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Effect of CGP 36742 on the extracellular level of neurotransmitter amino acids in the thalamus

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Abstract

We have evaluated the effect of the brain penetrating GABAb antagonist, CGP 36742 on GABAb receptors using in vivo microdialysis in the ventrobasal thalamus of freely moving rat. When a solution of 1 mM CGP 36742 in ACSF was dialyzed into the ventrobasal thalamus, 2–3-fold increases of extracellular Glu, Asp and Gly running parallel with significant decreases of contralateral extracellular Asp and Gly were observed. Unilateral applications of Glu receptor antagonists (0.5 mM MK801, 0.1 mM CNQX) evoked 2–3-fold decreases of CGP 36742-specific elevations of extracellular Asp, Glu and Gly. Administration of CNQX and MK801 in the absence of CGP 36742 did not alter the extracellular Glu and Gly concentrations whereas extracellular Asp concentrations diminished by 42–45% at both sides. By contrast, no changes of extracellular Gly accompanied the 5–10-fold enhancements of extracellular Asp and Glu, observed during application of the Glu uptake inhibitor, *t*PDC (1 mM). Suspensions of resealed plasmalemma fragments from the rat thalamus were mixed rapidly with the membrane impermeant form of the fluorescence indicator, bis-fura-2 and the changes in fluorescence intensity in response to CGP 36742 (0.5 mM), and the GABAb agonist, baclofen (0.1 mM), were monitored on the time scale of 0.04 ms–10 s. Progress of CGP 36742-mediated influx, and baclofen-mediated efflux of Ca^{++} ion, antagonized by CGP 36742, was observed in the 1 ms–10 s period of time. These data support the hypothesis that background ventrobasal activities and thalamocortical signaling are under the control of inhibitory GABAb receptors in the ventrobasal thalamus.

1. Introduction

A variety of evidence has promoted the suggestion that 3-aminopropyl-n-butyl phosphinic acid (CGP 36742), the brain penetrating GABAb antagonist facilitates the formation of the long term memory trace (Carletti et al., 1993; Mondadory et al., 1996; and references cited there). Application of phosphinic analogues of GABA to the ventrobasal thalamus produced characteristic increases of extracellular concentrations of glutamate and other amino acids. Thus, GABAb receptors were assessed in the ventrobasal thalamus by monitoring changes in the extracellular concentrations of various amino acids induced by the antagonists, 3-aminopropyl-(diethoxymethyl)-phosphinic acid, (CGP 35348) and N-{α-(*S*)-methyl-[3′,4′-dichloro]benzyl}-3-amino-2-(*S*)-hydroxy-propyl-benzyl-phosphinic acid hydrochloride (CGP 55845A) (Crunelli et al., 1992; Kardos et al., 1996; Nyitrai et al., 1996). We have therefore evaluated the effect of CGP 36742 on GABAb receptors using in vivo microdialysis in the ventrobasal thalamus. In addition, we describe a fast-kinetic method to study GABAb receptor-mediated Ca^{++} ion translocation in vitro. This method involves rapid mixing of the membrane impermeant hexapotassium salt of the fluorescence indicator, bis-fura-2 (Haugland, 1996), with GABAb receptor containing resealed plasmalemma fragments from the rat thalamus. By placing bis-fura-2, in the presence of

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Ca^{++} ion, on the external side of the membrane, Ca^{++} ion flux mediated by GABAb receptors can be studied by monitoring changes of fluorescence intensity of the bis-fura-2-Ca^{++} complex as Ca^{++} ion moves across the membrane in response to 2-(*R*)-*p*-chlorophenil-GABA (baclofen) or CGP 36742 on the time scale of 0.04 ms–10 s.

The results allow us to relate effect of CGP 36742 on the extracellular concentration of neurotransmitter amino acids to the mechanism by which GABAb receptor is functioning in the thalamus by comparing effects of various inhibitors, including inhibitor of glutamate uptake, L-*trans*-pyrrolidine-2,4-dicarboxilic acid (*t*PDC, Bridges et al., 1991), as well as inhibitors of glutamate receptors of the AMPA/Kainate type, 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX, Honoré et al., 1988) and NMDA type, 5-methyl-10,11-dihydro-5*H*-dibenzo[a,d]cyclohepten-5,10-imine maleate (dizocilpine, MK801; Wong et al., 1986).

