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Synaptosomal uptake and release of dopamine and 5-hydroxytryptamine in the nucleus accumbens in vitro following in vivo administration of lysergic acid diethylamide in rats[1]

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Summary

The uptake and the depolarisation-induced release of dopamine (DA) and serotonin (5-HT) were investigated after systemic application of LSD on synaptosomes of the nucleus accumbens of rats. For the release experiments synaptosomes were prelabelled with [^{14}C]-DA and [^{3}H]-5-HT, respectively, and superfused with physiological and potassium-enriched (50 mM) solutions. Low doses of LSD (0.1 and 0.5 mg/kg i. p.) induced a dose-dependent inhibition of the DA-release and an increase of the DA-uptake, respectively. LSD inhibited both the release and the uptake of 5-HT significantly.
The results are discussed with respect to a reliable characterization of the in vivo induced effects of LSD on the isolated synaptosomes.

Introduction

Lysergic acid diethylamide (LSD) requires growing interest as a useful tool in psychopharmacology and especially in the search for animal models of psychosis [1]. But despite extensive investigations the neurochemical basis of some pharmacological effects of LSD in laboratory animals and much more of the hallucinogenic action of LSD in man is poorly understood. Marked changes in the central 5-hydroxytryptamine (5-HT) system have been described [2, 3] and the decrease in 5-HT turnover [4–6] is believed to depend on the inhibition of the firing rate of raphe neurons [7]. On the other hand there is some evidence for an influence of LSD especially on the nigrostriatal dopamine (DA) system. But it is by no means clear, if these changes reflect a direct action of LSD on DA receptors or may be induced indirectly on the basis of the well known interaction between 5-HT and DA transmission systems [8, 9].
Recently it has been demonstrated by FINK et al. [10] that apomorphine- or amphetamine-induced hypermotility in rats is significantly potentiated by low doses of LSD and other hallucinogens, too. This potentiating effect has been shown to be triggered by a specific action of LSD on raphe neurons and seems to be mediated by the mesolimbic DA system in the nucleus accumbens [11].
These findings gave rise to a revaluation of the effects of LSD on 5-HT and DA systems especially in the nucleus accumbens [11]. According

[1] Dedicated to Prof. Dr. W. OELSZNER on the occasion of his 60th birthday

vations [12—15] distinct in vitro changes in functionally characteristic parameters of these transmission systems should be expected even after systemic administration of drugs. We therefore investigated the uptake and K^+-stimulated release of 5-HT and DA in crude synaptosomal fractions of the nucleus accumbens of rats following intraperitoneal injections of LSD.

Material and methods

Tissue preparation

We used male Wistar rats (VEB Versuchstierproduktion Schönwalde) weighing 150 ± 10 g and housed under standard conditions (temperature 22 ± 2 °C, 12 h light/dark schedule, food and water ad libitum). Lysergic acid diethylamide tartrate (LSD) (Spofa Praha, 0.1 or 0.5 mg/kg) was injected i.p. 30 min before killing. Control rats were treated with equivalent volumes of saline. After killing the rats by immersion in liquid nitrogen for about 7 s the brains were rapidly removed and dissected on ice cooled petridishes. Crude synaptosomal fractions were prepared from the nucleus accumbens. The tissue (30 ± 5 mg) was homogenized (teflon pestle, clearance 0.03, 10 strokes) in 0.32 M sucrose containing (mM): Na_2HPO_4 2.0, KH_2PO_4 0.7, $MgCl_2$ 1.0, disodium EDTA 3.0, *p*H 7.3. The homogenate was then centrifuged (1000 × *g* for 8 min, 4 °C) to remove nuclei and cell debris. The supernatant synaptosomal suspension was kept at 4 °C until use. The time period from killing the rats to the beginning of uptake incubation procedure did not exceed 15 min.

