Discussion. The present study demonstrated that hemiorchidectomy in adult rats results in approximately a 34% increase in the total Leydig cell mass in the remaining testis. The average Leydig cell profile area was larger in hemiorchidectomized rats than in controls. If these values (8 weeks) are compared on a volume basis ($127/104^{3/2} = 1.35$ it appears that the average Leydig cell in the hemiorchidectomized rats was about 35% larger than in controls. Average Leydig cell volume estimated using in independent method was about 32% larger than in controls. It thus appear that the increased total Leydig mass in the remaining testis after hemiorchidectomy is mainly due to a corresponding hypertrophy, and not hyperplasia, in the Leydig cells. This findings are in line with the observations of an increased Leydig cell nuclear diameter in partly castrated bulls[11] and a very moderate Leydig cell hyperplasia (5–7%) in hemiorchidectomized pubertal and adult rats[6,13]. Moreover, it has previously been demonstrated that there is a strong positive correlation between average Leydig cell size, and not Leydig cell number, and plasma testosterone levels in seasonally breeding animals[14].

Plasma testosterone concentration is maintained at normal values in hemiorchidectomized adult rats[4–6], but testis testosterone concentration is reported to be doubled[6]. These findings suggest that the Leydig cells in the remaining testis after hemiorchidectomy may produce twice as much testosterone as those in a normal testis. However, since total Leydig cell mass was only increased about 34% in these testes, it is likely that the average Leydig cell, apart from being large, also has a qualitatively increased capacity to produce testosterone. The mechanism behind the Leydig cell hypertrophy is unknown but it may be related to changes in the LH levels after the operation as suggested by Howland and Skinner[4]. Apart from the Leydig cell hypertrophy no other compensatory phenomena were noted in the remaining testes in hemiorchitectomized rats. These findings fit well with the general observation that hemiorchidectomy in adult rats does not influence the plasma concentration of FSH[4,5].

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Effect of des-Tyr^1-γ-endorphin on serotonin metabolism in rat brain regions

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Summary. Intracerebroventicular (i.c.v.) administration of des-Tyr^1-γ-endorphin (0.1 and 1.0 µg) caused a decrease of the serotonin (5-HT) concentration of the hippocampus. The concentration of 5-HIAA and the pargyline-induced alterations in 5-HT and 5-HIAA were not affected. No effects were noticed in other brain regions.

The β-lipotropin (β-LPH) derivative β-endorphin (β-LPH_{61-91}), which possesses opiate activities, affects, like narcotic drugs, serotonin (5-HT) metabolism in rat brain[4–6]. The β-endorphin fragment des-Tyr^1-γ-endorphin (β-LPH_{62-77}, DTγE), which is devoid of opiate activity, induces neuroleptic-like effects in rats[7] and has an anti-psychotic action in schizophrenic patients[8,9]. Since both serotonergic and dopaminergic receptors in the brain may be involved in the mechanism of action of neuroleptics[10], we studied the influence of DTγE on 5-HT metabolism in rat brain regions.

Methods. Male Wistar rats (Centraal Proefdieren Bedrijf TNO, Zeist, The Netherlands) weighing 175–205 g were used. They were housed under standard conditions (22 °C, lights on from 5.00 h to 19.00 h) and had access to food and water ad libitum. The rats received a polyethylene cannula in the lateral ventricle 9 days before the day of experimentation and were housed in single cages afterwards. The rats were fasted for 20 h before being decapitated. In the 1st experiment rats received either placebo (1 µl saline) or 1.0 µg DTγE in 1 µl saline intracerebroventricularly (i.c.v.). 30 min later 8 rats of each group were decapitated; the other 16 rats of each group received either pargyline (150 mg/kg; Aldrich) or vehicle (saline) i.p. and were subsequently decapitated 30 min later, i.e. 60 min after i.c.v. treatment. In a 2nd experiment the effect of higher and lower doses of DTγE on hippocampal 5-HT concentration was investigated. 4 groups of 8 rats received 1 µl saline or 0.01, 0.1 or 10.0 µg DTγE in 1 µl saline i.c.v. 30 min later all rats received 0.5 ml saline i.p., in order to create experimental conditions identical to those of the 1st experiment, and they were then decapitated 60 min following i.c.v. treatment. After decapitation the brains were rapidly removed and dissected according to Gispen et al.[11] on an ice-chilled glass plate. 5-HT and 5-hydroxy 3-indole acetic acid (5-HIAA) were assayed in the brain parts (indicated in table 1) according to Curzon and Green[12]. Concentrations are expressed as ng per mg tissue and given as means ± SEM. Student's t-test was used for statistical analysis of the data.

