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Research report

Long-term impoverished housing effects on morris maze performance after a fimbria lesion

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Abstract

Male Wistar rats received bilateral Fimbria lesions and were postoperatively housed in either standard social conditions or in impoverished conditions (one rat per cage) for 2 weeks in experiment I, and for 7 months in experiment II. The effects of lesion and housing conditions were investigated in the Morris maze spatial orientation task. Fimbria lesions increased the latency to reach the platform during acquisition in both experiments, which indicates that functional recovery of the Morris maze impairment does not occur in 7 months time. Post-operative impoverishment for 2 weeks or for 7 months reduced the lesion induced deficit in Morris maze acquisition, while it had a more general effect in the trial without platform. Interestingly, the impoverishment effects were not more severe after 7 months, but even less easily detected. These findings are interpreted as if impoverishment affects the reactiveness of animals to external stimuli, which may help the animal to compensate for the lesion-induced-deficit in Morris maze learning.

Keywords: Impoverished housing; Isolation; Fimbria lesion; Recovery; Morris maze.

1. Introduction

Animals housed singly in small cages (impoverished housing condition; IC) differ from those housed with other animals (standard housing condition; SC) in measures of behaviour. A considerate amount of studies on impoverished housing has started impoverishment before or just after weaning, and variety of effects have been reported; IC-rats showed less object contact in an open field [4,6], IC-rats explored more than SC-rats [1], IC-rats had deficits in sexual behaviour [14,15], IC-rats weighed more, probably because they ate more [1,8], and IC before (but not after) 50 days of age impaired radial arm maze learning [5]. Specifically impoverishment during week 4 and 5 decreases social interest later in life, and causes deficits in submissive behaviours when IC-rats are placed in the territory of a dominant male (T. Hol, thesis 1994). Einon has shown that IC effects on object contact and radial arm maze learning could not be induced when rats were first introduced to the impoverished condition after 45/50 days of age [5,6], but emergence from cover in an open field could be affected by impoverishment at any time [6]. Some behaviours seem to be susceptible to impoverishment starting well after weaning; rats impoverished at young adult age are slower to extinguish conditioned taste aversion [13], and upon resocialization after a period of impoverishment rats show an increase in social grooming and approach the other animal more [17]. When impoverishment lasts for weeks or even months several behavioural differences can be distinguished: rats become more aggressive [18], explore more in a hole-board task [7] and are hyperactive when introduced into a novel environment [11]. Impoverished housing for 2–3 weeks impaired the acquisition of the Morris maze spatial orientation task, but these effects were still reversible by a period of group housing, periodic exposure to loud noises or brief periods of physical restraint. However, as impoverishment lasted more than 3 weeks, the deficit grew more severe, and became increasingly harder to reverse [28].

The possibility to induce impoverishment effects in mature rats may have consequences for brain damage

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studies, since this type of restriction may affect the behaviour of a rat with a lesion. It is notable that impoverished housing is often used inadvertently in experiments which use brain lesions or canulae as a consequence of the surgical procedure, and which investigate behaviour (e.g. [16,25,27,29]). Since it is generally accepted that post-operative housing in enriched environments can affect behavioural deficits after cortical and hippocampal lesions [3,9], the present study concerned itself with the possible effects of postoperative impoverishment after a fimbria lesion. Lesions to the Fimbria, as well as slightly larger lesions to the Fimbria-Fornix disrupt spatial learning in several tasks [2,21,22,25,27] (note: in some of these studies rats were housed individually), and this effect is still present after 7 months [33]. In the present study, rats with a Fimbria lesion were housed immediately after surgery in impoverished conditions for a short period (2 weeks) in experiment I, and subjected to long-term impoverishment (7 months) in experiment II. Subsequently they were tested for housing effects on their spatial learning ability in the Morris maze.