Uptake assay

For dopamine (DA) uptake studies according to PALFREYMAN et al. [16] aliquots of the crude synaptosome suspension was diluted 1:5 with a modified Mc Ilwain buffer [17] containing (mM): NaCl 130.0, KCl 1.7, KH_2PO_4 1.3, Na_2HPO_4 10.4, $MgSO_4$ 1.3, $CaCl_2$ 1.3, glucose 11.0, sucrose 17.3, ascorbic acid 1.1, disodium EDTA 0.2, pargyline 0.125. The buffer was saturated with 5% carbon dioxide in oxygen and adjusted to *p*H 7.3. 5-hydroxytryptamine (5-HT) uptake studies according to COYLE and SNYDER [18] were made using crude synaptosomal fractions diluted 1:5 with a Krebs-Henseleit medium [19] with the following composition (mM): NaCl 119.0, KCl 4.6, $CaCl_2$ 2.5, KH_2PO_4 0.85, $MgSO_4$ 0.84, $NaHCO_3$ 24.8, glucose 10.0, disodium EDTA 0.05, ascorbic acid 0.56, pargyline 0.02. The buffer was saturated with carbon dioxide in oxygen and adjusted to *p*H 7.3.
After equilibrating the synaptosomes at 37 °C for 5 min either [^{14}C]-DA or [^{3}H]-5-HT (New England Nuclear, spec. act. 53.2 mCi/mmol and 25.6 Ci/mmol) was added to yield a final concentration of $4 \cdot 10^{-7}$ M and $3.9 \cdot 10^{-8}$ M, respectively. The synaptosomes were incubated an additional 10 min. To stop the reaction 2 ml of ice cold incubation medium were added. Then the samples were centrifuged at 18000 × *g* for 20 min at 4 °C, after which the pellets were washed twice with 1 ml ice cold saline. 1 ml of absolute ethanol was added to each tube and after rehomogenization (8 strokes) and centrifugation at 18000 × *g* for 15 min at 4 °C aliquots of the supernatant were transferred into counting vials. The scintillation solution consisted of 100 g naphthalene, 4 g PPO and 0.2 g POPOP dissolved in 1 l dioxan. Radioactivity was measured in a LKB scintillation counter (Model 1210, Ultrobeta). After correcting for blank values incubated at 0 °C and representing passive transport and unspecific binding the amine uptake values are expressed as dpm per mg protein [20] and were set to 100% in control animals for comparison with drug treated animals.

Synaptosomal transmitter release

For study of DA and 5-HT release crude synaptosomal suspensions were prelabelled with [^{14}C]-DA and [^{3}H]-5-HT according to the incubation procedure described above, then placed under light pressure on GFB Whatman filters and transferred into a superfusion chamber (inner volume 0.4 ml) modified according to SCHMIEDER et al. [21]. The superfusion rate was 0.3 ml/min. Fractions were collected every 2 min. After 10 min of superfusion with McIlwain medium for DA and Krebs-Henseleit buffer (each buffer contains doubled Ca^{2+} conc.) for 5-HT, respectively, synaptosomes were depolarized for 5 min by 50 mM K^+(substituting

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Discussion

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an equimolar concentration of NaCl) and further 10 min without K^+-enriched buffer. After finishing superfusion the GFB filter and aliquots of the collected fractions were transferred into counting vials and measured for radioactivity.

For comparison of synaptosomal transmitter release after in vivo application either of drugs or saline we estimated the difference between K^+-evoked and virtual unstimulated release (dpm/fraction during 5 min K^+-stimulation minus virtually dpm/fraction).

Statistical analysis was performed according to WILCOXON, MANN and WHITNEY on a Hewlett-Packard desk computer (Model 9825 A, Opt. 001).

Results

Release of DA and 5-HT

Fig. 1 and 2 demonstrate typical superfusion profiles after preloading the synaptosomes with [^{14}C]-DA and [^{3}H]-5-HT, respectively. The change from physiological to K^+-enriched superfusion medium induces immediately an increase of the transmitter overflow. In preliminary experiments we could show that the depolarisation-induced overflow of the transmitters was to a great extent Ca^{2+}-dependent. The radioactivity of every fraction represents 1.5—12% of the total activity taken up. The stimulated increase in release is calculated as the difference between the virtual overflow and the counted overflow after potassium. Intraperitoneal injections of LSD induced a significant inhibition of the overflow of both transmitters (Fig. 1, 2). The lower dose of 0.1 mg/kg LSD did not change the DA release significantly whereas 0.5 mg/kg LSD caused a marked decrease to about 58% (DA) and 60% (5-HT) of controls (Fig. 3, open columns).

