Chapter 8

Extension of the Sensitive Period in Chicks Reared in the Light

In previous experiments it has been shown that the sensitive period for imprinting may be extended by treating chicks with a mixture of KX during the first day of life followed by rearing them in complete darkness. The question that this chapter addresses is whether the same effect can be achieved in chicks that have been reared in the light.

One might expect that dark-rearing contributes to the extension of the sensitive period for imprinting in KX-treated chicks by either preventing them from forming an imprinting memory or learning the properties of their environment. Thus, light-rearing chicks may have the opposite effect of allowing chicks to form a stronger representation of their environment and so impair the formation of an imprinting memory. Classically, dark-rearing chicks prior to imprinting has been used as a method of extending the sensitive period for imprinting (e.g. Sluckin, 1962; Case and Graves, 1978) However, in Chapter 3 it was shown that, when using the imprinting paradigm of this thesis, the sensitive period for imprinting in dark-reared chicks ended sometime between days 2 and 4 post-hatching. Thus, the extension of the sensitive period for imprinting to day 8 post-hatching has been largely attributed to the drug treatments (KX, two doses of ketamine or MK-801) that were used. However, it is possible that the combination of dark-rearing and the drug treatments were necessary in order for the effects to be achieved, especially when considering the effects of light on the developing nervous system.

Depriving animals of light is also known to prevent activity-dependent changes from occurring in areas of the brain that usually receive visual stimulation. In the visual cortex of the cat correlated synaptic inputs originating from visual stimulation are thought to induce the segregation of cells into the appropriate ocular dominance columns

(Rauschecker, 1991). If kittens are reared in the dark, or if the synaptic transmission in this area is blocked with, for example, tetrodotoxin (Reiter *et al.*, 1986) or APV, a competitive NMDA receptor antagonist (Kleinschmidt *et al.*, 1987), ocular dominance columns are not formed. Thus, the neural activity produced by light exposure induces the formation of ocular dominance columns.

At the cellular level, dendritic development is also affected by the amount of visual stimulation. Galal *et al.* (1990) reported that light-reared chicks have a decreased density of dendritic spines in the left and right hyperstriatum accessorium compared to dark-reared chicks. While this region is involved in visual processing, it is not specifically implicated with imprinting. In the IMHV, which is involved in imprinting, there was a reduction in the density of dendritic spines only in the left IMHV of light reared chicks, but there was no change in the density of dendritic spines in the right IMHV. Galal *et al.* (1990) suggested that the function of this reduced dendritic spine density is to select a population of synapses that will then be ready for modification by experience. In fact, the word that these authors used was 'priming'. A direct comparison to the priming procedure frequently used before imprinting dark-reared chicks is difficult to avoid.

The priming procedure in the context of imprinting has been described on page 51. Half an hour of light exposure prior to imprinting has been shown to facilitate imprinting (Bateson and Wainwright, 1972). As yet, the minimum amount of light exposure needed to precipitate changes in the length of dendritic spines is not known. In the experiment of Galal *et al.* (1990) the light-reared chicks received 72 hours of diffuse light exposure, making it uncertain exactly how much light exposure is needed in order for the changes to occur. Changes in synaptic efficacy in response to electrical stimulation in sections from the left IMHV of dark-incubated chicks is also affected by the amount of light exposure that the chicks had previously received (see page 35). The probability of producing a potentiated response was below 40% until the chicks had been exposed to light for at least a day (Bradley *et al.*, 1991b). The duration of the priming period is thus too short for any significant changes in synaptic efficacy to occur. Nevertheless, priming

obviously has beneficial effects in the formation of an imprinting memory. Indeed, changes in synaptic morphology due to exposure to an imprinting stimulus (Bradley and Horn, 1979; Bradley *et al.*, 1981; Bradley and Galal, 1988) have been shown to occur in dark-reared chicks, in which the time of exposure to the imprinting stimulus, and hence light, was a matter of only a few hours.

Clearly, the amount of light-exposure that a chick receives will influence synaptic changes in regions of the brain which are concerned with visual functions, including imprinting. The question that the present experiment investigates is whether the sensitive period for imprinting can be extended in KX-treated chicks that had been reared to day 8 in the light.

8.1 Methods

Thirty-six australorp × leghorn chicks were used in this experiment. As in previous experiments the chicks were incubated and hatched in the dark incubator. Ten hours after hatching they were treated in the dark, with either sterile, pyrogen free 0.9% saline or the KX mixture (55 mg/kg ketamine + 6 mg/kg xylazine), injected into the gastrocnemius muscle. All animals remained in the dark incubator for a further 10-12 hours whereupon they were carried in a light-proof container to individual rearing cages situated in a room that was continuously illuminated by fluorescent lights on the ceiling. The dimensions of the cages were 21 × 21 × 30 cm (width × depth × height). These cages were the standard rearing cages used to house chicks for experiments in this laboratory. Three of the sides were made of galvanised sheet iron. The front was made of perspex, which in this case was covered from the inside with a sheet of paper. In order to minimise the reflection of the chicks image, older cages that had become tarnished were selected. Plain white material was suspended at a height of 10 cm over the tops of the cages to further ensure complete visual isolation. A constant supply of food and water was available to the chicks. The temperature of the room was maintained at 32-34° C for the first 2 days and then reduced to 27° C over the next four

days. Throughout the period of rearing extreme care was taken to ensure that the chicks could not see beyond their cages. Thus, the chicks received a normal amount of light stimulation, but had little perceptual experience.