2. Materials and methods

2.1. Materials

HEPES, sodium glutamate, mercaptoethanol and butylated hydroxy toluene (BHT) were obtained from SIGMA. CNQX and dizocilpine (MK801) were from RBI. Bis-fura-2 was purchased from Molecular Probes. Acetonitril, orto-phtalaldehyde (OPA), phosphoric acid, tetraethylammonium hydroxide, and tetrahydrofuran were obtained from Merck. $CaCl_2$, KCl, NaCl, NaOH and $MgCl_2$ were purchased from Fluka. The amino acid standards were from Serva.

2.2. Suspensions of resealed plasmalemma fragments

Suspensions of resealed plasmalemma fragments were prepared as described previously (Kardos et al., 1994, Serfõzõ and Cash, 1995). Male Wistar rats, 3–6 weeks old, were killed by decapitation with a guillotine. The brain was put in ice-cold Ca^{++}-HEPES buffer, containing 145 mM NaCl, 5 mM KCl, 1.2 mM $CaCl_2$, 1 mM $MgCl_2$, 10 mM glucose and 10 mM HEPES, adjusted to pH 7.5 with 1 mM NaOH. Three thalami were homogenized with a glass-Teflon homogenizer (20 strokes up and down by hand) in 10 ml Ca^{++}-HEPES buffer containing 20 μM BHT. 10 ml of the above buffer was added to the homogenate and centrifuged at 200 g for 4 min at 4°C (Varifuge 20 RS, Heraeus Sepatech). The supernatant was centrifuged at 3500 g for 15 min, and the pellet was washed twice by suspending it in 20 ml buffer and centrifuged for 15 min at 3500 g. The final pellet was resuspended in 6 ml of the above Ca-HEPES buffer. The protein concentration was adjusted to 0.320 mg/ml according to the Folin reagent method (Lowry et al., 1951).

2.3. Determination of the concentration of endogenous GABA in suspensions of resealed plasmalemma fragments

Aliquots (500 μl) of resealed plasmalemma fragments in Ca^{++}-HEPES buffer from five preparations were centrifuged at 10000 g for 5 min and the supernatant filtered through Millipore 0.22 μm pore size sterile syringe filters. Samples of buffer used for making up bis-fura-2 solutions and suspensions of resealed plasmalemma fragments were treated in the same way. Samples thus prepared were stored at −80°C. Concentration of GABA was determined as described below.

2.4. Microdialysis

Microdialysis probes were prepared as described earlier (Juhász et al., 1989). Briefly, 5000 D cut-off hollow (Travenol, diameter 0.2 mm, length 3 mm) was adjusted into 25-gauge stainless steel tubing. Glass capillaries pulled from Jencons glass tubing were used for the inlet and outlet of the probe. These glass capillaries were guided by stainless steel tubes. Animal experiments were carried out as previously described (Kardos et al., 1996; Nyitrai et al., 1996) on the basis of local ethical rules in accordance with the Guidelines on the Use of Living Animals in Scientific Investigations 1984. The rat (350–400 g) was anaesthetised with 1% halothane in air and placed into a stereotaxic frame. The probes were implanted into the ventrobasal thalamic nuclei bilaterally (A:−1.9, L: 2.5, V:−7 mm, according to the atlas of Pellegrino and Cushman, 1967). To minimise tissue damage the final position of the probes was reached slowly, in not less than 20 min.

Microdialysis experiments started at 24 h after the surgery. Perfusion with artificial cerebrospinal fluid (ACSF) containing 144 mM NaCl, 3 mM KCl, 1 mM $MgCl_2$ and 2 mM $CaCl_2$ in water bidistilled over $KMnO_4$ was performed at a rate of 1 μl/min. The pH of ACSF was adjusted to 7.4 with NaOH prior to the microdialysis experiment started. The purity of ACSF used in the experiment was checked by HPLC. The samples, 20 μl each, were collected every 20 min for 1 h (control). Thereafter different inhibitors like CGP 36742 (1 mM), CNQX (0.1 mM), MK801 (0.5 mM) and *t*PDC (1 mM) dissolved in ACSF were applied unilaterally via the microdialysis probe for 2 h and 1 h, respectively. Based on the in vitro calibration of the probes (Juhász et al., 1989) the estimated concentration of the drug proximal to the wall of the microdialysis probe is about 20–30% of its concentration