Uptake of DA and 5-HT

We used concentrations of DA and 5-HT near the K_m values described for striatum (K_m for DA = $1.3 \cdot 10^{-7}$ M and for 5-HT = $4.9 \cdot 10^{-8}$ M [22, 23]). In preliminary experiments a time-dependent uptake of DA as well as of 5-HT, reaching plateaus after 5—6 min could be demonstrated. Therefore all determinations for the uptake were performed 10 min after starting the experiments. For DA uptake an initial velocity of 18.4 ± 2.1 pmoles/mg protein/min was calculated. An unspecific uptake and binding at 0 °C of about 10% of the active uptake at 37 °C were determined for both systems. After an intraperitoneal injection of 0.5 mg/kg LSD marked changes in the uptake of DA and 5-HT could be demonstrated. The uptake of DA was significantly increased to about 156% of controls; on the other hand the 5-HT uptake decreased to about 43% of controls (Fig. 3, right columns).

Discussion

For the study of drug-induced changes in the turnover, release and reuptake of putative transmitters various in vivo and in vitro methods have been developed. In vivo methods — e.g. tracerkinetic methods, the use of inhibitors of synthesis or metabolization of transmitters — indicate changes of the turnover or the endogenous levels of metabolites without direct indications of the presynaptically released, that means, biologically active transmitter pool. On the other hand several in vitro methods (slices, subcellular particles) are available for characteriz-

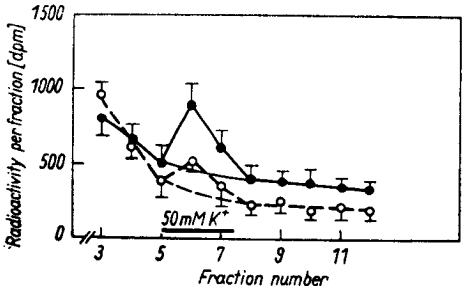

Fig. 1

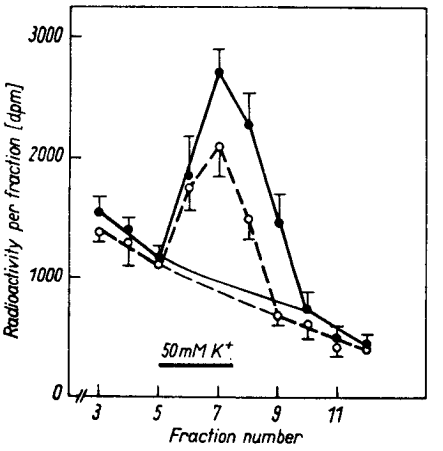

Fig. 2

Fig. 1. Effect of i. p. injected LSD on K+-stimulated release of preaccumulated [^{3}H]-5-HT (see methods)

● control; ○ 0.5 mg LSD/kg i. p. 30 min before killing. The smaller lines represent the unstimulated virtual overflow. The curves are based on the average of 4—5 experiments

Fig. 2. Effect of i. p. injected LSD on K+-stimulated release of preaccumulated [^{14}C]-DA (see methods)

● control; ○ 0.5 mg LSD/kg i. p. 30 min. before killing. The smaller lines represent the unstimulated virtual release. Each fraction represents a time period of 2 min. The curves are based in the average of 4—5 experiments

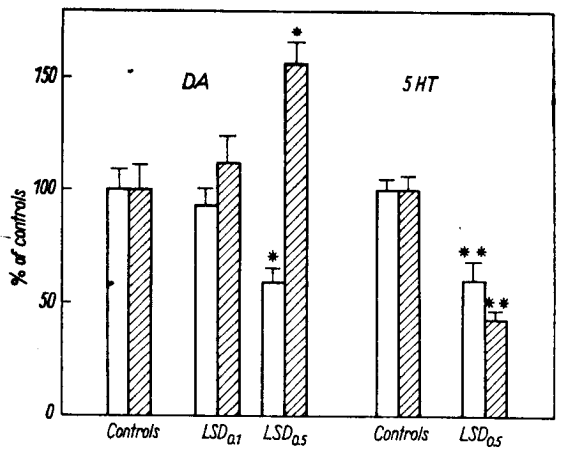

Fig. 3. Effect of i. p. injected LSD (0.1 mg/kg and 0.5 mg/kg) 30 min before killing on potassium evoked release (□) and uptake (▨) of [^{14}C]-DA and [^{3}H]-5-HT

Statistical analysis according to WILCOXON, MANN and WHITNEY ($n = 4-5$)

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ing synthesis, release and reuptake of transmitters under the direct influence of drugs. A combination of these two procedures, investigations in vitro following the application of drugs in vivo, has been scarcely employed.

