ELSEVIER

European Journal of Pharmacology 274 (1995) 41–46

ejp

2-Hydroxy-saclofen causes a phaclofen-reversible reduction in population spike amplitude in the rat hippocampal slice

Sarah J. Caddick, Ian M. Stanford, John E. Chad *

Department of Physiology and Pharmacology, University of Southampton, Bassett Crescent East, Southampton, SO9 3TU, UK

Received 11 October 1994; accepted 15 November 1994

Abstract

2-Hydroxy-saclofen is known to be active at $GABA_B$ receptors in the mammalian central nervous system, and we have investigated its effects on synaptic transmission in the rat hippocampal slice preparation. Orthodromic stimuli were applied to the stratum radiatum, and population spike responses from the CA1 pyramidal cell layer were recorded extracellularly. A second, identical stimulus was applied at a variable interpulse interval (IPI) after the initial conditioning stimulus. GABAergic synaptic inhibition was observed as a decrease in the spike amplitude of the second response compared to the first. Both the $GABA_B$ receptor antagonist phaclofen (1 mM) and 2-hydroxy-saclofen (200 μM) prevented a slow phase of inhibition for IPIs of 200–400 ms. However, these agents differed markedly in their effects on overall synaptic transmission. Phaclofen had no effect on the amplitude of the initial conditioning spike amplitude, whereas 2-hydroxy-saclofen reduced it significantly, in a manner similar to baclofen (1 μM). The direct actions of 2-hydroxy-saclofen were unexpected for a pure antagonist of $GABA_B$ receptors, but could be prevented by the co-administration of phaclofen (1 mM), but not bicuculline (1 μM). Reduction in conditioning spike amplitude due to antagonism of $GABA_B$ autoreceptors on inhibitory interneurones and subsequent enhancement of $GABA_A$ tonic inhibition would have been blocked by bicuculline. The blockade of the 2-hydroxy-saclofen effect by phaclofen implies a $GABA_B$ receptor partial agonist action. The possible sites of this action are discussed.

Keywords: GABA (γ-aminobutyric acid); $GABA_B$ receptor; 2-Hydroxy-saclofen; Hippocampus; (Inhibition); Presynaptic inhibition

1. Introduction

GABA (γ-aminobutyric acid) is the major inhibitory transmitter in the central nervous system (CNS). Its ability to modulate cellular excitability in the hippocampus is well documented (Karlsson and Olpe, 1989; Sivilotti and Nistri, 1991). GABA has been shown to act directly at two classes of receptor on the postsynaptic cell (Alger and Nicoll, 1982). Activation of $GABA_A$ receptors is known to increase membrane conductance to chloride and mediates the fast hyperpolarisation that immediately follows the excitatory event (Newberry and Nicoll, 1984). Activation of postsynaptic $GABA_B$ receptors increases membrane conductance to K^+ via a G-protein and this is responsible for the late slow hyperpolarisation following the $GABA_A$ receptor event (Dutar and Nicoll, 1988a,b; Solis and Nicoll, 1992; reviewed by Bowery, 1993). There are also presynaptic receptors thought to be primarily of the $GABA_B$ type located on the terminals of the inhibitory and excitatory cells which when activated modulate neurotransmitter release (Thompson et al., 1993). $GABA_B$ receptors are distinguished pharmacologically by the lack of effect of the $GABA_A$ receptor antagonist bicuculline (Bowery et al., 1981) and their sensitivity to phaclofen (Kerr et al., 1987; Seabrook et al., 1990) and its analogues. 2-Hydroxy-saclofen is a recently developed analogue (Kerr et al., 1988) which has been shown to be selective for the $GABA_B$ receptor and antagonise the actions of the $GABA_B$ receptor agonist baclofen in the trigeminal nucleus of the rat (Fromm et al., 1992). 2-Hydroxy-saclofen also blocked the agonist actions of 3-aminopropanephosphinic acid at $GABA_B$ receptors in CA1 neurones of the rat hippocampus (Lovinger et al., 1992) and antagonised the effect of baclofen on excitatory transmission (Harrison et al., 1990). This study

* Corresponding author. Tel. (703) 594292, fax (703) 594319.