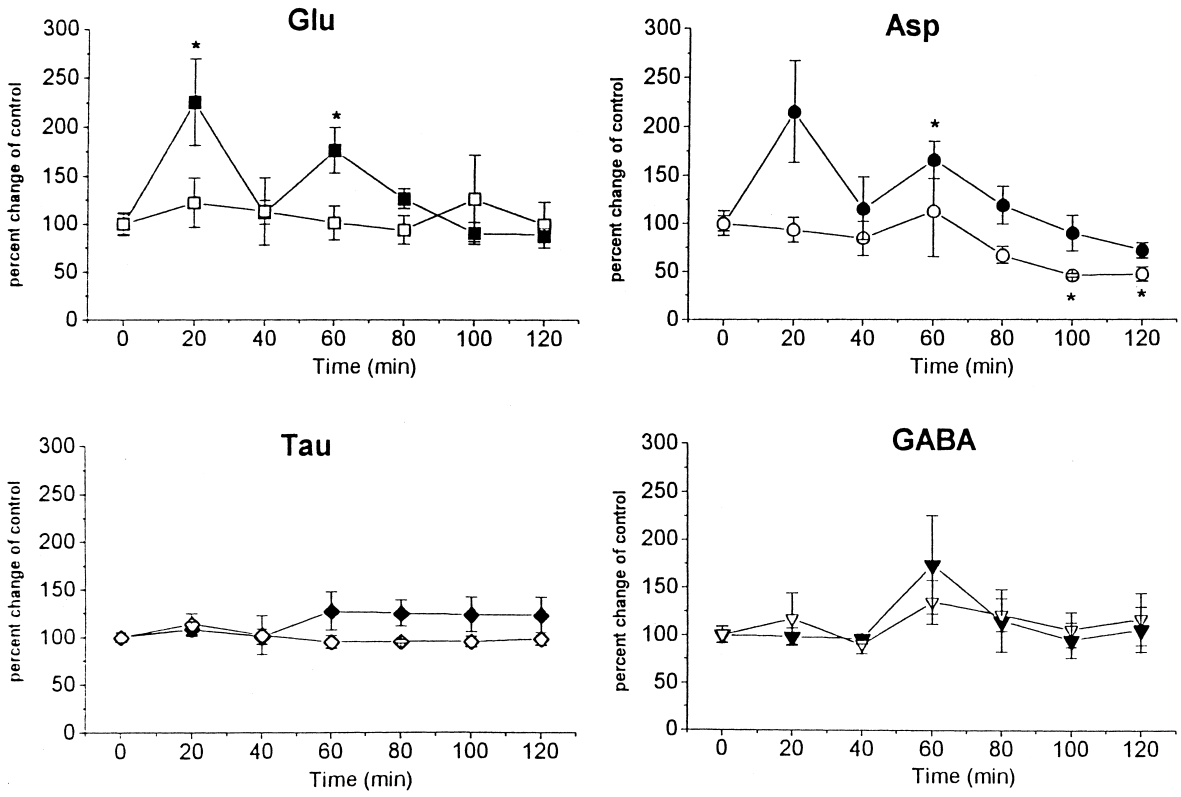

Fig. 1. Contralateral changes in the extracellular concentrations of different amino acids monitored during unilateral application of CGP 36742 (1 mM) in the ventrobasal thalamic nuclei of freely moving rat. Square (Glu), circle (Asp), diamond (Tau) and triangle (GABA) symbols: sides of drug (solid) and ACSF (open) applications. Data from experiments are expressed as mean percentage (±SEM) of control taken as the average concentration of three samples collected for an hour before the solution of 1 mM CGP 36742 in ACSF was introduced into the microdialysis probe. Student's *t*-test indicated values significantly different from 100% at $P < 0.05$ (*).

inside the probe. Probes implanted symmetrically in the contralateral thalamus were perfused with ACSF. After the experiment the brain was removed and placed into 10% paraformaldehyde. Anatomical localisation of the dialysis probes was checked by histological analyses of Nissl-stained coronal sections.

2.5. Determination of the concentration of Glu, Asp, Gly, GABA and Tau in the microdialysis samples

Precolumn derivatization with OPA was performed in the presence of mercaptoethanol at pH 10.4. Quantitative analysis of the OPA derivatized amino acids was performed in an automated HPLC-combined fluorescence detection system (Pharmacia AminoSys) using 305–395 nm excitation and 430–470 nm emission filters and HP Hypersyl ODS reversed phase column with the following eluents: 0.1 M phosphate buffer containing 0.5% (vol/vol) tetrahydrofuran and 0.02% (vol/vol) tetraethylammonium hydroxide, pH 6.0 (A); 70% acetonitrile mixed with 0.1 M phosphate buffer adjusted to pH 6.0 with NaOH (B). The gradient profile was 3% B at 0 min, 11% at 1.5 min, 22% B at 16 min, 40% B at 20 min, 60% B at 25 min, 100% B at 29 min, 2% B at 37 min. External standards of 10 μM amino acids were injected after every 10 samples. Chromatograms were evaluated by PE Nelson 2000 software. Detection limits for amino acids were 0.5–5 pmoles in 10 μl sample.