2. Materials and method

2.1. Animals

The subjects were 73 Male Wistar rats (R.M.I livestock, Utrecht). Upon arrival at the laboratory they were placed for 2 weeks into standard conditions prior to surgery, to habituate them to their new surroundings. Their day night cycle was reversed (low red light from 8.00 hours to 20.00 hours) and the temperature kept constant at 21 ± 2°C. Food (standard rat chow) and water was provided ad libitum. All animals were handled twice a week during cage maintenance.

2.2. Surgery

Fimbria lesion (Fim). The rats ($\pm$ 200 g) were anaesthetized with an intramuscular injection of Hypnorm (Duphar, Weesp, NL) which contains flunisone (10 mg/ml) and pentanylcitrate (0.2 mg/ml) prior to surgery. The head was fixed in a stereotactic apparatus. The nose clip was elevated +4.0 mm resulting in a slope of the skull of 30° varying from horizontal. A mechanical lesion, using a specially designed knife, was made through a groove in the skull, position 0.5 mm anterior, 3.0 mm lateral from Bregma to 1.0 mm posterior, 1.5 mm lateral to Bregma (adapted from [20]). The transection was placed from caudo-medial to rostro-lateral at a depth of 5.5 mm below the skull surface. The fimbria was bilaterally transected during this procedure: the fornix remained intact. (Sham operations consisted of skin incising and drilling of the skull; the cortex was not damaged.)

2.3. Post-operative environments

After surgery rats were either placed pairwise in a standard macrolon cage ($42 \times 26 \times 15$ cm, with a metal top), referred to as standard condition: SC, or alone in a small macrolon cage ($26 \times 20 \times 13$ cm with a metal top) referred to as impoverished condition: IC. The rats remained in these conditions for 2 weeks in experiment I, and for 7 months in experiment II. Group size was in Exp.I: Sham/SC $n=8$, Sham/IC $n=11$, Fim/SC $n=9$, Fim/IC $n=10$, and in Exp.II: Sham/SC $n=7$, Sham/IC $n=10$, Fim/SC $n=8$, Fim/IC $n=10$. The rats remained in these conditions throughout the testing period. All cages were transported to the room which contained the Morris maze 3 days before testing began and remained there throughout the experiment.

2.4. Apparatus and task

Morris maze. A Morris maze apparatus was used with a black pool (diameter 200 cm, depth 40 cm) filled with water (temperature $27°C \pm 1°C$). Low red light conditions resulted in a black water surface in which the black platform could not be detected. In quadrant 1 of four fixed quadrants a black escape platform (a cylinder $\varnothing$10 cm, 30 cm high) was placed 1 cm below the surface. Cues were provided by two white boards with black signs placed around the rim of the pool. Observations were made using an automated system described below.

Acquisition. All rats received 16 trials during acquisition training, 4 trials each day on four consecutive days with an intertrial interval of 10 min. A rat was entered facing the wall at random on one of four entrypoints, and allowed to swim for 120 s. The latency till the rat mounted the platform was recorded. If the rat failed to find the platform within 120 s it was guided there by hand (latency was set at 120 s) and allowed to remain on the platform for 30 s.

Probe trial (=trial without platform). On the fifth day the platform was removed. All rats entered at a fixed point and allowed 60 s to swim, during which their swimming pattern was recorded by the automated system. During analysis the time and travelled distance in the quadrant which had previously contained the platform was measured.

2.5. Automated motion tracking system

The output of the video camera, mounted above the Morris maze, was directly fed into a computerized image analysis system that records the rats position approximately twice per second. The test arena can be divided into zones, and the time and travelled distance per zone

can be quantified. For a detailed description of the system see [23].

2.6. Statistical analysis

All data were imported into the SYSTAT software package. The Morris maze acquisition was analysed with a two-way analysis of variance (ANOVA) with repeated measurements over the factors Housing (SC and IC) and Lesion (Sham versus Fimbria lesion), followed in case of significance by a post-hoc Tukey HSD test for each day separately. The data from the probe trial was analysed using a two-way ANOVA, over the factors Housing and Lesion.