SSDI 0014-2999(94)00702-0

examines the effects of 2-hydroxy-saclofen on orthodromic evoked population responses in the CA1 region of the adult rat hippocampus. Preliminary accounts of this work have been presented (Caddick et al., 1992; Caddick and Chad, 1992).

2. Materials and methods

2.1. Tissue preparation

Methods of slice preparation have been previously described (Andersen et al., 1987). In brief, male Wistar rats (approx 200 g) were decapitated under halothane anaesthesia, the brains removed and immersed in cold (4°C) artificial cerebrospinal fluid (ACSF). The hippocampi were carefully dissected out and transverse slices were cut (400–500 μm) using a McIlwain tissue chopper and transferred to an oxygenated holding chamber for at least 1 h. Slices were transferred to the recording chamber and held between two nylon nets fully submerged under a continuous flow of warm ACSF (34°C) oxygenated with 95% O_2/5% CO_2. The composition of the ACSF was (mM): NaCl 118, $NaHCO_3$ 26, KCl 3.3, KH_2PO_4 1.25, $MgSO_4 \cdot 7H_2O$ 1, $CaCl_2$ 2.5, D-glucose 10, at a pH of 7.4.

2.2. Extracellular recordings

Extracellular voltage recordings from area CA1 were obtained using glass microelectrodes containing 3 M NaCl with a tip resistance of 4–10 MΩ placed in the stratum pyramidale. A bipolar platinum stimulating electrode was positioned in the stratum radiatum, 1–2 mm from the recording electrode, for orthodromic stimulation of the Schaffer collateral/commissural afferents (0–30 V, 0.2 ms). Recordings were filtered at 1 kHz, digitally sampled at 10 kHz and stored to disc. Subsequent analysis averaged 6 individual responses under each condition to reduce noise before measurement of the size of the population response amplitude and the field excitatory postsynaptic potential (e.p.s.p.) slope. The population response amplitude was measured as the difference of the peak from the value of the underlying waveform linearly extrapolated from the values immediately before and after the spike. The field e.p.s.p. slope was calculated from a linear approximation of the initial rise of the waveform. Data are presented graphically as mean ± S.E.M., and statistical significance assessed with paired *t*-tests.

2.3. Paired pulse inhibition

GABAergic inhibition was assessed by means of a paired pulse protocol. Two identical consecutive stimuli were applied to the excitatory afferents which resulted in a first, conditioning response and a second, test response. Stimulus amplitude was routinely set to achieve half-maximal stimulus amplitude of the conditioning response under control conditions. The respective amplitudes of the conditioning response (C) and test responses (T) were measured and inhibition quantified as the percentage ratio of the decrease in response to the conditioning response amplitude $[((C - T)/C) \times 100]$. The interpulse interval (IPI) was varied between 10 and 500 ms in order to determine the progression of synaptic inhibition following the conditioning stimulus. Only slices showing clear inhibition at 10 ms interpulse interval were included in the study.

2.4. Drugs

The drugs used in these experiments were: phaclofen 1 mM, Tocris; 2-hydroxy-saclofen 200 μM, Tocris; baclofen 1 μM, Tocris; bicuculline 1 μM, Sigma. Concentrations used were based on those shown to be effective in modifying synaptic transmission in the rat hippocampus in previous studies (Davies et al., 1990; Harrison et al., 1990; Nathan et al., 1990). Stock solutions were prepared and frozen until required. On usage, the stock solutions were diluted to the required concentration in warm oxygenated ACSF and perfused through the recording chamber.

3. Results

3.1. Effect of phaclofen and 2-hydroxy-saclofen on paired pulse inhibition evoked in CA1 pyramidal cells

Extracellular population responses recorded from CA1 pyramidal cells following paired pulse stimulation showed a reduction in amplitude of the second, test response compared to the first, conditioning response (Fig. 1). The reduction in amplitude of the test response at short interpulse intervals (10–30 ms) revealed a fast early component of inhibition. This inhibition could be blocked by bicuculline (1 μM, $n = 15$), a $GABA_A$ receptor antagonist. Under control conditions the inhibition at 10 ms interpulse interval was $76 \pm 6\%$, and was reduced to $43 \pm 7\%$ ($P < 0.01$) by bicuculline. Paired pulse stimulation at longer interpulse intervals (200–400 ms) revealed a second weaker component of inhibition under control conditions, which was not significantly reduced by bicuculline (at 300 ms interpulse interval; control $10 \pm 3\%$; bicuculline $13 \pm 2\%$).

