Learning and Memory: Pharmacology

LMP1
DOPAMINERGIC MODULATION OF GLUTAMATERGIC TRANSMISSION IN SENSORIMOTOR CORTEX DURING CONDITIONING

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The influence exerted by dopaminergic pathways on glutamate transmission in cortical neurons is important regarding to the higher cognitive functions. The aim of this study was to investigate the dopaminergic effects on the glutamatergic transmission in the sensorimotor cortex of behaving cats. The animals were trained to respond on a sound click by a placing reaction. The extracellular impulse activity and effects of iontophoretical microapplication of synaptically active substances were investigated by means of glass multibarrels microelectrodes. Background and activity evoked by conditional click were investigated before, during and after application of glutamate (Glu), levodopa (L-d), haloperidol (Hal), sulpiride (Sul), SCH-23390 (Sch) and their combinations. Biceps electromyogram response was used as an indicator of a beginning of the conditioned movement. Perievent histograms triggered by stimulus and movement onsets were constructed. Application of Glu increased the background and evoked responses and this potentiation was preserved even 10-20 minutes after the end of the application. Dopamine precursor L-d provoked a comparable increase in the activity. The impulse activity for a joint application of both substances did not exceed levels observed with a separate application of each substance. The application of Hal increased the firing rates after the end of its application, especially, in neurons with a low initial background activity. Joint application of Glu and Hal decreased the movement-related activity for up to 10-15 min after the end of the iontophoresis. The application of D2-receptor antagonist Sul increased the discharge rate of neurons with low firing activities and decreased background activity of neurons with initially high firing rate. The main effect of D1-receptor antagonist Sch was a late potentiation of the evoked activity after the end of its application. Joint application of Glu and Sch as well as that of Glu and Sul enhanced the responses to the conditioned stimulus Discharges of some neurons that begun responses to stimulus only after beginning of movement during action of dopamine-receptor blockers change to reaction that overtake of the movement. These results suggest that dopaminergic pathways exert an inhibitory influence on the potentiation of glutamatergic transmission. The occlusion observed with joint application of Glu and L-d provides strong evidence of possible participation of G-proteins in learning processes. Further analysis of the association between spike trains will investigate the hypothesis that the dopaminergic system might regulate associative responses as a function of computational demands.

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LMP2

DOPAMINE D1 AND D2 DIFFERENTIALLY MODULATE REACTION TO SPATIAL AND NON-SPATIAL CHANGE IN MICE

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Experimental evidence suggests a role of nucleus accumbens in spatial learning, however, possible differences between the two dopamine receptors subclasses has not yet been examined. For this reason we investigated the effects of local administrations of D1 D2 receptors antagonists into the nucleus accumbens in a non-associative spatial task. The task consists in placing mice in an open field containing five objects and, after three sessions of habituation, examining their reactivity to object displacement (spatial novelty) and object substitution (object novelty) and it has been designed to estimate the ability of mice to encode spatial and non-spatial relationship between discrete stimuli. Focal administration of the D2 antagonist, sulpiride (50 and 100 ng/side), induce a dose dependent impairment in reactivity to spatial novelty, and a similar effect was also observed in reactivity to non-spatial novelty, exploration, as well as locomotor activity. Focal administrations of the D1 antagonist SCH23390 (12.5 and 50 ng/side) also decreased reactivity to spatial change, however, no effect on locomotor activity and exploration was observed. Moreover, reactivity to non-spatial change was affected only with the high dose of the D1 antagonist. These results confirm the observation of an involvement of the mesoaccumbens dopaminergic system in the modulation of spatial learning. Furthermore, while the overall effect induced by the D2 antagonist seems to suggest a possible motivational or motor deficit, blockade of D1 receptors seems to play a rather selective in the acquisition or processing of spatial information.