On day 8 post-hatching the chicks were imprinted on either the red and black box or the rotating fowl. The standard imprinting procedure used in previous experiments was followed (see page 46). This included placing the chicks in the priming boxes for half an hour to give the chicks the same experience immediately prior to the imprinting test as those in other experiments. After training the chicks were returned to their rearing cages, then tested 1 h and 24 h later.

8.2 Results

8.2.1 Activity in training

Table 8-2 presents the activity of the chicks during the training period. The activity of the chicks during the training period was analysed using a three-factor analysis of variance (treatment × stimulus × direction) with a repeated measure on direction. This data was transformed using a log transformation prior to analysis. There was no significant main effect due to treatment ($F_{1,32} = 1.16$, $p = 0.46$) or stimulus used in training ($F_{1,32} = 0.63$, $p = 0.43$). There was, however, a significant main effect of direction which the chicks moved during the training period ($F_{1,32} = 8.94$, $p = 0.01$). Significantly more activity was directed towards the imprinting stimulus than away from it. There were no significant interactions between any of the factors (treatment × stimulus $F_{1,32} = 1.89$, $p = 0.43$; direction × treatment $F_{1,32} = 0.66$, $p = 0.43$; treatment × direction $F_{1,32} = 3.36$, $p = 0.08$; direction × treatment × stimulus $F_{1,32} = 0.54$, $p = 0.47$).

Table 8-1. Activity of chicks during training

Age	Stimulus	Number Trained	Total activity (revolutions)	Activity towards (revolutions)	Activity away (revolutions)
Saline	box	9	333 ± 301	274 ± 25	59 ± 48
	hen	8	105 ± 69	53 ± 35	52 ± 35
KX	box	9	483 ± 221	378 ± 223	106 ± 42
	hen	10	259 ± 158	221 ± 138	38 ± 22

Table presents the mean ± SEM activity of the chicks in training. Activity is presented in revolutions of the imprinting wheels.

8.2.2 Activity in the preference tests

The activity of the chicks in each of the testing periods is presented in Table 8-2. For each testing period the data was log transformed and analysed separately using a two-factor analysis of variance the factors were treatment and stimulus.

In the test 1 h after training there was no significant main effect of treatment ($F_{1,19}$ = 0.72, p = 0.41) or stimulus ($F_{1,19}$ = 2.81, p = 0.11). There was no significant interaction between the factors ($F_{1,19}$ = 0.58, p = 0.45).

In the test 24 h after training there was no significant main effect of treatment ($F_{1,22}$ = 0.01, p = 0.93) or stimulus ($F_{1,22}$ = 0.02, p = 0.90). There was no significant interaction between the factors ($F_{1,22}$ = 0.00, p = 0.96).

Table 8-2. Activity in preference tests

		1 hour after training			24 hours after training		
Treatment	Stimulus	Reached activity criterion n	%	Total activity (revolutions)	Reached activity criterion n	%	Total activity (revolutions)
Saline	box	5	56	30.1 ± 13	5	56	19.0 ± 11.6
	hen	6	86	6.0 ± 2.1	6	86	16.2 ± 8.8
KX	box	5	63	31.0 ± 5.1	4	50	20.9 ± 8.5
	hen	7	70	22.0 ± 11.9	7	70	16.9 ± 8.8

Mean ± SEM total activity during both testing periods. Activity is presented in revolutions of the imprinting wheels. There were no significant differences in the activity of the groups in either of the tests. Also presented in the table is the number (n) and percentage of chicks that reached the activity criterion in each of the testing periods.

8.2.2.4 Number of chicks that reached the activity criterion

As is clear from Table 8-2, the number of chicks from each group that reached the activity criterion in both testing periods was practically the same. The only factor that nearly had a significant effect was stimulus ($X^2 = 3.13$, df = 1, $0.05 < p < 0.10$).