3. Results

3.1. Experiment I: 2 weeks impoverishment

The latency to reach the platform over the 16 acquisition trials is shown in Fig. 1, which depicts means of four trials. Rats with a Fimbria lesion (Fim) had significantly longer latencies than rats with a sham lesion ($F(1,33)=35.797$, $P<0.001$). IC rats had shorter latencies than SC rats (housing effect $F(1,33)=14.799$, $P<0.001$); but the interaction between Lesion and Housing was not significant. One-way ANOVAs per time interval yielded significant group effects over all days ($P<0.01$) Post-hoc Tukey HSD tests revealed that on day 3 and 4 Fim/SC rats differed from sham-operated rats and Fim/IC rats (Fim/SC-Sham/SC day 3: $P<0.001$, day 4: $P<0.001$, Fim/SC-Sham/IC day 3: $P<0.001$, day 4: $P<0.001$, Fim/SC-Fim/IC day 3: $P<0.05$, day 4: $P<0.05$). IC-Fim and -Sham rats did not differ significantly. This indicates that isolation could reduce the lesion induced deficit in Morris maze acquisition. Impoverishment appeared to affect both Sham and Fim animals; there was a slight but significant difference of latency in IC-Sham rats when compared to SC-Sham rats on day 1 (Tukey HSD: $P<0.01$).

In the probe trial the travelled distance and the time spent in the quadrant which previously contained the platform were quantified (Fig. 2 and Fig. 3). Rats with a fimbria lesion spent less time in the quadrant than sham rats ($F(1,33)=8.12$, $P<0.01$). There was no significant difference in travelled distance in this area. IC rats spent more time in the quadrant ($F(1,33)=12.9$,

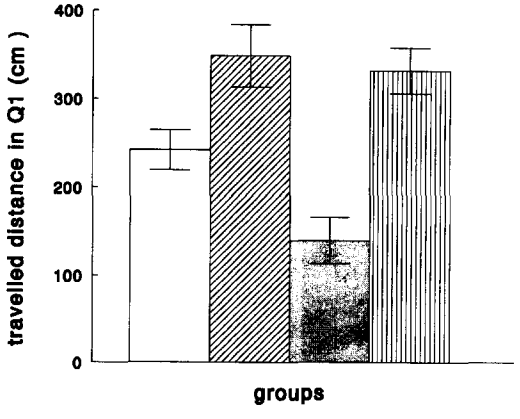

Fig. 2. Mean travelled distance in Quadrant 1 in the Morris maze (in cm)±SEM. for each group during the trial without platform. Quadrant 1 held the platform during acquisition trials. Impoverishment lasted for 2 weeks after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=8$ (open bar), Sham/IC $n=11$ (hatched bar), Fim/SC $n=9$ (gray bar), Fim/IC $n=10$ (vertically striped bar).

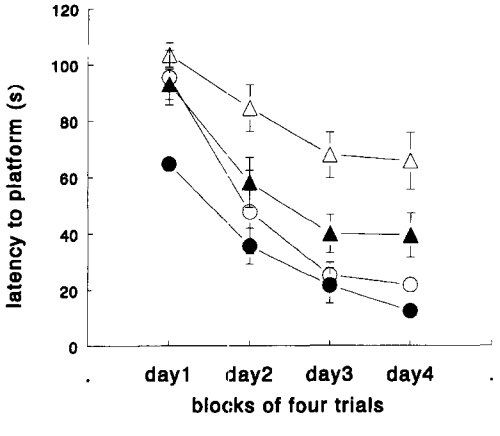

Fig. 1. Mean latencies (in s)±SEM. to reach the platform in the Morris maze for each group per day. Each day depicts a mean of four trials. Impoverishment lasted for 2 weeks after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=8$ (○), Sham/IC $n=11$ (●), Fim/SC $n=9$ (△), Fim/IC $n=10$ (▲).

