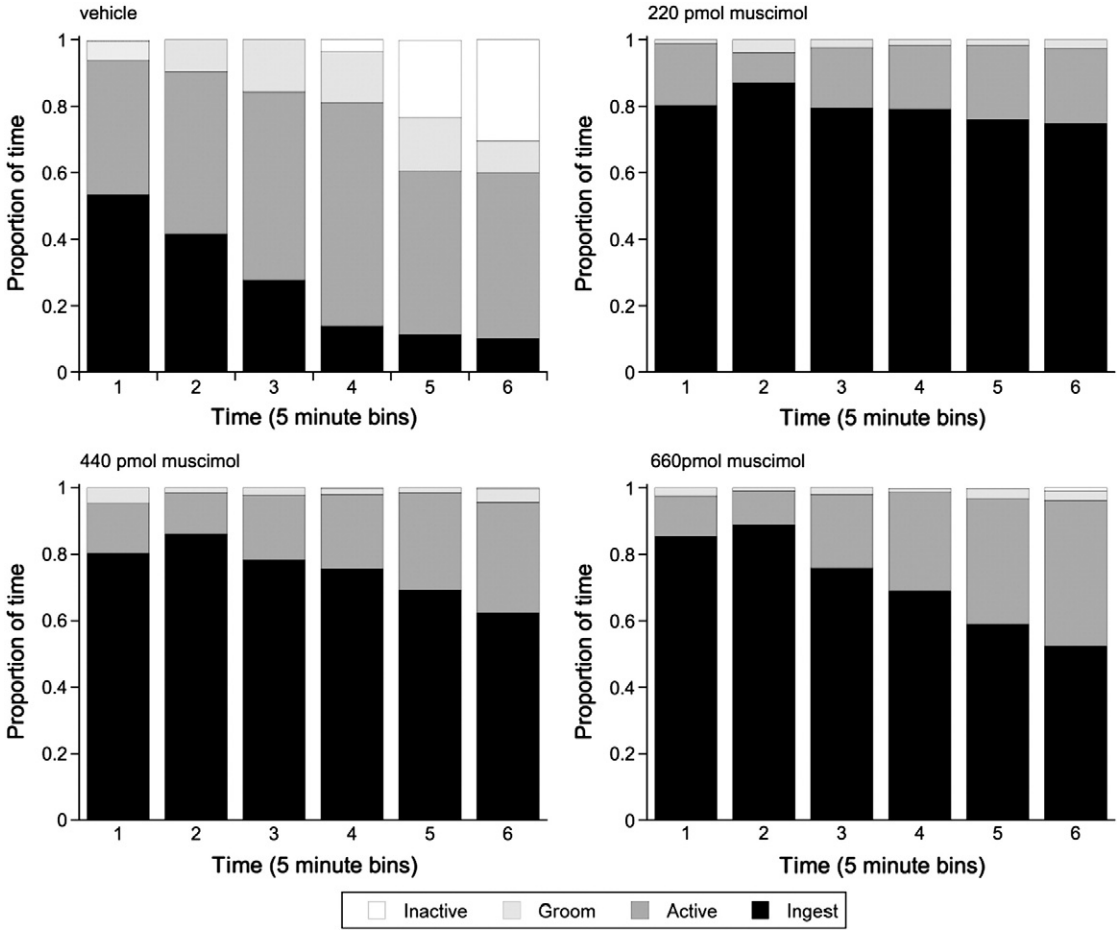

Fig. 4. The effect of intra-accumbens shell infusion of muscimol (0, 220, 440, 660 ρmol) on the components of feeding related behaviour.

of short periods of food withdrawal on the behavioural satiety sequence using a palatable mash as the test diet. The changes in the sequence reported in that study were similar to those seen here despite differences in both recording technique and diet type. In that study, and here, withdrawal led to a marked increase in the time spent feeding during the earlier part of the sequence and a delayed transition towards grooming and inactivity. Ishii et al. (2003b) also examined the effects of both quinine and saccharin adulteration of the palatable mash. Saccharin, at the concentrations used, failed to enhance intake and produced some small changes within the sequence that resembled the stronger action of quinine, suggesting an aversive component to the response. Other non-pharmacological manipulations of palatability have not been widely explored in this paradigm.