The application of phaclofen (Fig. 1A; 1 mM) had little effect on the amplitude of the conditioning response or the early inhibition of the test responses (interpulse intervals 10–30 ms), but prevented the slow inhibition (interpulse intervals 200–400 ms) in a re-

versible manner. In contrast, 2-hydroxy-saclofen (Fig. 1B; 200 μM) reduced the amplitude of all the responses recorded including the conditioning response. Furthermore, there was an apparent reduction in the early inhibition and prevention of the slow inhibition, in that the test spikes for interpulse intervals of 300 ms were similar in size to the conditioning response. All these changes were reversible on washing. Baclofen (1 μM) also reduced the conditioning responses to a similar degree (Fig. 1C), but changed the early inhibition (interpulse intervals 10–20 ms) into a strong facilitation which extended throughout the region of facilitation observed in controls (50–100 ms).

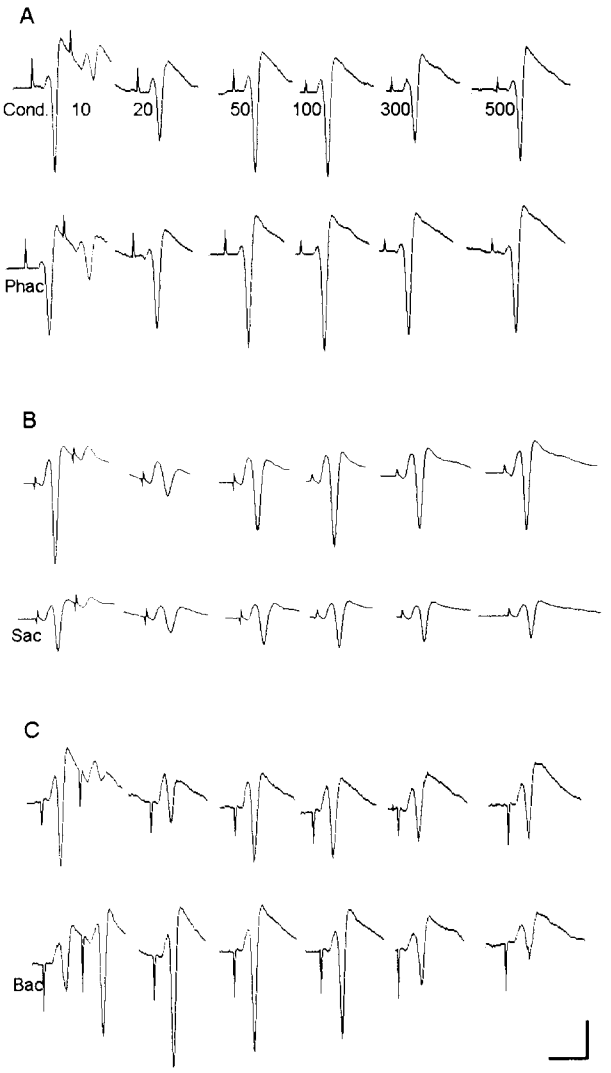

Fig. 1. Extracellular field recordings from CA1 pyramidal cells, showing the conditioning and test spikes following paired stimuli to Schaffer collateral/commissural under control conditions (top trace) and after 10 min exposure to the drug (lower trace of each pair). From left to right in each row the first conditioning spike is shown (Cond.) with the test spike after 10 ms interpulse interval. For longer interpulse intervals only the test spikes are shown for intervals of 20–500 ms in successive columns as labelled. Early inhibition is seen as a reduction in the test spike at intervals of 10–20 ms and late inhibition is seen as the reduction in the test spike seen at 300 ms under control conditions. (A) Phaclofen (1 mM) reduces the inhibition at 300 ms interpulse interval but has no significant effect on the conditioning response or the early inhibition. (B) 2-Hydroxy-saclofen (200 μM) reduces the amplitude of the conditioning and all test spikes, as well as reducing both the early and late inhibitions. (C) Baclofen (1 μM) reduces the conditioning response, but causes facilitation to be observed at 10–100 ms interpulse intervals. Calibration 10 ms and 1 mV for B, 10 ms and 2 mV for A and C.