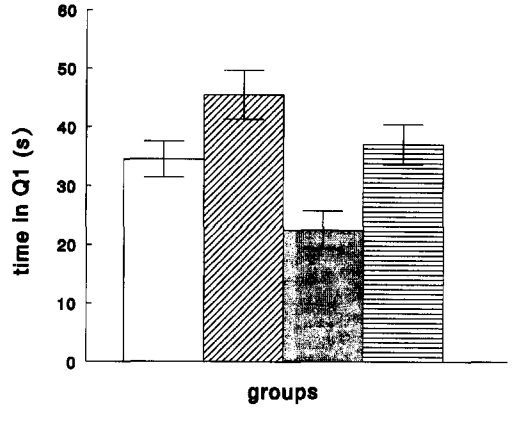

Fig. 3. Mean time spent in Quadrant 1 in the Morris maze (in s)±SEM. for each group during the trial without platform. Quadrant 1 held the platform during acquisition trials. Impoverishment lasted for 2 weeks after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=8$ (open bar), Sham/IC $n=11$ (hatched bar), Fim/SC $n=9$ (gray bar), Fim/IC $n=10$ (horizontally striped bar).

$P<0.001$), and had a higher travelled distance than SC rats ($F(1,33)=18.158$, $P<0.001$). There was no significant interaction between housing and surgery.

3.2. Experiment II: 7 months impoverishment

Rats with a fimbria lesion had been allowed 7 months for recovery, during which they were housed in SC or in IC. The latency to reach the platform is shown in Fig. 4. In spite of these 7 months animals with lesions were still impaired in Morris maze acquisition ($F(1,31)=15$, $P<0.001$). A two-way ANOVA with repeated measurements did not yield any significant effect of housing condition, nor an interaction Housing × Lesion. However, the largest differences could be observed on the second half of the task. One way ANOVA's over each day did reveal group differences on day 2, 3 and 4. Post-hoc Tukey HSD tests were performed. On day 2 Fim/IC differed from Sham/IC ($P<0.05$). On day 3, Fim/SC had higher latencies than all three other groups (Fim/SC-Sham/SC $P<0.01$, Fim/SC-Sham/IC $P<0.001$, Fim/SC-Fim/IC $P<0.05$). Fim/IC did not differ significantly from either sham group. On day 4 Fim/SC had higher latencies than both sham groups (Fim/SC-Sham/SC $P<0.06$, Fim/SC-Sham/IC $P<0.01$). There was no significant difference between Fim/IC and all three other groups, indicating that the measures for this group were intermediate. In the probe trial (Fig. 5 and Fig. 6) the impairment of rats with a fimbria lesion could be detected: their travelled distance in the correct quadrant was shorter (ANOVA: $F(1,31)=6.105$, $P<0.05$). There was a significant effect of housing on the travelled distance in quadrant 1 ($F(1,31)=4.442$, $P<0.05$) as well. However, the time in the correct quadrant failed to reach significance for both factors.

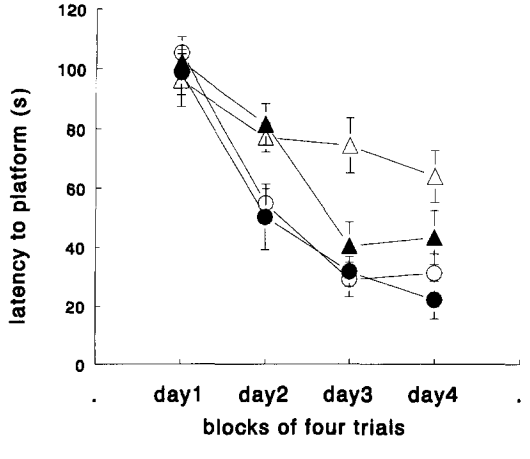

Fig. 4. Mean latencies (in s)±SEM. to reach the platform in the Morris maze for each group per day. Each day depicts a mean of four trials. Impoverishment lasted for 7 months after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=7$ (○), Sham/IC $n=10$ (●), Fim/SC $n=8$ (△), Fim/IC $n=10$ (▲).