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LMP3

ENHANCED CONDITIONED APPROACH RESPONSES IN TRANSGENIC MICE WITH IMPAIRED GLUCOCORTICOID RECEPTOR FUNCTION

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Motivated behaviour can be divided into an instrumental component, such as preparatory responses for food, and a consummatory component, such as eating the food. Anticipation of food reward requires learning about the nature of the reward and about the environmental conditions under which this reward can be expected. Glucocorticoids are secreted in response to rewarding stimuli such as food, and these

rewarding effects have been suggested to be mediated by glucocorticoid-induced stimulation of dopaminergic (DA) transmission in the nucleus accumbens. The long-term consequences of impaired glucocorticoid receptor (GR) function on reward-related learning were studied in transgenic mice with impaired GR function in a series of experiments taxing conditioned and unconditioned approach responses to stimuli predictive of food. There was a double-dissociation in that transgenic mice with impaired GR activity showed enhanced conditioned exploration in situations when stimuli predicted reward, while free-feeding food consumption over 24 h was reduced. Previous experiments have shown altered accumbens dopaminergic activity in these animals. In line with these findings, we observed an enhanced behavioural stimulation of transgenic mice following administration of *d*-amphetamine (2 mg/kg). This suggests that the increase in preparatory responses in transgenic mice may be mediated via an enhanced accumbens dopaminergic activity, possibly secondary to alterations in other brain systems.

LMP4

NMDA GLUTAMATE RECEPTOR ANTAGONISTS SELECTIVE EFFECTS ON SYNAPTIC PLASTICITY AFTER NOCICEPTIVE SENSITIZATION IN SNAIL *Helix lucorum*

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Recent reports have indicated that various types of glutamate receptors are of importance in synaptic mechanisms of learning. N-methyl-D-aspartate (NMDA) glutamate receptors involvement in mechanisms of synaptic plasticity during elaboration of simple form of learning (nociceptive sensitization) was investigated in L-RPl1 neurons of semiintact preparation in snail *Helix lucorum.* Specific skin receptor site for the neurons is snail "head";. Sensory stimulation of the site evoked neuronal response with maximal parameters. An other site, snail "foot", is a nonspecific site for the L-RPl1 neurons and its stimulation evoked smaller response. Sensitizing stimuli (600 ul, 10% quinine solution) were applied onto specific skin site (snail "head") or nonspecific one (middle part of snail "foot"). Application of sensitizing stimuli onto snail "head"; or middle part of snail "foot" in control animals initiated slight depression of L-RPl1 neurons responses evoked by tactile or chemical sensory stimulation during short-term period and significant facilitation of neural responses during long-term period of sensitization. Sensitization during application of NMDA glutamate receptor antagonists (AP5 or MK801) produced the same changes in neuronal responses evoked by tactile stimulation of snail "head"; or middle part of "foot" as well as chemical sensory stimulation of middle part of "foot" as in control animals. However in these conditions significant depression of neuronal responses evoked by chemical stimulation of snail "head" during short- and long-term periods of sensitization was determined. We suggested that NMDA glutamate receptors are selectively involved in plasticity induction mechanisms of synaptic "inputs" processing chemical sensory stimulation from snail "head" specific skin site of L-RPl1 neurons in *Helix lucorum.*

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LMP5

ROLE OF NUCLEUS ACCUMBENS NMDA RECEPTORS IN MEMORY CONSOLIDATION IN A NON-ASSOCIATIVE TASK IN MICE

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Many studies show that nucleus accumbens is not only involved in reward and motivation but also in learning and memory processes. However, it is often difficult to dissociate effects of manipulation of nucleus accumbens on memory and motivation because of the positive or negative reinforcement present in most learning paradigms. Moreover, it is not completely clear in which stage of the memorisation process the nucleus accumbens is involved. For this reason, in this study we investigated the effects of immediate post-trial administrations of the non-competitive NMDA antagonist AP-5 intracerebroventricularly as well as into the nucleus accumbens in a non-associative spatial task. This task consist in placing mice in an open field containing five objects and, after three sessions of habituation, examining 24 hrs later their reactivity to object displacement (spatial novelty). In order to assess the possible occurrence of plastic changes in the nucleus accumbens, the effect of immediate post-trial administrations of oligonucleotides antisense for CREB was also examined. The results show that intracerebroventricular administrations of the competitive NMDA antagonist, AP-5 (0.15 and 0.3 µl/side), immediately after the last session of habituation induced a dose dependent impairment of the ability of mice to detect spatial novelty. The results of the second experiment show that post-training focal administration of AP-5 (0.3 µl/side) in nucleus accumbens induced similar effects on the ability of mice to detect the change on test trial. Moreover, post-trial administrations of oligonucleotides antisense but not sense, into the nucleus accumbens, induced an impairment in reactivity to spatial change on test day. These findings demonstrate an involvement of NMDA receptors located in the nucleus accumbens in the consolidation of spatial information. Furthermore they suggest possible plastic changes in the nucleus accumbens during the consolidation process.