Results. The results of the 1st experiment are shown in tables 1 (5-HT) and 2 (5-HIAA). 60 min after i.c.v. DTγE administration the 5-HT concentration of the hippocampus was decreased as compared with that after saline treatment. No differences were found in 5-HT concentration in the other brain parts and in 5-HIAA concentration in any of the brain regions. Pargyline administration resulted in an increase in 5-HT and decrease in 5-HIAA concentrations in all regions. There were no significant effects of peptide treatment on the pargyline-induced alterations of 5-HT and 5-HIAA concentrations. In the 2nd experiment it was found that also a dose of 0.1 µg DTγE caused a decrease in hippocampal 5-HT concentration (728 ± 21 ng/g vs 809 ± 19 ng/g

Table 1. Effect of DTγE (administered i.c.v.) on 5-HT concentrations and on pargyline-induced accumulation of 5-HT in rat brain regions

Group	Treatment	5-HT concentration (ng/g tissue) Rostral cortex	Amygdala	Hypo-thalamus	Thalamus	Hippo-campus	Mesen-cephalon	Medulla
1	Sal	811±36	1562±66	2882±127	1700±58	930±46	1593±56	1432±55
2	DTγE	812±19	1539±63	2757± 73	1694±76	854±32	1558±48	1448±26
3	Sal-Sal	735±28	1572±56	2716± 59	1532±40	940±24	1472±34	1465±62
4	Sal-Parg	960±36*	1931±88*	3633±126*	2081±82*	1289±30*	2059±77*	1964±76*
5	DTγE-Sal	707±28	1471±55	2569± 79	1498±52	796±35**	1434±64	1457±50
6	DTγE-Parg	932±27*	1810±75*	3418± 83*	1996±60*	1192±56*	1962±89*	1872±94*

Rats of groups 1 and 2 received placebo (1 µl saline; group 1) or 1.0 µg DTγE i.c.v. (group 2) 30 min prior to decapitation. Rats of groups 3–6 received, 30 min after i.c.v. administration of placebo (groups 3 and 4) or DTγE (groups 5 and 6), either saline (groups 3 and 5) or pargyline (150 mg/kg; groups 4 and 6) i.p. and were decapitated 30 min later, i.e. 60 min after i.c.v. treatment. Values are means ± SEM (n = 7–8). * $p < 0.01$ for differences with controls receiving saline instead of pargyline (groups 3 and 5 respectively). ** $p < 0.01$ for difference with saline-saline-treated controls (group 3).

Table 2. Effect of DTγE (administered i.c.v.) on 5-HIAA concentrations and on pargyline-induced decrease in 5-HIAA concentration in rat brain regions

Group	Treatment	5-HIAA concentration (ng/g tissue) Rostral cortex	Amygdala	Hypo-thalamus	Thalamus	Hippo-campus	Mesen-cephalon	Medulla
1	Sal	296±12	481±38	638±47	606±45	450±35	864±23	595±44
2	DTγE	319±14	436±19	688±50	605±41	442±35	878±33	585±34
3	Sal-Sal	299±14	463±25	682±43	606±31	533±16	903±72	657±34
4	Sal-Parg	205± 7*	262±13*	460±26*	402±23*	322±16*	611±17*	462±21*
5	DTγE-Sal	317±16	444±15	665±48	646±50	472±31	861±29	680±43
6	DTγE-Parg	214± 7*	277±16*	449±26*	415±30*	343±26*	621±37*	464±34*

For details see table 1. Values are means ± SEM (n = 7–8). * $p < 0.01$ for differences with controls receiving saline instead of pargyline (groups 3 and 5 respectively).

for saline-treated controls, $p < 0.02$; n = 8). Interestingly, both a low dose (0.01 µg) and a high dose (10.0 µg) of the peptide were ineffective (768 ± 20 and 820 ± 30 ng/g respectively).

Discussion. Although the present data reveal that DTγE reduces hippocampal 5-HT concentrations, it is as yet impossible to indicate its mechanism of action, since no effects were evident on 5-HIAA levels and on either pargyline-induced 5-HT accumulation or 5-HIAA disappearance. Van Loon and De Souza[4] have reported that β-endorphin decreases hippocampal 5-HT turnover, while it has an opposite effect in other brain regions. Though the dose used (15 µg, intracisternally) was higher than those found to be effective in our experiments with DTγE, it is clear that the effect of DTγE is different from that of β-endorphin. An effect on 5-HT concentration of the same magnitude as that observed in the present study has also been found after des-enkephalin-γ-endorphin (β-LPH_{66-77}) administration, i.c.v. in doses of 0.1 and 1.0 µg, in the dorsal hippocampus and the raphe area of the mesencephalon (Versteeg et al., unpublished results). It, thus, appears that γ-type endorphins selectively cause a slight, but significant decrease in 5-HT concentrations in specific brain regions.

It has been shown that ^{3}H-spiperone binds to both serotonergic and dopaminergic receptors in the brain[10]. There is evidence that DTγE affects the activity of dopamine systems in the brain[13,14]. The present results indicate that the peptide also influences brain 5-HT systems. Although DTγE does not displace ^{3}H-spiperone in vitro[15,16], recently Pedigo et al.[17] reported that DTγE inhibits the in vivo binding of ^{3}H-spiperone in the brain. DTγE, however, in contrast to neuroleptics, preferentially acts in dopamine-rich brain regions: it inhibits ^{3}H-spiperone binding maximally in striatal and mesolimbic regions and is less effective in the frontal cortex[17]. Unfortunately, data on the characterisation of neuroleptic binding in the hippocampus is lacking. It thus remains to be elucidated whether the effect of γ-type endorphins on hippocampal 5-HT is a direct one or brought about trans-synaptically via other transmitter systems.

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