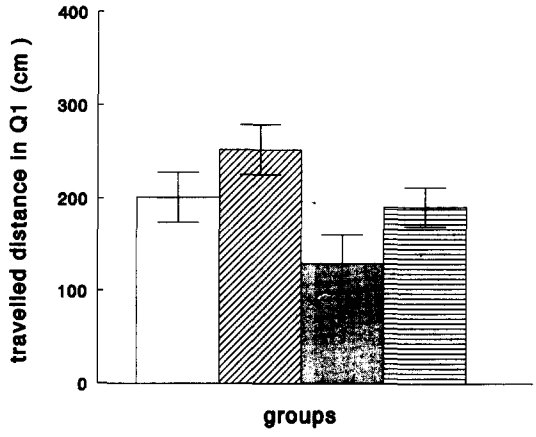

Fig. 5. Mean travelled distance in Quadrant 1 in the Morris maze (in cm)±SEM. for each group during the trial without platform. Quadrant 1 held the platform during acquisition trials. Impoverishment lasted for 7 months after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=7$ (open bar), Sham/IC $n=10$ (hatched bar), Fim/SC $n=8$ (gray bar), Fim/IC $n=10$ (horizontally striped bar).

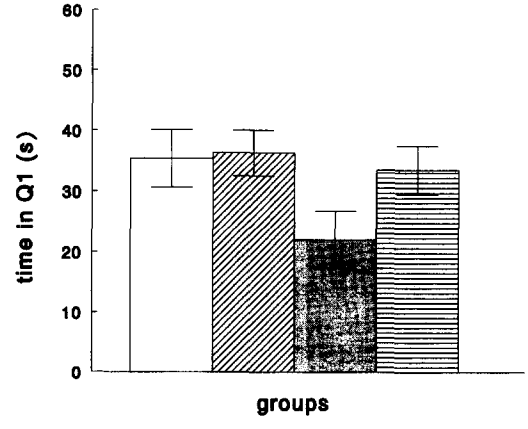

Fig. 6. Mean time spent in Quadrant 1 in the Morris maze (in s)±SEM. for each group during the trial without platform. Quadrant 1 held the platform during acquisition trials. Impoverishment lasted for 7 months after the lesion. Sham, sham lesion; Fim, fimbria lesion; SC, rats were housed in standard conditions; IC, rats were housed impoverished. Group sizes were Sham/SC $n=7$ (open bar), sham/IC $n=10$ (hatched bar), Fim/SC $n=8$ (gray bar), Fim/IC $n=10$ (horizontally striped bar).

4. Discussion

The present study demonstrates that lesioning of the Fimbria impaired the performance in the Morris maze, and that after a 7-month post-operative period no functional recovery had occurred. These findings are consistent with reports about impairments in spatial orientation tasks after lesions to the fimbria [27], fimbria-fornix [19,21,22,29] and hippocampus [18].

Post-operative impoverishment for 2 weeks reduced the lesion-induced deficit in Morris maze acquisition, while it had a more general effect in the trial without platform, where it raised the time and travelled distance in the platform quadrant independent of the lesion. The effects of long-term impoverishment (7 months) are similar to those after 2 weeks; a slight reduction of the latency to reach the platform of rats with lesions during acquisition, and a general effect on the travelled distance in the trial without platform. However, the impoverishment effects were not more severe after 7 months, but even less easily detected. This is in contrast with the expectations, based on the report by Wade and Maier, that impoverishment for 2–3 weeks impaired Morris maze performance of rats without a lesion, and these deficits grew more severe as the period of impoverishment increased [28]. After long-term impoverished housing rats develop an array of behavioural changes, including, amongst others, increased aggression [14,26], high locomotor activity [12] and altered social behaviour [17]. Several authors have contributed the impoverishment effect to a 'hyperreactivity to environmental stimuli' or 'hyperarousal' [6,10,14]. Wade and Maier concluded that the Morris maze task may have interacted with the exaggerated arousability of the rats, and the subsequent level of arousal was detrimental to learning.