The pattern of paired pulse inhibition is similar between healthy slices, and normalisation to the amplitude of control spike (see Materials and methods) to provide an index of percentage inhibition allows the pooling of data from different experiments. This allows an analysis of the dependence of paired pulse inhibition on interpulse interval and the effects of drugs, as shown in Fig. 2. Under control conditions (Fig. 2A; $n = 29$) the larger, early inhibition (interpulse interval 10 ms; $67 \pm 6\%$) and late inhibition (interpulse interval 300 ms; $9 \pm 2\%$) are clearly seen, separated by a region of facilitation (negative inhibition). 2-Hydroxy-saclofen (Fig. 2B; 200 μM) reduced the late inhibition at 300 ms interpulse interval (paired controls $12 \pm 3\%$; 2-hydroxy-saclofen $-2 \pm 2\%$; $n = 9$; $P < 0.01$). There was also a significant reduction in the early inhibition at 10 ms interpulse interval (paired controls $89 \pm 2\%$; 2-hydroxy-saclofen $46 \pm 15\%$; $P < 0.01$). Phaclofen (Fig. 2C; 1 mM) had little effect on the early inhibition (10 ms interpulse interval; paired controls $51 \pm 18\%$; phaclofen $60 \pm 11\%$), but reduced late inhibition (300 ms interpulse interval; control $14 \pm 5\%$; phaclofen $-4 \pm 6\%$; $n = 7$; $P < 0.01$). Baclofen (Fig. 2D; 1 μM; $n = 7$) reduced both early and late inhibition producing a general facilitation, which was maximal between 50 and 100 ms interpulse interval.

3.2. Effect of 2-hydroxy-saclofen upon the conditioning response amplitude

2-Hydroxy-saclofen reduced late inhibition similarly to phaclofen, but also attenuated the conditioning response amplitude similarly to the effect of baclofen (Figs. 1 and 2). This effect was investigated in more detail in a series of experiments ($n = 5$) in which sets of individual supra-maximal stimuli (5 at 0.1 Hz), were repeated every 5 min, whilst drugs were perfused through the recording chamber. Sets of recordings were averaged to give a single amplitude value at each time point for each experiment and normalised to the initial value during the control period. Representative recordings from each phase, and the time course of population spike amplitude changes are shown in Fig. 3. Under control conditions the spike amplitudes were steady, and upon addition of 2-hydroxy-saclofen (200 μM) there was a reduction to a lower amplitude in both experimental sets. In the first set of experiments (■), the further addition of bicuculline at 60 min (1 μM; in continued presence of 2-hydroxy-saclofen) did

not appear to produce any further change in spike amplitude. Washing led to a return of the spike amplitude towards control levels. Representative recordings from each phase are shown as the upper inset series.

In the second set of experiments (▲) the same procedure was repeated showing the reduction in conditioning spike amplitude produced by 2-hydroxy-saclofen as before, but testing the effect of the further addition of phaclofen (1 mM). Representative recordings from each phase are shown as the lower inset series. As the phaclofen/saclofen ACSF was perfused through the experimental chamber, the amplitude of the spike returned toward control levels, and no further change was observed on washing.

To test the numerical significance of these observations, the data taken after 10 min equilibration time in each condition (20 samples per slice) were pooled (Table 1). The P-value is shown for each successive change. In both sets of experiments, 2-hydroxy-saclofen reduced the population spike amplitude by approximately 20% ($P = 0.01$). The addition of bicuculline (sac/bic) produced no significant change in amplitude, but the addition of phaclofen (sac/phac) produced a significant recovery in amplitude ($P = 0.01$).