2.6. Transmembrane Ca^{++} ion flux measurements

Transmembrane Ca^{++} ion flux was followed by rapid mixing of resealed plasmalemma fragments in 75 μl buffer with an equal volume of buffer solution containing 1 μM bis-fura-2 (membrane impermeant form) in the presence or absence of CGP 36742 (1 mM) and/or baclofen (0.2 mM). Fast mixing of thermostatted (30.0 ± 0.1°C) reactants was performed in a SF-61 DX2 Stopped–Flow/ UV Fluorescence Detection System (Hi-Tech). Under these conditions the decrease of the fluorescence intensity of bis-fura-2, monitored at 500 nm using a 260–390 nm excitation filter, was corresponded to the influx of Ca^{++} ion into *native* plasma membrane vesicles. The percent fluorescence intensity in time (0.04 ms–10 s) was recorded on a logarithmic time base (Kovács et al., 1998). To reduce interference of light scattering from vesicles with the

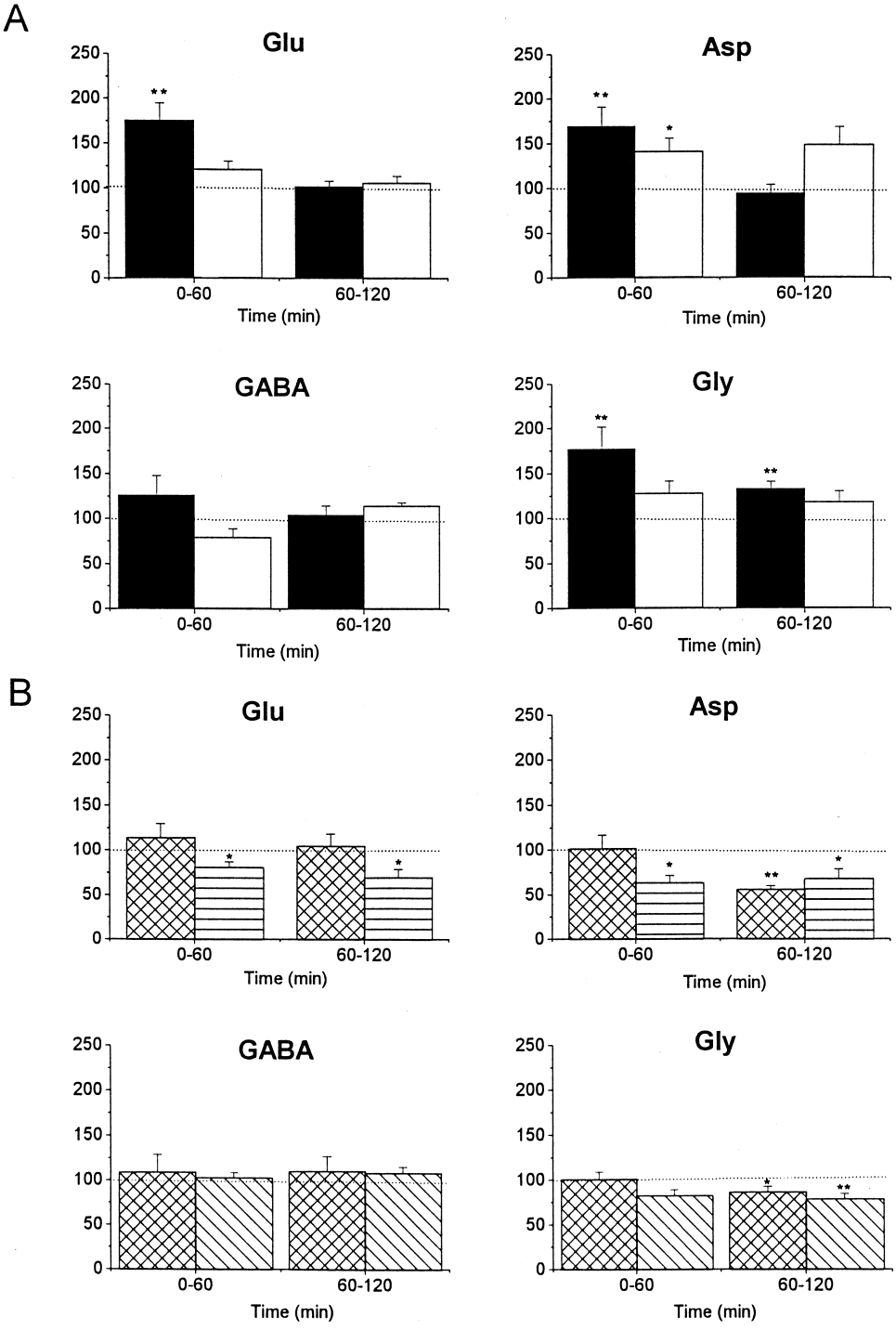

Fig. 2. Comparison of contralateral changes observed in the extracellular concentrations of neurotransmitter amino acids evoked by unilateral application of CGP 36742 (1 mM) and CGP 36742 (1 mM) together with CNQX (0.1 mM) and MK801 (0.5 mM) in the ventrobasal thalamic nuclei of freely moving rat. (**A**) side of treatment; solid columns CGP 36742 application, open columns CGP36742 applied with CNQX and MK801. (**B**) contralateral side; criss-cross columns CGP 36742 application, horizontally hatched columns CGP 36742 applied with CNQX and MK801. Data from two experiments expressed as mean percentage (±SEM) of controls taken as the average concentration of three samples collected for 1 h before either the solution of 1 mM CGP 36742 or the solution of 1 mM CGP 36742 with 0.1 mM CNQX and 0.5 mM MK801 was introduced into the microdialysis probe, were averaged over the 0–60 min and 60–120 min period of drug application. Student's *t*-test indicated values significantly different from 100% at $P < 0.05$ (*) and $P < 0.01$ (**).

fluorescence emission of bis-fura-2, dilute 3% (vol/vol) suspensions were used. Traces representing averages of 3–4 experiments, each performed in 7 repeated measurements, comprise 640 data acquired automatically. Transformation of the percent fluorescence data into the *percent change of fluorescence* was performed with substraction of background trace measured without additives. Traces are plotted so that the negative values represent the influx of Ca^{++} ion.

2.7. Data evaluation