A close inspection of the experimental methods shows that Wade and Maier's circumstances of isolation are further along the line of impoverishment of the environment than the ones used in the present study. In their settings the isolates are barely handled, ours are handled twice a week. Their rats are housed on a wire mesh bottom, and thus lack the experience to manipulate sawdust. Their rats are kept free of disturbances other than cage maintenance, our animals were housed in a well-used stable. As a consequence their isolation may well result in a higher level of arousal. This may explain the discrepancy in results, since a slight level of arousal may be beneficial to the performance, if the increase in general reactivity causes the rat to swim around more (as may be deduced from the trial without platform data, where IC in general increased the time and travelled distance of the rats); while exaggerated arousal would interfere overly much with the learning process.

It is also interesting to note that the Morris maze performance of Wade and Maier's rats was probably guided by external cues, and an increased reactivity to all (relevant and non-relevant) cues may have worked distracting. However, the fimbria lesion directly disrupts cue-oriented spatial learning [27]. Rats with either a hippocampal lesion or a fimbria(-fornix) lesion may supposedly improve their performance in the Morris water maze task by using a non-hippocampal mediated search strategy [18,24,30]. It may be argued that because rats with a fimbria lesion are not supposed to use the cues, their performance could not deteriorate by overt distraction. Even though this may serve to explain why no impairment of Morris maze performance was found in the present study, it fails to elucidate the observed beneficial effect of IC in rats with a lesion.

Even though the explanations for the impoverishment effect are still highly speculative, the presence of an effect has consequences for the methodological design of lesion studies in general. Animals are often housed singly after an operation (e.g. [16,25,27,29]), without consideration for the possible effect of housing conditions on behaviour. This may lead to a wrong interpretation of the symptoms seen after the lesion. In a design similar to the present study it may even have led to a false assumption of functional recovery of the lesion-induced deficit.

It is well-known that post-operative housing in enriched environments can affect behavioural deficits after cortical and hippocampal lesions [3,9,31,32]. In a different study we have shown in an experiment somewhat similar to the design of the present study that post-operative environmental enrichment (lasting 6 weeks) could also attenuate the Morris maze deficit arising after a fimbria-fornix lesion [34]when animals with a lesion were compared to standard housed animals. Thus it seems that both impoverishment and enrichment can affect the Morris maze performance of animals with a lesion of the fimbria fornix when compared to standard housed animals. However, mostly the effects of impoverishment and enrichment are in opposite directions; for instance in a study by Will and Kelche [31] where impoverished rats with a hippocampal lesion performed worse in a shuttle box avoidance task when compared to both standard housed rats and enriched rats with the lesion. It is, however, interesting that Will and Kelche [32] reported that enrichment and impoverishment of rats with a hippocampal lesion had an opposite effect in either a standard Morris maze or a dry version of the maze where a food cup with pellets was hidden under sawdust in a comparable arena. In the standard Morris maze the deficit was much larger in enriched animals when compared to impoverished. Thus a relative beneficial effect of impoverishment was found. However, in the dry version enriched animals with a dorsal hippocampal lesion performed at sham level whereas the performance of impoverished animals with a lesion was impaired. They concluded that the differential effect may have been caused by the different functional demands of the two tasks. Both required spatial memory, but the motivational, time, response and sensory characteristics did vary greatly. The 'wet' test, where impoverishment seemed to have a positive effect, is considered more stressful than the 'dry' version, where impoverishment had no positive effect. This may indicate that impoverished animals are better able to react to a stressful situation. This test also shows that even though both

housing conditions can affect the performance of animals with brain lesions, the effects of each housing condition possibly do not rely on the same principle. The effect of enrichment is often supposed to rely on an enhancement of the adaptive capacity of the animals [9] which could help the animals with a lesion to switch more easily to alternative search strategies [34], but whereas the effect of impoverishment, though not fully understood, may rely on a difference in arousability, a different reaction to stress or a higher reactivity to cues [6,10,14]. However, it is not clear from the present data whether the impoverished rats may have also used the alternative search strategy mentioned in the enrichment study, since the search pattern of the animals has not been studied in greater detail.