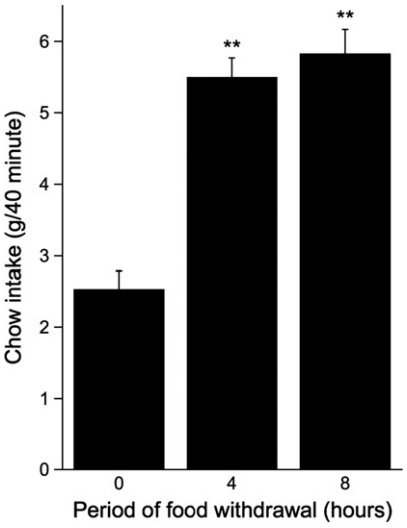

Fig. 5. The effect of food -withdrawal (0, 4, 8 h) on intake of chow.

The similarity of the effects of intra-accumbens baclofen and food withdrawal suggests that it may elicit a broader, motivational, effect beyond the enhancement of feeding related motor behaviours attributed to intra-accumbens muscimol. Earlier reports have shown that muscimol enhanced the intake of different macronutrients and also of sucrose solutions, but had no effect on the consumption of palatable saccharin or saline solutions (Basso and Kelley, 1999). Intra-accumbens muscimol also failed to influence instrumental responding for food on progressive ratio schedules (Zhang et al., 2003) or to potentiate the acquisition of a food-motivated instrumental response (Hanlon et al., 2004). However all of these studies used doses of muscimol that were well above the threshold for increasing food intake in satiated rats and which, in the present study, led to the exclusion of almost all behaviour other than the basic components of ingestion. The effects of intra-accumbens baclofen on feeding have not been explored in terms of macronutrient selection or using any instrumental paradigm.

Intra-accumbens infusions of $GABA_A$ agonists (or glutamate antagonists) also elicit varying effects on positive and aversive responses to food and the environment in which it is consumed depending on their rostro-caudal position within this structure. Reynolds and Berridge (2001, 2002) have shown that more rostral infusions of muscimol elicit appetitive responses to food and support the development of place preferences whereas more caudal infusions result in defensive treading