Since diffusion of amino acids into the microdialysis probe is complex, concentrations of amino acids in the dialysate are not identical with the extracellular concentration of amino acids (Benveniste and Huttemeier, 1990; Shimizu et al., 1993) therefore concentrations of amino acids measured in dialysates collected during various drug applications were related to averaged [amino acid] of control samples collected for an hour previous to drug application and were given as percent changes. In the case of CGP 36742 application data obtained in every 20 min were pooled from six animals and averaged (mean ± SEM). In the other cases values of [amino acid] in three sequential dialysis samples collected in the 0–60 min and 60–120 min periods pooled from two animals were averaged (mean ± SEM). For statistical analysis of data we used Students *t*-test. Percent change of control value was considered significant at $P < 0.05$ level.

3. Results

Concentration of Glu, Asp, Gly, Tau and GABA in the control dialysate samples remained constant for an hour previous to drug application, and found to be: 0.44 ± 0.07 μM Glu, 0.29 ± 0.03 μM Asp, 2.3 ± 0.5 μM Gly, 1.9 ± 0.23 μM Tau, 0.09 ± 0.02μM GABA, respectively.

3.1. Changes in the extracellular concentrations of amino acids during the application of CGP 36742 in the ventrobasal thalamus

Dialysis of ACSF containing 1 mM CGP 36742 through the probe placed in the ventrobasal thalamus of freely moving rat increased extracellular concentrations of Glu and Asp (Fig. 1). Percent changes in the extracellular concentration of Glu showed a two release-pulse pattern with significant increase 226 ± 44% and 176 ± 24% displayed at 20 min and at 60 min ($P < 0.05$), respectively. Changes detected in the dialysate samples collected at 40 min (112 ± 13%), 80 min (126 ± 11%), 100 min (90 ± 12%) and 120 min (88 ± 7%) after the start of CGP 36742 application were not significant and varied near to the control value. Increases in the extracellular [Asp] were significant 1 h after the start of CGP 36742 microdialysis (166 ± 20%, $P < 0.05$). Percent changes in the extracellular concentrations of Tau and GABA did not exceed the control levels significantly (Tau: 109 ± 8%, 101 ± 8%,128 ± 20%, 125 ± 14%, 124 ± 18%, 123 ± 18%; GABA: 97 ± 9%, 95 ± 5%, 172 ± 52%, 114 ± 33%, 94 ± 18%, 105 ± 23%; Fig. 1) throughout the experiment. Administration of CGP 36742 produced significant increase in extracellular [Gly] (0–60 min: 176 ± 26%, 60–120 min: 132 ± 9%, $P < 0.05$, Fig. 2). In the contralateral thalamus, where only ACSF was perfused, significant decreases in extracellular [Asp] and [Gly] were observed in 60–120 min: 55 ± 5% and 85 ± 7%, respectively; $P < 0.05$, Fig. 2).