GLOWINSKI and coworkers could demonstrate a diminished synthesis of 5-HT in striatal slices of rats after intraperitoneal injections of MAO-inhibitors [24] and LSD [12], respectively. Amphetamine, given systemically, caused a dose dependent inhibition of synaptosomal DA synthesis [13]. On the other hand neuroleptics induced an increase in DA synthesis in slices and synaptosomes [14, 15]. Amphetamine and benztropine inhibited the uptake of DA and 5-HT in striatal slices and synaptosomes dose-dependently after in vivo application [25]. Δ^8-tetrahydrocannabinol induced in stressed rats a marked increase of DA uptake in striatal synaptosomes [26]. LSD has been shown to reduce 5-HT release [12]. This inhibitory effect can be induced, in contrast to the inhibition of synthesis, by LSD added in vitro to the slices. After intraperitoneal injections of thioproperazine the release and synthesis of DA in striatal slices were stimulated [15]. These effects could not be reproduced by incubating the slices with this drug indicating the importance of an interneuronal feedback mechanism for DA release.

These general findings support the conclusion that after systemic administration of drugs functional changes in nerve terminals of distinct neurons are induced which persist for a certain time period after killing the rats. These alterations for instance in biosynthesis, release and uptake of transmitters are demonstrable in brain slices or synaptosomes in vitro. Our results about significant changes in the synaptosomal uptake and release of DA and 5-HT in the nucleus accumbens of rats following intraperitoneal injections of LSD are in agreement with the above mentioned observations. This combined procedure offers some striking advantages in comparison to usual in vivo or in vitro experiments.

For investigating the release of DA and 5-HT we used a special superfusion technique [21], by which false conclusions can be excluded. By the distribution of synaptosomes in a very thin layer and a rapid superfusion rate it is unlikely that changes in the release of transmitters are mediated by modulatory influences of other transmitters released from a different population of synaptosomes or that the released transmitter is taken up again.

An evaluation of specific LSD-induced alterations mentioned above in our experiments needs a comparison with results already published and obtained by in vivo and in vitro studies. After systemic administration of low doses of LSD the firing rate of raphe neurons of rats is completely inhibited [7]. Due to this inhibition a decreased 5-HT turnover rate after LSD treatment has been demonstrated [4—6]. The LSD action on raphe neurons appears to be functionally comparable with alterations after raphe lesion. A reduced 5-HT content in several brain areas and tryptophane hydroxylase activity, too, was found following lesion of the B8 region [27, 28].

In vitro the high affinity uptake of 5-HT in synaptosomes is reduced by LSD dose-dependently [29]. The electrically stimulated release of 5-HT from brain slices was decreased by addition of LSD to the superfusion medium [30]. Recently, CERRITO and RAITERI [31] and GÖTHERT and WEINHEIMER [32] reported that 5-HT inhibited its own stimulated release from hypothalamic synaptosomes and cortical slices, respectively, obviously by activating presynaptic 5-HT autoreceptors.

Confirming recent observations on slices [12] in own in vitro experiments (unpublished) LSD markedly depresses the synaptosomal release of 5-HT.

Our in vitro results demonstrating a significant decrease in the K^+-stimulated release of 5-HT and a pronounced inhibition of 5-HT uptake following systemic administration of LSD are in accordance with results obtained by in vitro or in vivo studies. It is concluded that the LSD-induced diminished release and uptake, respectively, in synaptosomes of the nucleus accumbens of rats depends on functional changes in nerve terminals due to an inhibition of the firing rate of raphe neurons or to an activation of presynaptic 5-HT receptors on synaptosomal membranes (release) or by local blocking of the synaptosomal uptake mechanism.