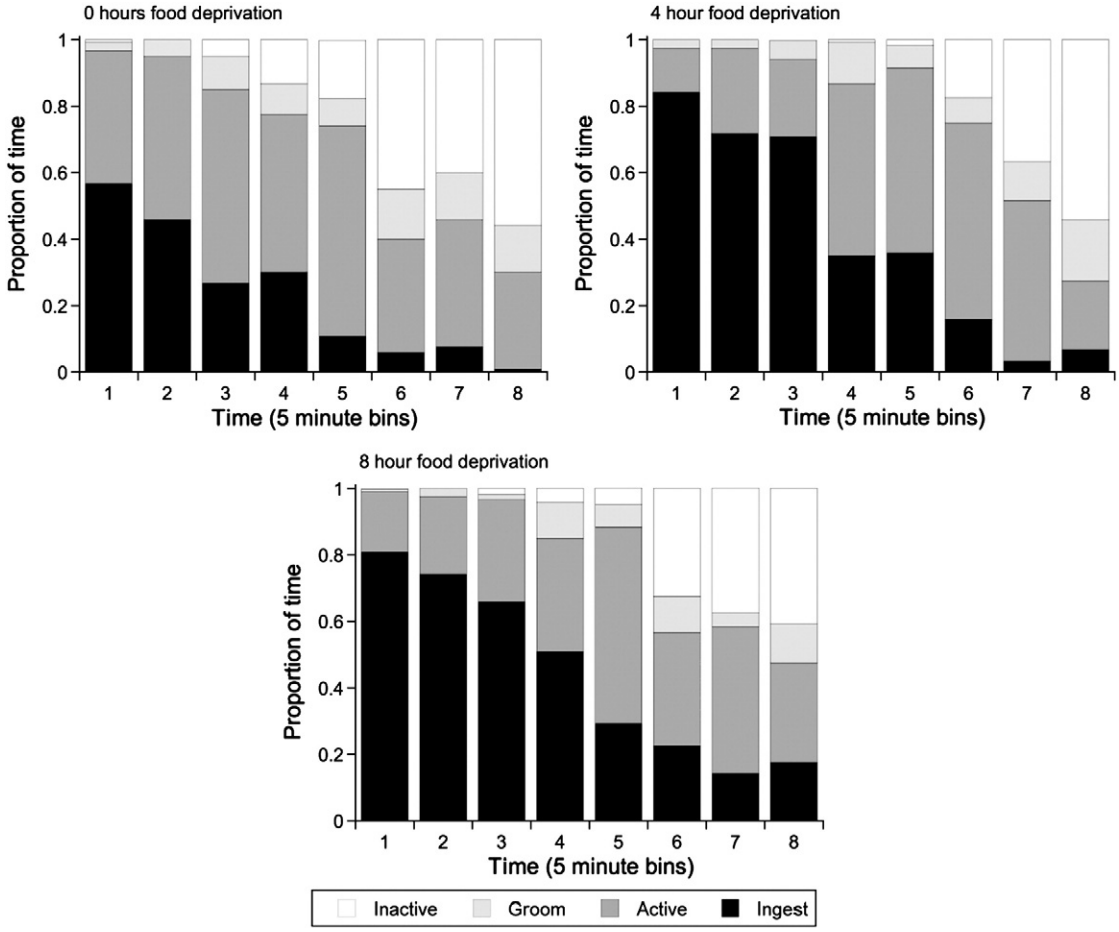

Fig. 6. The effect of food withdrawal (0, 4, 8 h) on the components of feeding related behaviour.

behaviour and can support the development of conditioned place aversions. Furthermore, infusions that most robustly increase intake fall within a restricted region within which concurrent taste reactivity responses indicate that the food is actually disliked (Reynolds and Berridge, 2002). A similar pattern of responses is elicited by infusions of the glutamate antagonist DNQX (Reynolds and Berridge, 2003). However the boundary and extent of this gradient in responsiveness is strongly modulated by context, at least in the case of infusions of glutamate antagonists (Reynolds and Berridge, 2008). In a familiar and non-threatening context, aversive responses become relatively less likely even at more caudal placements (Reynolds and Berridge, 2008). The placements for animals in the present studies, in which animals were tested in a very familiar environment, fell within the area in which aversive responses would be less likely.

Differentiation, at a behavioural level, of the effects of activating $GABA_A$ and $GABA_B$ receptors within the nucleus accumbens would not be surprising given their very different patterns of expression. $GABA_A$ receptors are located postsynaptically on the dendrites of the medium spiny neurons, which act as the major output pathway from the nucleus accumbens (Galvan et al., 2006). Additional $GABA_A$ receptors are expressed on (GABA-ergic) interneurons. Broadly speaking the post-synaptic location of $GABA_A$ receptors is consistent with the view that they mediate fast phasic inhibition. By contrast, $GABA_B$ receptors are most commonly found presynaptically either as auto- or hetero-receptors and also extrasynaptically (Galvan et al., 2006). Presynaptic $GABA_B$ receptors either inhibit neurotransmitter release or mediate slow inhibition through an extrasynaptic location (Otis and Mody, 1992). For example, $GABA_B$ receptors within the nucleus accumbens are able to modulate the release of glutamate and, as a consequence may also affect opioid peptide and cholinergic signalling (Calabresi et al., 2000). Differential interactions between the two GABA receptor subtypes and opioid receptors have been demonstrated by Znamensky et al (2001) in the context of the induction of feeding behaviour. They suggest that these effects may be in part attributable to the location relative to opioid receptors of $GABA_A$ and $GABA_B$ receptors.

In summary, the data reported here demonstrate that, at least in the behavioural satiety sequence, the effects of intra-accumbens infusions of baclofen more closely resemble those of food withdrawal than is the case for muscimol. Accumbens $GABA_B$ receptors are located in a manner that would allow them to modulate neurotransmission by glutamatergic and other systems within the accumbens in addition to any effects on the output pathways from the accumbens. This raises the possibility that modulation of accumbens $GABA_B$ receptors may be capable of influencing a wider range of feeding related behaviours, including instrumental responding, than actions at $GABA_A$ receptors.

References

Basso AM, Kelley AE. Feeding induced by GABA(A) receptor stimulation within the nucleus accumbens shell: regional mapping and characterization of macronutrient and taste preference. Behav Neurosci 1999;113:324–36.