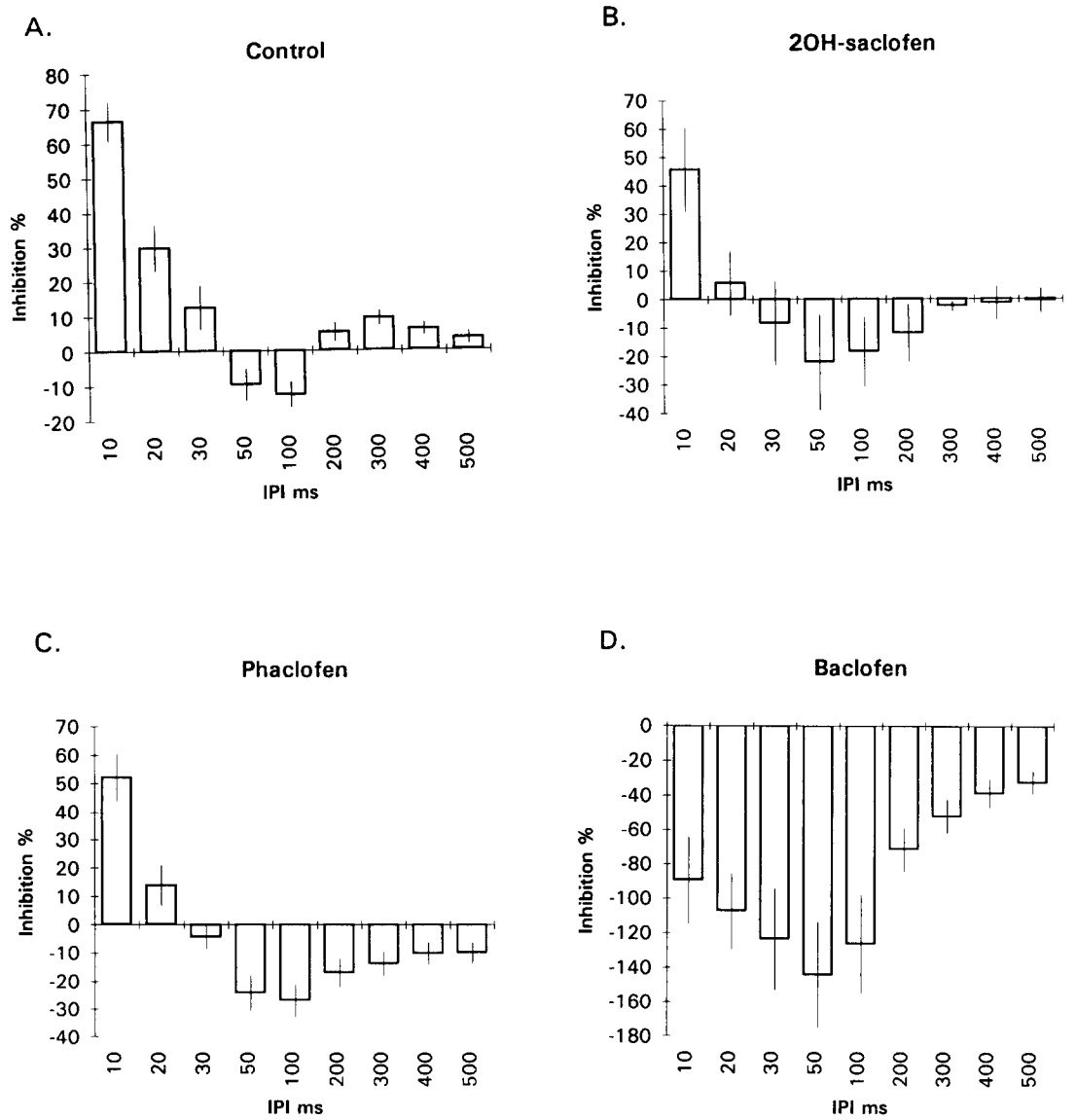

Fig. 2. The effect of 2-hydroxy-saclofen (200 μM; $n = 9$), phaclofen (1 mM; $n = 7$) and baclofen (1 μM; $n = 7$) on paired pulse inhibition of the population spike amplitude. Inhibition was calculated as described in Materials and methods. Data was taken after 10 min exposure to drug. (A) Under control conditions ($n = 22$) two phases of inhibition are observed, an early inhibition for interpulse intervals of 10–20 ms, and a smaller, late inhibition for interpulse intervals of 200–500 ms. All data are represented as the mean ± S.E.M. (B) 2-Hydroxy-saclofen reduces both the early and late inhibitions, increasing the range of facilitation observed. (C) Phaclofen has little effect on the early phase of inhibition but reduces the late phase. (D) Baclofen produces facilitation at all interpulse intervals tested.