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LMP6

SELECTIVE CHOLINERGIC AND SEROTONERGIC LESIONS USING 192 IGG-SAPORIN AND 5,7-DIHYDROXYTRYPTAMINE IN THE RAT: NEUROCHEMICAL AND BEHAVIOURAL EFFECTS

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In the literature, evidence has accumulated suggesting that drug- or lesion-induced disruption of central serotonergic function may potentiate cognitive consequences of damage to central cholinergic neurons or blockade of cholinergic (mainly muscarinic) receptors. So far, however, the cognitive effects of combined lesions with toxins selective for each system of neurotransmitters have not been assessed. In the present study, Long-Evans female rats (three months old) sustained intracerebroventricular injections of either 150 µg 5,7-dihydroxytryptamine (5,7-DHT), 2 µg 192 IgG-saporin (SAPO), or a combination of both (5,7-DHT + SAPO). Rats given sham-injections (SHAM) were used as controls; those given 5,7-DHT were pretreated with desipramine (30 mg/kg, i.p., 20 minutes before anaesthesia). Between 10 days and 2.5 months after surgery, all rats were tested for home-cage activity, forced alternation in a T-maze, sensorimotor capabilities in a beam-walking test, and spatial memory in both a water maze (reference and working memory) and a radial maze (working memory). Diurnal and nocturnal locomotor activity was significantly increased in rats with 5,7-DHT injections, alone or combined to SAPO, as compared to SHAM or SAPO rats. In the T-maze, only rats with combined lesions were significantly impaired as compared to each of the three other groups. Sensorimotor capabilities were altered in all lesion groups, but less dramatically in rats with 5,7-DHT lesions. In the water-maze task, only 5,7-DHT + SAPO rats showed impaired working memory performance; spatial reference memory was affected by neither lesion. Finally, in the radial-maze test, 5,7-DHT + SAPO rats were again the only ones to exhibit a (modest but significant) deficit. These results will be discussed in the light of neurochemical determinations. As such, they show that **i)** 192 IgG-saporin lesions produce severe sensorimotor deficits, presumably because of damage to Purkinje cells in the cerebellum, but fail to affect locomotor activity as well as spatial learning/memory performances ii) 5,7-DHT lesions produce diurnal and nocturnal hyperactivity, modest sensorimotor deficits, and do not alter cognitive capabilities *per se*, iii) the combination of cholinergic and serotonergic lesions alters cognitive capabilities, a finding supporting a role for cholinergic/serotonergic interactions in cognitive functions. It is noteworthy, however, that in comparison with previous studies combining 5,7-DHT lesions to less specific lesions of basal forebrain cholinergic neurons, or to antimuscarinic drugs given systemically, the cognitive deficits found in our rats with the combined lesions are of much lower amplitude. Also, the absence of any cognitive deficit induced by 192 IgG-saporin alone is at some variance (insufficient amount?) with the cholinergic hypothesis of learning/memory.