3.2. Changes in the effect of CGP 36742 in the presence of CNQX and MK801

Coadministration of NMDA (Wong et al., 1986) and Kainate/AMPA type (Honoré et al., 1988) glutamate receptor antagonists (0.5 mM MK801 and 0.1 mM CNQX, respectively), diminished the CGP 36742 induced increase in extracellular [Glu], [Asp] and [Gly] (Fig. 2). Increases in Glu (175 ± 20), Asp (169 ± 23%) and Gly (176 ± 26%) concentrations in the 0–60 interval observed with CGP 36742 were reduced to one third (Glu: 121 ± 10% and Gly: 127 ± 15%) or half (Asp: 140 ± 16%; $P < 0.05$).

By monitoring the contralateral ventrobasal thalamus, the decreases in extracellular [Asp] (67 ± 11%) and [Gly] (77 ± 6%) in 60–120 min interval observed with CGP 36742 were unaltered when CGP 36742, CNQX and MK801 were applied together, whereas decreased extracellular [Glu] were detected through the whole period of observation (0–60 min: 80 ± 6%, 60–120 min: 69 ± 10%; $P < 0.05$, Fig. 2).

Administration of a mixture of CNQX (0.1 mM) and MK801 (0.5 mM), in the absence of CGP 36742, caused significant decreases of the basal extracellular Asp concentrations in 0–120 min 55 ± 5% and 58 ± 15% at the lateral and contralateral sides, respectively ($P < 0.05$). Whereas, administration of the mixture of CNQX (0.1 mM) and MK801 (0.5 mM) for two h showed no significant effects on the extracellular concentrations of Glu (laterally: 90 ± 11%, contralaterally: 88 ± 8%), Gly (laterally: 87 ± 9%, contralaterally: 76 ± 15%) and Tau (laterally: 115 ± 7%, contralaterally: 100 ± 3%). However, we did observe some elevation of the extracellular GABA concentration during application of CNQX and MK801 (laterally: 121 ± 14%, contralaterally: 131 ± 10%) during the above 2-h treatment.

Table 1
The effect of *t*PDC application on the extracellular Glu, Asp, Gly and Tau concentrations in the thalamus of freely moving rats ($^{*}P < 0.05$, $^{**}P < 0.01$)

		Percent Change of [amino acid][a]			
Probe Position	Time (min)	Glu	Asp	Gly	Tau
Side of treatment[b]					
	−60–0	100 ± 6	100 ± 5	100 ± 3	100 ± 3
	0–60	1260 ± 120**	451 ± 50**	127 ± 13	142 ± 8**
	60–120	228 ± 19**	123 ± 13	80 ± 10	111 ± 9
Contralateral side					
	−60–0	100 ± 12	100 ± 14	100 ± 14	100 ± 14
	0–60	82 ± 12	68 ± 5**	56 ± 8**	115 ± 8
	60–120	108 ± 18	90 ± 18	59 ± 18	109 ± 6

[a] Average concentrations in the control (100%) dialysate samples were: 0.29 ± 0.03 μM Asp, 0.44 ± 0.07 μM Glu, 2.3 ± 0.5 μM Gly and 1.9 ± 0.23 μM Tau.

[b] The following experimental protocol has been applied: −60–0 min ACSF, 0–60 min *t*PDC, 60–120 min ACSF.

3.3. The effect of tPDC on the extracellular concentrations of amino acids

Application of the Glu uptake blocker *t*PDC (1 mM, 0–60 min) in the ventrobasal thalamus of freely moving rat produced an order of magnitude higher extracellular [Glu] as well as five-fold increase in extracellular [Asp] (1260 ± 120% and 451 ± 50%, $P < 0.01$, Table 1). One hour after finishing up the application of *t*PDC, the [Glu] remained elevated (60–120 min 228 ± 19%, $P < 0.01$). In contrast to significant alterations of extracellular [Glu] and [Asp] there was no change in the extracellular [Gly] produced by *t*PDC (0–60 min 127 ± 13%, 60–120 min 80 ± 10%). Administration of *t*PDC (0–60 min) caused a transient increase in the extracellular concentration of Tau (0–60 min: 142 ± 8%, 60–120 min: 111 ± 9%, $p < 0.05$, Table 1).