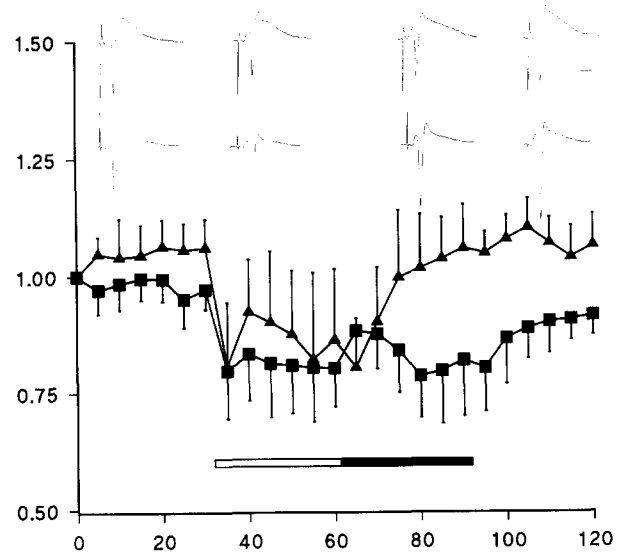

Fig. 3. Reversal of the 2-hydroxy-saclofen reduction in population spike amplitude by phaclofen but not bicuculline. Time course data from two sets of experiments are shown graphically as mean ± S.D. ($n = 5$), normalised to the initial values recorded. In both sets of experiments, after a 30 min control phase, perfusion of 2-hydroxy-saclofen (200 μM; open bar) reduced the population spike amplitude within 5 min. After a further 30 min a second drug was added to the perfusion (solid bar). Phaclofen (1 mM; ▲) increased the amplitude to control levels and there was no further change on washout. In the second set of experiments bicuculline (1 μM; ■) was used as the second drug, but did not increase the amplitude, although there was a recovery on washing. The inset data show individual traces during each phase of the two sets of experiments, the upper set showing effect of bicuculline and the lower the effect of phaclofen. Calibrations 1 mV and 4 ms.

Washing caused a significant recovery from 2-hydroxy-saclofen/bicuculline but there was no significant increase on washing from 2-hydroxy-saclofen/phaclofen. The measured initial slope values of the field e.p.s.p. show a similar pattern of changes.

Table 1
Reversal of the effects of 2-hydroxy-saclofen by phaclofen

	Mean	S.E.M.	P		Mean	S.E.M.	P
Population spike amplitude							
Control	0.98	0.02		Control	1.06	0.03	
sac	0.81	0.05	0.01	sac	0.87	0.08	0.01
sac/bic	0.81	0.05	0.44	sac/phac	1.03	0.05	0.01
Wash	0.90	0.03	0.01	Wash	1.07	0.02	0.14
Initial field e.p.s.p. slope							
Control	0.94	0.11		Control	1.14	0.21	
sac	0.80	0.10	0.06	sac	1.00	0.23	0.13
sacbic	0.64	0.15	0.03	sac/phac	1.26	0.22	0.11
Wash	0.80	0.08	0.03	Wash	1.30	0.35	0.43

sac: 2-hydroxy-saclofen; bic: bicuculline.

4. Discussion

The extracellular recordings from CA1 pyramidal neurones presented here reveal a qualitative difference in the actions of the $GABA_B$ ligands phaclofen and 2-hydroxy-saclofen. In these experiments, both 2-hydroxy-saclofen and phaclofen reduced late (bicuculline insensitive) inhibition, mediated by $GABA_B$ receptors, with similar quantitative differences to those described previously (Dutar and Nicoll, 1988a,b; Kerr et al., 1988; Lambert et al., 1989; Davies et al., 1990). However, 2-hydroxy-saclofen has also been shown to have direct effects on the amplitude of the population spike responses of the CA1 neurones to orthodromic stimuli (Figs. 1 and 3), similar to the actions of the $GABA_B$ receptor agonist baclofen, distinguishing its activity from phaclofen which had no significant direct actions. This effect of 2-hydroxy-saclofen was also observed by Nathan et al. (1990).