LMP7

WORKING MEMORY AND LEARNING IMPAIRMENTS IN DELAYED MATCHING AND NON-MATCHING TO POSITION CAUSED BY FIMBRIA-FORNIX LESIONS BUT NOT INTRA-HIPPOCAMPAL INJECTIONS OF 192-IgG SAPORIN

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Past studies have used lesions of the fimbria-fornix (FF) or medial septum/vertical limb (MS/VDB) region to study the involvement of subcortical inputs to the hippocampus in learning and memory. However, the chemical nature of these structures is complex, involving not only cholinergic, but GABA-ergic inputs to the hippocampus as well as cholinergic projections from the MS/VDB to the entorhinal and cingulate cortices. Thus, behavioural effects observed following lesions of the FF or MS/VDB cannot be clearly attributed to the removal of any one projection per se. The present study used the delayed matching to position (DMTP) paradigm to assess the role of the cholinergic septo-hippocampal projection in spatial working memory by comparing the effects of FF lesions to those of hippocampal injections of 192-IgG saporin (SAP), an immunotoxin that selectively destroys cholinergic cells. Rats were trained to asymptotic performance in a variable-delay (0, 4, 8,12, 16, 24, 32 sec) non-matching to position task (DNMTP). They were then divided into four groups, receiving either aspirative FF lesion (Group FF, n=8), intrahippocampal SAP injections (Group SAP-HPC, n=10), or the appropriate sham operation (Controls, n=10). Starting two weeks after surgery , animals were run for 15 days on the variable-delay DNMTP before being trained on a reversal of the matching contingency (i.e., DMTP) with a single delay (0 sec). Following reversal acquisition, variable delays were again introduced for a further 15 sessions. In DNMTP performance, group FF showed a delay-dependent impairment, with performance decreasing more rapidly than controls at delays longer than 0 sec, suggesting a spatial working memory deficit. Group SAP-HPC did not differ from controls. All groups acquired the matching reversal at similar rates. However, when variable delays were reintroduced, FF rats showed a significant reduction in percent correct responses at the 0-sec delay, suggesting an impairment in the performance of a previously well-acquired task in the face of novel testing conditions. Again, SAP-HPC rats were unaffected relative to controls. By the end of the 2 weeks of testing, the delay performance of Controls and SAP-HPC rats had reached near pre-reversal levels; however, FF rats demonstrated a clear delay-dependent deficit. These results suggest a potentially important role for the GABA-ergic component of the septo-hippocampal pathway and/or septo-cingulate/septo-entorhinal cholinergic projections in spatial working memory in the DMTP and DNMTP. The cholinergic septo-hippocampal pathway may not be necessary for the performance of such tasks.

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LMP8

THE EFFECTS OF SCOPOLAMINE AND D-AMPHETAMINE ON RATS INTOXICATED WITH ORGANOPHOSPHATES WORKING ON A DELAYED SPATIAL ALTERNATION TASK

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Organophosphates compounds (Ops) are a large class of chemical, many of wich are used as insecticides. It is well established that the main effect of Ops is the inhibition of acetylcholinesterase (AchE) activity, leading to accumulation of acetilcholine at central and peripheral cholinergic synapses. This overstimulation produce a downregulation of cholinergic receptors as a compensatory mechanism. This adaptative mechanism can result on delayed cognitive deficits, and an increased susceptibility to, at least, cholinergic substances. The aim of this experiment was to study the effects of scopolamine and d-amphetamine on rats intoxicated with organophosphates compounds as DFP and Chlorpyriphos working on an animal model of short term memory. 24 male Wistar rats were used as a subjects for this experiment. All subjects were trained in a delayed spatial alternation task with 3 delays: 0, 10 and 20 sec., and with 90 trials per session (30 per delay at random blocks of 10 trials). Subjects were divided into three groups (N = 8) attending to the organophosphate administered: 125 mg/kg of Chlorpyriphos in a single dose, 0.2 mg/kg of DFP during 25 days, or olive oil during 25 days. When behavioral results do not revelated differences between groups, rats were administered with scopolamine (0.007, 0.013, 0.025, 0.05, 0.1, 0.25 and 0.5mg/kg) and d-amphetamine (0.25, 0.5 and 1.0 mg/kg). Administrations were i.p. and in 1 ml/kg. Dependent variables were: percent of correct responses, errors type I and II, nose-pokes, latency to lever pressing, and number of trials completed. Just the variable number of trials completed had a differential effect between groups, being less the number of trials completed on groups treated with organophosphates. We will discuss these results in the light of contradictory results in literature on the effects of organophosphates on cognitive and motivation processes.