Calabresi P, Centonze D, Gubellini P, Marfia GA, Pisani A, Sancesario G, Bernardi G. Synaptic transmission in the striatum: from plasticity to neurodegeneration. Prog Neurobiol 2000;61:231–65.

Clifton PG, Barnfield AM, Philcox L. A behavioural profile of fluoxetine-induced anorexia. Psychopharmacology 1989;97:89–95.

Galvan A, Kuwajima M, Smith Y. Glutamate and GABA receptors and transporters in the basal ganglia: what does their subsynaptic localization reveal about their function? Neuroscience 2006;143:351–75.

Halford JC, Wanninayake SC, Blundell JE. Behavioral satiety sequence (BSS) for the diagnosis of drug action on food intake. Pharmacol Biochem Behav 1998;61:59–68.

Hanlon EC, Baldo BA, Sadeghian K, Kelley AE. Increases in food intake or food-seeking behavior induced by GABAergic, opioid, or dopaminergic stimulation of the nucleus accumbens: is it hunger? Psychopharmacology 2004;172:241–7.
Ishii Y, Blundell JE, Halford JCG, Rodgers RJ. Effects of systematic variation in presatiation and fasting on the behavioural satiety sequence in male rats. Physiol Behav 2003a;79:227–38.
Ishii Y, Blundell JE, Halford JCG, Rodgers RJ. Palatability, food intake and the behavioural satiety sequence in male rats. Physiol Behav 2003b;80:37–47.
Kelley AE, Baldo BA, Pratt WE, Will MJ. Corticostriatal-hypothalamic circuitry and food motivation: integration of energy, action and reward. Physiol Behav 2005;86:773–95.
Otis TS, Mody I. Differential activation of GABAA and GABAB receptors by spontaneously released transmitter. J Neurophysiol 1992;67:227–35.
Paxinos G, Watson C. The Rat Brain in Stereotaxic Coordinates. London: Academic Press, Ltd.; 1998.
Reynolds SM, Berridge KC. Fear and feeding in the nucleus accumbens shell: rostrocaudal segregation of GABA-elicited defensive behavior versus eating behavior. J Neurosci 2001;21:3261–70.
Reynolds SM, Berridge KC. Positive and negative motivation in nucleus accumbens shell: bivalent rostrocaudal gradients for GABA-elicited eating, taste "liking"/"disliking" reactions, place preference/avoidance, and fear. J Neurosci 2002;22:7308–20.
Reynolds SM, Berridge KC. Glutamate motivational ensembles in nucleus accumbens: rostrocaudal shell gradients of fear and feeding. Eur J Neurosci 2003;17:2187–200.
Reynolds SM, Berridge KC. Emotional environments retune the valence of appetitive versus fearful functions in nucleus accumbens. Nat Neurosci 2008;11:423–5.
Richter CP. A behavioristic study of the activity of the rat. Comp Psychol Monogr 1922;1:1-55.
Stratford TR, Kelley AE. GABA in the nucleus accumbens shell participates in the central regulation of feeding behavior. J Neurosci 1997;17:4434–40.
Taha SA, Fields HL. Encoding of palatability and appetitive behaviors by distinct neuronal populations in the nucleus accumbens. J Neurosci 2005;25:1193–202.
Taha SA, Fields HL. Inhibitions of nucleus accumbens neurons encode a gating signal for reward-directed behavior. J Neurosci 2006;26:217–22.
Vickers SP, Clifton PG, Dourish CT. Behavioural evidence that d-fenfluramine-induced anorexia in the rat is not mediated by the 5-HT1A receptor subtype. Psychopharmacology 1996;125:168–75.
Ward BO, Somerville EM, Clifton PG. Intra-accumbens baclofen selectively enhances feeding behavior in the rat. Physiol Behav 2000;68:463–8.
Zhang M, Balmadrid C, Kelley AE. Nucleus accumbens opioid, GABaergic, and dopaminergic modulation of palatable food motivation: contrasting effects revealed by a progressive ratio study in the rat. Behav Neurosci 2003;117:202–11.
Znamensky V, Echo JA, Lamonte N, Christian G, Ragnauth A, Bodnar RJ. γ-Aminobutyric acid receptor subtype antagonists differentially alter opioid-induced feeding in the shell region of the nucleus accumbens in rats. Brain Res 2001;906:84–91.