Assuming selectivity for $GABA_B$ receptors, antagonism of $GABA_B$ receptors could only account for these observations if they were located on inhibitory interneurones. For instance, this effect could be produced by the enhancement of a tonic inhibition by antagonism of presynaptic autoreceptors on basket cell synapses, leading to an increase in $GABA_A$ inhibition. In this case the reduction in population spike amplitude would be indirect and should be prevented by blockade of postsynaptic $GABA_A$ receptors. However, this is not the case: bicuculline at a dose sufficient to attenuate $GABA_A$ inhibition in our experiments failed to reverse the effects of 2-hydroxy-saclofen.

Alternatively, 2-hydroxy-saclofen could have an agonist action on $GABA_B$ receptors leading to a reduction in population spike amplitude, similar to baclofen (Harrison et al., 1990). The reduction in population spike amplitude could be conceivably produced by either pre- or post-synaptic agonism of $GABA_B$ receptors, or a combination of both, and can be antagonised by the actions of phaclofen (Fig. 3). Presynaptic receptors are known to be present in the hippocampus and appear to decrease neurotransmitter release when activated at both inhibitory and excitatory terminals (Harrison et al., 1990; Thompson et al., 1993). Any post-synaptic receptor agonist actions would compound these effects.

Phaclofen has been suggested to be a more effective antagonist of baclofen at post- rather than pre-$GABA_B$ receptors in the hippocampus (Dutar and Nicoll, 1988b), and 2-hydroxy-saclofen had little effect on field e.p.s.p.s recorded in the stratum radiatum (Harrison et al., 1990). Taken together, this would implicate agonism of 2-hydroxy-saclofen at post-synaptic receptors. However, the reduction of $IPSC_A$ observed by Davies et al., 1990 could be interpreted as showing some pre-synaptic effect of 2-hydroxy-saclofen. Our record-

ings from the stratum pyramidale are not ideally suited to analysis of field e.p.s.p.s, but the pooled data show a similar pattern of changes in slope as in population spike amplitude. The reasons behind this discrepancy are not clear; Harrison et al. (1990) used 2-hydroxy-saclofen from RBI, whilst this study and Davies et al. (1990) used Tocris. However, contamination seems an unlikely explanation, as the contaminant would have to be an effective $GABA_B$ receptor agonist, at sufficiently high concentration to overcome the antagonistic effects of 200 μM 2-hydroxy-saclofen. A plausible explanation is that the observation of this small effect is dependent upon the exact state of the slice preparation, and that our selection procedures of using only slices showing strong early inhibition (interpulse interval 10 ms) allows us to observe it.

We postulate that 2-hydroxy-saclofen is a $GABA_B$ receptor partial agonist, which could account for both the reduction in population spike amplitude and reduction of late inhibition. Agonism at a pre-synaptic site could also account for the anomalous observations of a reduction in early, $GABA_A$ mediated, paired pulse inhibition (Fig. 2B) and $IPSC_A$ (Davies et al., 1990). It would also provide an explanation for the lack of increase in population spike amplitude observed when bicuculline was added in the presence of 2-hydroxy-saclofen. 2-Hydroxy-saclofen activating presynaptic $GABA_B$ receptors of inhibitory interneurones would reduce their release of GABA. Overall, this suggests that the exact site of actions of 2-hydroxy-saclofen are worthy of further investigation.

References

Alger, B.E. and R.A. Nicoll, 1982, Feedforward dendritic inhibition in rat hippocampal pyramidal cells studied in vitro, J. Physiol. 328, 105.

Andersen, P., J. Storm and H.V. Wheal, 1987, Thresholds of action potentials evoked by synapses on the dendrites of pyramidal cells in the rat hippocampus in vitro, J. Physiol. 383, 509.