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LMP9

NERVE GROWTH FACTOR ADMINISTRATION ANTICIPATES THE APPEARANCE OF SPATIAL DISCRIMINATION IN DEVELOPING MICE

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The present study investigates the role of the neurotrophin Nerve Growth Factor (NGF) in the emergence of spatial discrimination performances in developing mice. Much evidence has indicated that the ability

to recognise and remember the spatial characteristics of the surrounding environment depends largely on the function of forebrain cholinergic systems, and in particular of septo-hippocampal connections. During development, NGF synthesised in the hippocampus exerts a major trophic and tropic role on septal cholinergic neurones, guiding the growing axons to establish the proper synaptic contacts with the target. Indeed we have previously shown that NGF administration during critical development phases anticipates the maturation of behavioural responses under cholinergic control. Fifteen-day old CD-1 mice received intracerebroventricular (icv) administration of NGF (20μg). Behavioural effects of this treatment were investigated on pnd 18 using the spatial open field test with four objects (a test in which response to both spatial and object novelty is assessed). While at this age control mice were unable to detect a rearrangement of two of the four objects, NGF-treated animals reacted to the spatial changes in the test environment. Control and NGF-treated mice showed comparable novelty responses when an unfamiliar object was presented into the arena. To evaluate the neurochemical effects of NGF treatment, choline acetyltransferase activity (a marker of cholinergic function) has been also measured in hippocampus, striatum and cortex. These findings are compared with previous rat data from our laboratory indicating that basal forebrain cholinergic neurones are critical for detecting spatial arrangements but not necessarily for detecting novelty. NGF effects on developing cholinergic system result in a earlier appearance of the ability to process spatial information and detect spatial changes in the environment.

LMP10

PERI-NATAL CHOLINE SUPPLEMENTATION REVEALS A DISSOCIATION BETWEEN TWO TYPES OF SPATIAL STRATEGIES

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Choline supplementation improving memory functions in rodents is assumed to increase the synthesis and release of acetylcholine in the brain. We have found that a combined pre- and postnatal supplementation results in long-lasting facilitation of spatial memory in juvenile rats when training was conducted in presence of a local salient cue. The present work was aimed at analysing the effects of peri- and postnatal choline supplementation on spatial abilities of naive adult rats. Rats given a perinatal choline supplementation were trained in various cued procedures of the Morris navigation task when aged 5 months. The treatment had a specific effect of reducing the escape latency of the rats when the platform was at a fixed position in space and surrounded by a suspended cue. This effect was associated with an increased spatial bias when the cue and platform were removed. In this condition, the control rats showed impaired spatial discrimination following the removal of the target cue, most likely due to an overshadowing of the distant environmental cues. This impairment was not observed in the treated rats. Further training with the suspended cue at unpredictable places in the pool revealed longer escape latencies in the control than in the treated rats suggesting that this procedure induced a selective

perturbation of the normal but not of the treated rats. A special probe trial with the cue at an irrelevant position and no escape platform revealed a significant bias of the control rats toward the cue and of the treated rats toward the uncued spatial escape position. This behavioural dissociation suggests that a salient cue associated with the target induces an alternative "non spatial" guidance strategy in normal rats, with the risk of overshadowing of the more distant spatial cues. In this condition, the choline supplementation facilities a spatial reliance on the cue, that is an overall facilitation of learning a set of spatial relations between several visual cues. As a consequence, the improved escape in presence of the cue is associated with a stronger memory of the spatial position following disappearance of the cue. This and previous observations suggest that a specific spatial attention process relies on the buffering of highly salient visual cues to facilitate integration of their relative position in the environment.