References

[1] Baenninger, L.P., Comparision of behavioural development in socially isolated and grouped rats, *Anim. Behav.*, 15 (1967) 312–323.

[2] Bresnahan, E.L., Kametani, H., Spangler, E.L., Chachich, M., Wiser, P.R. and Ingram, D.K., Fimbria fornix lesions in yound rats impair acquisition in a 14-unit T maze similar to prior observed performance deficits in aged rats, *Psychobiology*, 16 (1988) 243–250.

[3] Dalrymple-Alford, J.C. and Kelche, C.R., Behavioral effects of preoperative and postoperative differential housing in rats with brain lesions: a review. In B.E. Will, P. Schmitt and J.C. Dalrymple-Alford (Eds.), *Brain Plasticity, Learning and Memory*, Plenum Press, New York, 1985, pp. 441–448.

[4] Einon, D. and Morgan, M., Habituation of object contact in socially reared and isolated rats (*Rattus norvegicus*), *Anim. Behav.*, 24 (1976) 415–420.

[5] Einon, D.F., Spatial memory and response strategies in rats: age, sex and rearing differences in performance, *Quart. J. Exp. Psychol. [B]*, 32 (1980) 473–489.

[6] Einon, D.F. and Morgan, M.J., A critical period for social isolation in the rat, *Dev. Psychobiol.*, 10 (1977) 123–132.

[7] Enginar, N. and Eroglu, L., Long term isolation as an animal model of depression, *Anim. Models Psychopharmacol.*, 3 (1991) 225–229.

[8] Fiala, B., Snow, F.M. and Greenough, W.T., 'Impoverished' rats weigh more than 'enriched' rats because they eat more, *Dev. Psychobiol.*, 10 (1977) 537–541.

[9] Finger, S., Environmental attenuation of brain lesion symptoms. In S. Finger (Ed.), *Recovery from Brain Damage: Research and Theory*, Plenum Press, New York, 1978, pp. 297–329.

[10] Frances, H., Lienard, C., Fermanian, J. and Lecrubier, Y., Isolation-induced social behavioral deficit: a proposed model of hyperreactivity with a behavioral inhibition, *Pharmacol. Biochem. Behav.*, 32 (1989) 637–642.

[11] Garzon, J., Fuentas, J.A. and Del Rio, J., Antidepressants selectively antagonize the hyperactivity induced in rats by long term isolation, *Eur. J. Pharmacol.*, 59 (1979) 293–296.

[12] Gentsch, C., Lichtensteiner, M., Frischknecht, H.R., Feer, H. and Siegfried, B., Isolation induced locomotor hyperactivity and hypoalgesia in rats are prevented by handling and reversed by resocialisation, *Physiol. Behav.*, 43 (1988) 13–16.

[13] Giardini, V., Influence of housing conditions and state of partner on conditioning and extinction of taste aversion to lithium and chlorpromazine, *Psychopharmacology*, 86 (1985) 96–101.

[14] Hole, G.J., Einon, D.F. and Plotkin, H.C., The role of social experience in the development of sexual competence in rattus norvegicus, *Behav. Process.*, 12 (1986) 187–202.

[15] Hurd, E. and Larsson, K., Dependence of adult mating behaviour in male rats on the presence of littermates in infancy, *Brain Behav. Evol.*, 1 (1968) 405–419.

[16] Leis, T., Pallage, V., Toniolo, G. and Will, B., Working memory theory of hippocampal function needs qualification, *Behav. Neural Biol.*, 42 (1984) 140–157.

[17] Niesink, R.J.M. and Van Ree, J.M., Short-term isolation increases social interaction of male rats: a parametric analysis, *Physiol. Behav.*, 29 (1982) 819–825.