Bowery, N.G., 1993, $GABA_B$ receptor pharmacology, Annu. Rev. Pharmacol. Toxicol. 33, 101.

Bowery, N.G., A. Doble, D.R. Hill, A.W. Hudson and J.S. Shaw, 1981, Bicuculline-insensitive GABA receptors on peripheral autonomic nerve terminals, Eur. J. Pharmacol. 71, 53.

Caddick, S.J. and J.E. Chad, 1992, Phaclofen antagonizes the 2-OH-saclofen induced reduction in extracellular responses of CA1 pyramidal cells in the rat, Pharmacol. Commun. 2, 152.

Caddick, S.J., J.E. Chad and I.M. Stanford, 1992, 2-OH-saclofen affects both early and late inhibition in the rat hippocampus, Br. J. Pharmacol. 104, 465P.

Davies, C.H., S.N. Davies and G.L. Collingridge, 1990, Paired pulse depression of monosynaptic GABA mediated inhibitory responses in rat hippocampus, J. Physiol. 424, 513.

Dutar, P. and R.A. Nicoll, 1988a, A physiological role for $GABA_B$ receptors in the central nervous system, Nature 332, 156.

Dutar, P. and R.A. Nicoll, 1988b, Pre- and postsynaptic $GABA_B$ receptors in the hippocampus have different pharmacological properties, Neuron 1, 585.

Fromm, G.H., K. Sato and M. Nakata, 1992, The action of $GABA_B$ antagonists in the trigeminal nucleus of the rat, Neuropharmacology 31, 475.

Harrison, N.L., D.M. Lovinger, N.A. Lambert, T.J. Teyler, R. Prager, J. Ong and D.I.B. Kerr, 1990, The actions of 2-hydroxy-saclofen at pre-synaptic $GABA_B$ receptors in the rat hippocampus. Neurosci. Lett. 119, 272.

Karlsson, G. and H.R. Olpe, 1989, Inhibitory processes in normal and epileptic-like rat hippocampal slices: the role of $GABA_B$ receptors, Eur. J. Pharmacol. 163, 285.

Kerr, D.I.B., J. Ong, R.H. Prager, B.D. Gynther and D.R. Curtis, 1987, Phaclofen; a peripheral and central baclofen antagonist, Brain Res. 405, 150.

Kerr, D.I.B., J. Ong, G.A.R. Johnston, J. Abbenante and R.H. Prager, 1988, 2-Hydroxy-saclofen: an improved antagonist at central and peripheral $GABA_B$ receptors, Neurosci. Lett. 92, 92.

Lambert, N.A., N.L. Harrison, D.I.B. Kerr, J. Ong, R.H. Prager and T.J. Teyler, 1989, Blockade of the late IPSP in rat CA1 hippocampal neurones by 2-OH-saclofen, Neurosci. Lett. 107, 125.

Lovinger, D.M., N.L. Harrison and N.A. Lambert, 1992, The actions of 3-aminopropane-phosphinic acid at $GABA_B$ receptors in rat hippocampus, Eur. J. Pharmacol. 211, 337.

Nathan, T., M.S. Jensen and J.D.C. Lambert, 1990, $GABA_B$ receptors play a major role in paired-pulse facilitation in area CA1 of the rat hippocampus. Brain Res. 531, 55.

Newberry, N.R. and R.A. Nicoll, 1984, Direct hyperpolarising action of baclofen on hippocampal pyramidal cells, Nature 308, 450.

Seabrook, G.R., W. Howson and M.G. Lacey, 1990, Electrophysiological characterisation of potent agonists and antagonists at pre- and postsynaptic $GABA_B$ receptors on neurones in rat brain slices, Br. J. Pharmacol. 101, 949.

Sivilotti, L. and A. Nistri, 1991, GABA receptor mechanisms in the central nervous system, Prog. Neurobiol. 36, 35.

Solis, J.M. and R.A. Nicoll, 1992, Pharmacological characterisation of $GABA_B$ mediated responses in the CA1 region of the rat hippocampal slice, J. Neurosci. 12, 3466.

Thompson, S.M., M. Capogna and M. Scanziani, 1993, Pre-synaptic inhibition in the hippocampus, Trends Neurosci. 16(6), 222.