LSD given systemically increases the synthesis of DA in the nigrostriatal and mesolimbic system [8, 9, 33]. In own tracerkinetic experiments the formation of dihydroxyphenylacetic acid (DOPAC) was found to be increased but simultaneously the synthesis of homovanillic acid (HVA) was decreased [34]. Using the push-pull technique a reduced DA outflow from cat brain has been shown after administration of LSD [35]. This confirms the inhibition of HVA synthesis regarding HVA as a marker for released DA. Our experiments with synaptosomes following in vivo administration of LSD resulted in an inhibition of the K^+-evoked release and an increase in DA uptake. This stimulated uptake seems to be responsible for the increased DOPAC-synthesis mentioned above.

The LSD-induced alterations of DA uptake and release can be explained by different actions. They can be mediated by direct actions of LSD on DA receptors, either on somatodendritic receptors in the A 10 region or on presynaptic receptors on nerve terminals. There is some evidence for such a DA like activation by LSD thus inducing a decrease in biosynthesis and release of DA [8, 34]. The stimulated uptake of DA is difficult to explain, but similar results could be achieved in own in vitro experiments [34]. On the other hand the observed alterations in the DA system can be triggered by an inhibition of the firing rate of raphe neurones, thus depressing an inhibitory input of the 5-HT system on DA nerve cells in A 10 region or on DA nerve terminals in the nucleus accumbens. By the present data this question cannot be answered and further experiments are needed.

In general, our results provide evidence that the combined in vivo/in vitro procedure exhibits a new possibility in order to demonstrate in vivo changes of the functional activity of transmitter systems, especially in their release and uptake parameters.

Acknowledgement

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References

[1] BOARDER, M. R.: Essays Neurochem. Neuropharmac. **2**, 21 (1977)
[2] BÜRKI, H. R., H. ASPER, N. RUCH, and P. E. ZÜGER: Psychopharmacology **57**, 227 (1978)
[3] GALLAGER, D. W., and G. K. AGHAJANIAN: J. Pharmac. exp. Ther. **193**, 785 (1975)
[4] ANDEN, N. E., H. CORRODI, K. FUXE, and J. L. MEEK: Eur. J. Pharmac. **25**, 176 (1968)
[5] SCHUBERT, J., H. NYBÄCK, and G. SEDVALL: Eur. J. Pharmac. **10**, 215 (1970)
[6] KEHR, W., R. NEUMEISTER, and R. ZIMMERMANN: Dopaminergic Ergot Derivatives and Motor Function, Stockholm 1978, p. 173. K. FUXE and D. B. CALNE (Eds.). Pargamon Press, Oxford and New York 1979
[7] AGHAJANIAN, G. K.: Fedn Proc. Fedn Am. Socs exp. Biol. **31**, 91 (1972)
[8] KEHR, W., and (1978)
[9] HETEY, L., and
[10] FINK, H., R. M (1979)
[11] OELSSNER, W., F Pharmacologica
[12] HAMON, M., S. I
[13] KUCZENSKI, R.,
[14] KAPATOS, G., ar
[15] CHERAMY, A., M
[16] PALFREYMAN, M (1974)
[17] MCILWAIN, H.:
[18] COYLE, J. H., a
[19] KREBS, H. A., a
[20] LOWRY, O. H., 265 (1951)
[21] SCHMIEDER, S.,
[22] HORN, A. S.: Ac
[23] HYTTEL, J.: Ps
[24] HAMON, M., S. I
[25] ROSS, S. B., and
[26] MACLEAN, K.
[27] COSTALL, B.,
[28] GEYER, M. A., 106, 257 (1976)
[29] UEBELHACK, R.
[30] FARNEBO, L.-O.
[31] CERRITO, F., an
[32] GÖTHERT, M., a (1979)
[33] PERSSON, S. A.:
[34] HETEY, L., H.-
[35] DA PRADA, M., Res. **94**, 67 (19