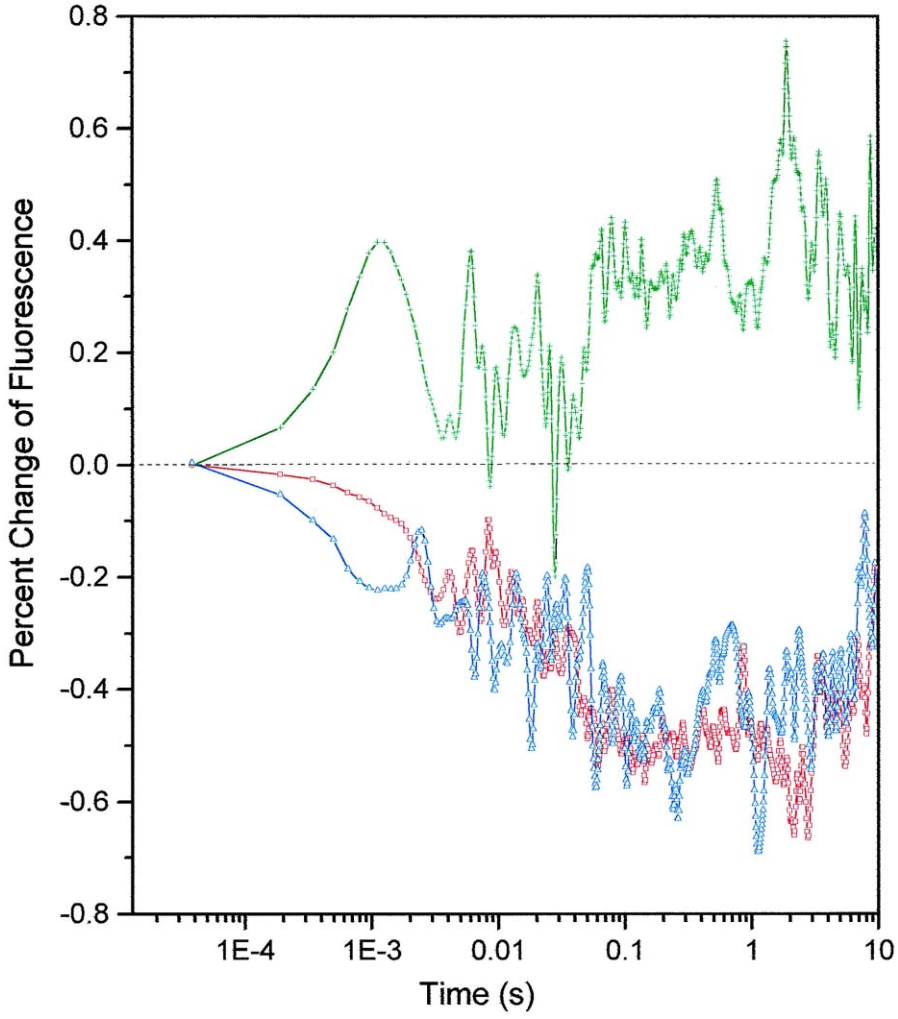

Fig. 3. The effect of GABAb receptor antagonist, CGP 36742, and agonist, baclofen, on the transmembrane Ca^{++} ion flux in resealed plasmalemma fragments from the rat thalamus. Symbols: 0.5 mM CGP 36742 (red □), 0.1 mM baclofen (green +), 0.1 mM baclofen with 0.5 mM CGP 36742 (blue △).

3.4. The effect of CGP 36742 and baclofen on the transmembrane Ca^{++} ion flux in resealed plasmalemma fragments from the rat thalamus

After the addition of 0.5 mM CGP 36742 to suspensions of resealed plasmalemma fragments isolated from the rat thalamus the progress of transmembrane Ca^{++} ion influx can be observed (Fig. 3), whereas baclofen (0.1 mM) induced efflux. CGP 36742 inhibited most of the transmembrane Ca^{++} ion efflux induced by baclofen over the entire range of response (Fig. 3). By measuring concentrations of endogenous GABA in suspensions of resealed plasmalemma fragments, as well as GABA content of buffers used in the stopped-flow experiments, the values obtained for a 1:1 mixture of the buffer and the suspension of resealed plasmalemma fragments were found to be: [GABA] = 0.30 ± 0.12 μM. The analyses, showing presence of a significant quantity of [GABA] in the membrane preparation, were supported by the appearance of Ca^{++} ion influx which is seen above to be appeared in the presence of CGP 36742.