LMP11

CORRELATION OF HISTOLOGICAL AND BEHAVIOURAL PHARMACOLOGICAL EFFECTS OF BRX-COMPOUNDS IN GERBIL ISCHAEMIA TEST

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The transient bilateral carotid artery occlusion (BCo) in Mongolian gerbil is a widely used model of global forebrain ischaemia (1,4). In this *in vivo* model the animals exhibit dysfunction in neurons in the hippocampus, frontal cortex and striatum, the brain regions important in learning and memory functions (3). Evaluation of the ischaemia occurs generally histologically (4), but various behavioural examinations have been employed to evaluate functional impairment of animals after ischaemia: hypermotility, Morris water maze, 8-arm radial maze test, passive avoidance (5,6). Y-maze test (2) is one of the suitable behavioural pharmacological tests, which can complete the ischaemia/hipoxia models as an additional observation method besides histological evaluation. The 5-min forebrain ischaemia decreases the spontaneous alternation (SA) behaviour of animals 2-4 days after BCo surgery (delayed amnesia) with 18% and induces about 70% hypermotility. The number of pyramidal cells in the hippocampus CA1 area decreases with 68%. In the present study the correlation of histological and behavioural pharmacological parameters (hypermotility and SA) are investigated in gerbil BCo model on the 4th day after occlusion and treatment with BRX-compounds. These compounds are synthesized for the neuroprotective project in Biorex R & D Co. Comparing histological and behavioural effects of nine BRX-compounds (30 and/or 50 mg/kg i.p. 30-min postoccl.) close correlation exists among the three parameters. The correlation between the results of motility and spontaneous alternation is about 90%, between motility and CA1 neuroprotection is more than 70%, while between SA and CA1 data the correlation is close to 70%.

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(1) Calapai *et al.*, (1993) *Drugs Exp. Clin. Res.* XIV, 4:159; (2) Dennis (1939) *J. Comp. Psychol.* 28:305; (3) Hiramatsu *et al.*, (1996) *Eur. J. Pharmacol.* 315:119; (4) Izumiyama & Kogure (1988) *Stroke* 19:1003; (5) Katoh et al.(1992), *Brain Res.* 577:57; Shuaib *et al.*, (1995) *Brain Res.*, 702:199.

LMP12
BDNF ADMINISTRATION IN THE CNS OF ADULT RATS AFFECTS PAIN THRESHOLD AND SPONTANEOUS BEHAVIOUR BUT NOT MEMORY RETENTION IN A MORRIS WATER MAZE TASK

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BDNF, a member of the neurotrophin family, has been shown to be involved in specific aspects of activity dependent synaptic plasticity. The present study examined the possible action of this neurotrophin and of its antibody (AbsBDNF) on memory retention in a Morris Water Maze (MWM) spatial navigation task. Sixty-day-old male Sprague Dawley rats were trained to locate a hidden platform for 3 consecutive days (8 trials per day) in a MWM. On day 3 all subjects were divided into three treatment groups (ten subjects per group), anaesthetised with Equitesin and injected intracerebroventricularly (icv) with: i) BDNF (24mg); ii) AbsBDNF (25mg); iii) vehicle (injection volume 10ml). On day 5 (animals were given one day of post operative recovery) all subjects were tested for memory retention in a probe trial, followed by a reversal task to test reacquisition. In order to dissociate learning and performance effects, all subjects were tested on the same day in a hot plate and in an open field test and a number of behavioural categories were scored. In the MWM task no differences were found as a function of treatment in the probe trial nor in the reversal task. In fact, upon removal of the platform, all groups spent significantly more time in the target quadrant and, when the platform was moved to the opposite location, they did not show differences in learning the new position. BDNF, however, affected both pain threshold in the hot plate test as well as spontaneous behaviour in the open field test. BDNF treated subjects showed a longer latency to lick their hindpaw and a tendency to show a lower frequency to lick their forepaw in the hot plate test while exhibiting a longer grooming duration in the open field test. Overall, while results from the hot plate and the open field test confirm previous data on BDNF effects on midbrain structures, data obtained in the MWM test suggest that, at least with this learning paradigm, this neurotrophin does not affect memory retention.

LMP13
EXPRESSION OF THE $GABA_A$ RECEPTOR g4-SUBUNIT GENE mRNA IN THE DOMESTIC CHICK FOREBRAIN FOLLOWING IMPRINTING TRAINING

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The learning process of imprinting involves morphological, electrophysiological and biochemical changes in a region of the chick (*Gallus gallus domesticus*) forebrain known as the intermediate and