Zusammenfassung

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[8] KEHR, W., and W. SPECKENBACH: Naunyn-Schmiedebergs Archs Pharmac. **301**, 163 (1978)
[9] HETEY, L., and W. OELSSNER: Proc. Eur. Soc. Neurochem. **1**, 441 (1978)
[10] FINK, H., R. MORGENSTERN, and W. OELSZNER: Pharmac. biochem. Behav. **11**, 479 (1979)
[11] OELSSNER, W., H. FINK, and R. MORGENSTERN: Proceedings of the Congress of Hungarian Pharmacological Society, Budapest 1979, in press
[12] HAMON, M., S. BOURGOIN, J. JAGGER, and J. GLOWINSKI: Brain Res. **69**, 265 (1974)
[13] KUCZENSKI, R., and D. S. SEGAL: Eur. J. Pharmac. **30**, 244 (1975)
[14] KAPATOS, G., and M. J. ZIGMOND: J. Pharmac. exp. Ther. **208**, 468 (1979)
[15] CHERAMY, A., M. J. BESSON, and J. GLOWINSKI: Eur. J. Pharmac. **10**, 206 (1970)
[16] PALFREYMAN, M. G., E. S. PALFREYMAN, and S. G. CLARK: Eur. J. Pharmac. **28**, 379 (1974)
[17] MCILWAIN, H.: Biochem. J. **49**, 382 (1951)
[18] COYLE, J. H., and S. H. SNYDER: J. Pharmac. exp. Ther. **170**, 221 (1969)
[19] KREBS, H. A., and K. HENSELEIT: Hoppe Seyler's Z. physiol. Chem. **210**, 33 (1932)
[20] LOWRY, O. H., N. J. ROSEBROUGH, A. L. FARR, and R. J. RANDALL: J. biol. Chem. **193**, 265 (1951)
[21] SCHMIEDER, S., E. RUDOLPH, and H.-D. FISCHER: Acta biol. med. germ. **37**, 1707 (1978)
[22] HORN, A. S.: Adv. biochem. Psychopharmac. **19**, 25 (1978)
[23] HYTTEL, J.: Psychopharmacology **60**, 13 (1978)
[24] HAMON, M., S. BOURGOIN, and J. GLOWINSKI: J. Neurochem. **20**, 1727 (1973)
[25] ROSS, S. B., and A. L. RENYI: Acta pharmac. tox. **36**, 56 (1975)
[26] MACLEAN, K. J., and J. M. LITTLETON: Eur. J. Pharmac. **41**, 171 (1977)
[27] COSTALL, B., D. H. FORTUNE, and R. J. NAYLOR: Neuropharmacology **14**, 859 (1975)
[28] GEYER, M. A., A. PUERTO, D. B. MENKES, D. S. SEGAL, and A. J. MANDELL: Brain Res. **106**, 257 (1976)
[29] UEBELHACK, R., L. FRANKE, and K. SEIDEL: Acta biol. med. germ. **37**, 1135 (1978)
[30] FARNEBO, L.-O., and B. HAMBERGER: Acta physiol. scand. Suppl. **371**, 35 (1971)
[31] CERRITO, F., and M. RAITERI: Eur. J. Pharmac. **57**, 427 (1979)
[32] GÖTHERT, M., and G. WEINHEIMER: Naunyn-Schmiedebergs Archs Pharmac. **310**, 93 (1979)
[33] PERSSON, S. A.: Eur. J. Pharmac. **43**, 73 (1977)
[34] HETEY, L., H.-D. FISCHER, and E. RUDOLPH: In preparation
[35] DA PRADA, M., A. SANER, W. P. BURKARD, G. BARTHOLINI, and A. PLETSCHER: Brain Res. **94**, 67 (1975)

Zusammenfassung

L. HETEY und K. QUIRING: Aufnahme und Freisetzung von Dopamin und Serotonin an der Synaptosomenfraktion des Nucleus accumbens der Ratte in vitro nach in vivo-Injektion von Lysergsäurediäthylamid

Nach systemischer Lysergsäurediäthylamid (LSD)-Applikation wurden Aufnahme und Depolarisations-induzierte Freisetzung von Dopamin (DA) und Serotonin (5-HT) an den Synaptosomen des Nucleus accumbens von Ratten untersucht. Für die Freisetzungsversuche wurden die Synaptosomen mit [^{14}C]-DA bzw. [^{3}H]-5-HT vormarkiert und mit physiologischer sowie Kalium-angereicherter (50 mM) Lösung superfundiert. Kleine Dosen von LSD (0,1 und 0,5mg/kg i. p.) hemmen die DA-Freisetzung bzw. stimulieren die DA-Aufnahme dosisabhängig. LSD hemmt die Freisetzung und Aufnahme von 5-HT signifikant.
Die Ergebnisse werden in bezug auf eine zuverlässige Charakterisierung der in vivo-induzierten Effekte von LSD an den isolierten Synaptosomen diskutiert.