[18] O'Keefe, J., Spatial memory within and without the hippocampal system. In W. Seifert (Ed.), *Molecular, Cellular and Behavioural Neurobiology of the Hippocampus*, Academic Press, New York, 1982, pp. 375–403.

[19] Olton, D.S. and Papas, B.C., Spatial memory and hippocampal function, *Neuropsychologia*, 17 (1979) 669–682.

[20] Paxinos, G. and Watson, C., *The Rat Brain in Stereotactic Coordinates*, Academic Press, 1986,

[21] Pitsikas, N., Spruijt, B.M., Josephy, M., Algeri, S. and Gispen, W.H., Effect of Org2766, an ACTH(4-9) analogue, on recovery after bilateral transection of the fimbria fornix in the rat, *Pharmacol. Biochem. Behav.*, 38 (1991) 931–934.

[22] Spruijt, B., Pitsikas, N., Algeri, S. and Gispen, W.H., Org2766 improves performance of rats with unilateral lesions in the fimbria fornix in a spatial learning task, *Brain Res.*, 527 (1990) 192–197.

[23] Spruijt, B.M., Hol, T. and Rousseau, J., Approach and avoidance behavior of individually recognized animals automatically quantified with an imaging technique, *Physiol. Behav.*, 51 (1992) 747–752.

[24] Sutherland, R.J., Kolb, B. and Whishaw, I.Q., Spatial mapping: definitive disruption by hippocampal or medial frontal cortical damage in the rat, *Neurosci. Lett.*, 31 (1982) 271–276.

[25] Sutherland, R.J. and Rodriguez, A.J., The role of the fimbria fornix and some related subcortical structures in place learning and memory, *Behav. Brain Res.*, 32 (1989) 265–277.

[26] Valzelli, L. and Bernasconi, S., Psychoactive drug effects on behavioural changes induced by prolonged socio-environmental deprivation in rats, *Psychol. Med.*, 6 (1976) 271–276.

[27] Van Der Staay, F.J., Raaijmakers, W.G.M., Lamers, A.J.J.C. and Tonnaer, J.A.D.M., Selective fimbria lesions impair acquisition of working and reference memory of rats in a complex discrimination task, *Behav. Brain Res.*, 32 (1989) 151–161.

[28] Wade, S.E. and Maier, S.F., Effects of individual housing and stressor exposure upon the acquisition of watermaze escape, *Learn. Motiv.*, 17 (1986) 287–310.

[29] Walker, J.A. and Olton, D.S., Spatial memory deficit following fimbria-fornix lesions: independent of time for stimulus processing, *Physiol. Behav.*, 23 (1979) 11–15.

[30] Will, B., Deluzarche, F. and Kelche, C., Does post-operative environment attenuate or exacerbate symptoms which follow hippocampal lesions in rats? *Behav. Brain Res.*, 7 (1983) 125–132.

[31] Will, B.E. and Kelche, C., Effects of postoperative environments on the avoidance behavior of rats with hippocampal lesions: recovery or improvement of function? *Behav. Neural Biol.*, 27 (1979), 96–106.

[32] Will, B.E. and Kelche, C., Environmental approaches to recovery of function from brain damage: a review of animal studies (1981–1991). In Rose F.D. and Johnson D.A. (Eds.), *Recovery from Brain Damage*, Plenum Press, New York, 1992, pp. 79–103.

[33] Van Rijzingen, I.M.S., van Doremalen, E., Jospehy, M., Gispen, W.H. and Spruijt, B.M., ACTH(4–9) analog Org2766 treatment 7 months delayed still improves Morris maze performance of fimbria fornix lesioned rats, *Pharmacol. Biochem. Behav.*, 53 (1996) 163–169.

[34] Van Rijzingen, I.M.S., Gispen, W.H. and Spruijt, B.M., Post-operative environmental enrichment attenuates fimbria fornix lesion-induced impairments in Morris maze performance., *Neurobiol. Learn. Mem.*, in press.