4. Discussion

Increased extracellular Glu, Asp and Gly in the ventrobasal thalamus observed with CGP 36742 support previous findings (Kardos et al., 1996, Nyitrai et al., 1996) that the extracellular concentration of Glu, Asp and Gly is under the control of inhibitory GABAb receptors in the ventrobasal thalamus in vivo. By contrast, CGP 36742 produced significant decrease of extracellular Asp and Gly in the contralateral ventrobasal thalamus. This depressant effect was extended to extracellular Glu when CGP 36742 administered in combination with NMDA and AMPA/Kainate receptor antagonists (MK801 and CNQX).

Opposite contralateral changes of extracellular neurotransmitter amino acids elicited by unilateral application of a GABAb antagonist (CGP 36742) in the rat ventrobasal thalamus are not documented. Presumably, it may be due to thalamocortical network signaling, however, involvement of other brain compartments, like glia or endothelium, cannot be excluded, also. Supporting this, we found decreases of the extracellular Asp and Glu concentrations in the contralateral thalamus during *t*PDC application also. However no anatomical evidence was found (Jones, 1985), electrophysiological measurements suggested that thalami of both sides are functionally interconnected (Jones, 1985). Most likely, the effects of increased Asp and Glu concentrations reach out the contralateral thalamus via consecutive thalamocortical, cortico–cortical and corticothalamic pathways. Contralateral Asp and Gly levels can be decreased by increased reticular inhibition at both sides.

The role of Gly is as yet unclear, although it is relevant to note that Gly inhibited excitatory responses to kainate, quisqualate and NMDA in the rat ventrobasal thalamus in vivo (Salt, 1989). Blockade of these inhibitory responses to Gly by strychnine revealed a facilitatory action of Gly on NMDA responses, also (Salt, 1989). It is thus possible that in addition to a non-selective inhibitory action, Gly facilitates NMDA receptor-mediated responses in the ventrobasal thalamus in vivo.

To extend and confirm this hypothesis we have examined the effect of a Glu uptake inhibitor, *t*PDC in the rat ventrobasal thalamus. Robust increases of extracellular Glu and Asp and no changes in Gly with *t*PDC can be contrasted with moderate increases of extracellular Glu, Asp and Gly observed during CGP 36742-inhibition of GABAb receptors. These moderate increases of extracellular Glu and Asp may arise from excessive Gly-mediated inhibition within the ventrobasal thalamus caused by increased basal extracellular Gly concentrations.

Blockade of NMDA and AMPA/kainate type Glu receptors eliminated the increases of Glu and Gly levels by CGP 36742, almost completely. The Glu receptor sensitive component of the increased extracellular Glu and Gly concentrations is likely due to Glu receptor activation by Glu released by GABAb receptor blockade. In turn, activated Glu receptors might elicit Glu and Gly release. Elevated extracellular concentration of Glu and Asp observed during *t*PDC application failed to change Gly concentration, by the fact itself suggesting a role for GABAb receptor in the control of extracellular concentration of Gly. By contrast, the increase of the extracellular Asp level by CGP 36742 was attenuated, but not eliminated, by the presence of Glu receptor antagonists. When Glu receptor antagonists were applied without CGP 36742 the concentration of extracellular Asp decreased parallel to minor increases of extracellular GABA level with no changes in Glu and Gly levels. Collectively these results suggest that mechanisms controlling extracellular concentration of Asp and Glu with Gly are different.

The calcium signal for transmitter secretion in presynaptic terminal (Katz and Miledi, 1967) have been used for a characterization of thalamic GABAb receptors. Consistent with previous observations (Kardos et al., 1996), we found, that the presence of CGP 36742 caused a transmembrane Ca^{++} ion influx in resealed plasmalemma fragments from the rat thalamus containing considerable amount of endogenous GABA. The results obtained with resealed plasmalemma fragments are in agreement with the presence of inhibitory GABAb receptors in the thalamus and suggest that

presynaptic modulation of Ca^{++} ion flux by GABAb receptors may be involved in the control of the basal release of neurotransmitter amino acids in the rat thalamus in vivo.

Overall increases of extracellular Glu, Asp and Gly elicited by CGP 36742 in the rat ventrobasal thalamus in vivo were attenuated in the presence of both NMDA and AMPA/Kainate type Glu receptor antagonists. Such results may imply modulation of thalamocortical glutamatergic transmission, superimposed on the control of the ventrobasal background activity, that characterize ventrobasal GABAb receptor function.

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