8.2.3 Percent preference scores

8.2.3.1 Test one hour after training.

Figure 8-1 illustrates the mean percent preference scores for the light-reared chicks imprinted on day 8 post-hatching and tested 1 h after training. The percent preference scores were arcsine transformed and analysed by means of a two-factor analysis of variance. The factors were treatment and stimulus. There was no significant main effect of treatment ($F_{1,19} = 2.98$, $p = 0.13$). The main effect of stimulus only approached significance ($F_{1,19} = 3.58$, $p = 0.06$). There was, however, a significant interaction between treatment and stimulus ($F_{1,19} = 7.64$, $p = 0.01$). Fisher's LSD tests revealed that the saline-treated group that was trained on the hen had significantly lower percent preference scores than all other groups ($p < 0.01$).

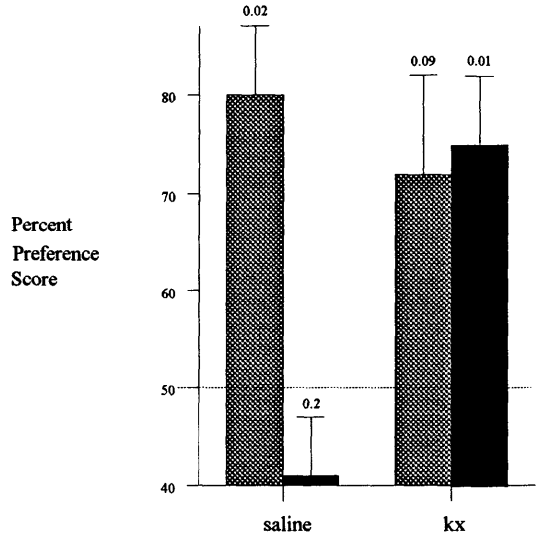

Figure 8-1. Presents the mean ± SEM percent preference scores of light-reared chicks imprinted on day 8 and tested 1 h after training.
Gray bars represent the box-trained groups, black bars represent the hen-trained groups. The percent preference score of the saline-treated group that was trained on the hen was significantly lower than each of the other groups. The values above the error bars represent the p values from two-tailed t-tests comparing the percent preference score of that group with the no-preference level of 50%.

Individual two-tailed t-tests comparing the group means with the no-preference level of 50% revealed that only the saline-treated group trained on the box ($t = 4.1$, $p = 0.02$) and the KX-treated group trained on the hen had percent preference scores significantly higher than the no-preference level of 50%. The percent preference scores of the saline-treated group trained on the hen ($t = -1.5$, $p = 0.19$) and the KX-treated group trained on the box ($t = 2.2$, $p = 0.09$) were not significantly different from the no-preference level.

8.2.3.2 Test 24 hours after training.

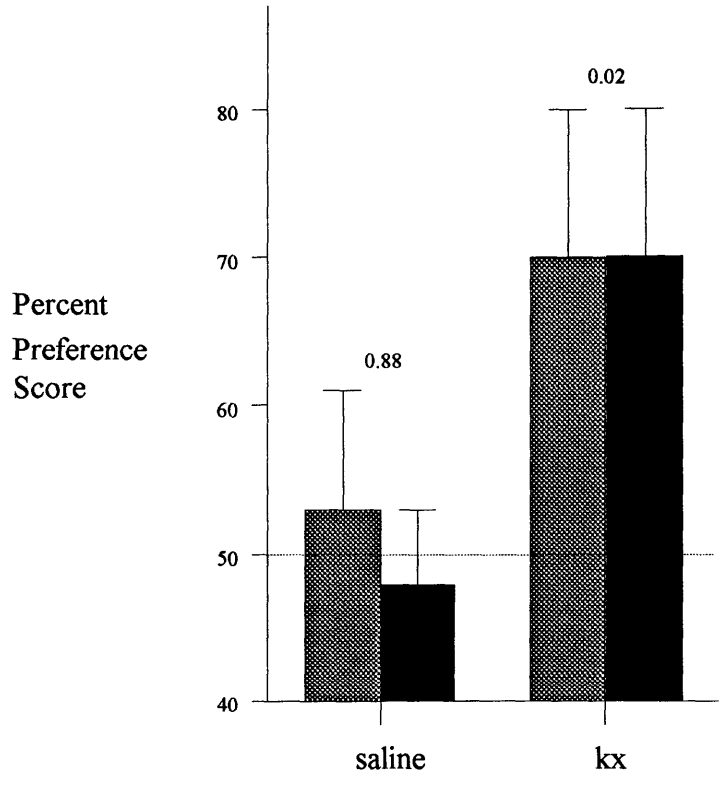

Figure 8-2. Presents the mean ± SEM percent preference scores of light-reared chicks imprinted on day 8 and tested 24 h after training.
Gray bars represent the box-trained groups, black bars represent the hen-trained groups. The percent preference scores of the KX-treated groups were significantly higher than the percent preference scores of the saline-treated groups. The values above the error bars represent the p values of t-tests performed on the combined groups (box + hen).

In the test 24 h after training there was a significant main effect of treatment ($F_{1,22}$ = 4.41, p = 0.05). There was no significant main effect of stimulus ($F_{1,22}$ = 0.06, p = 0.81) nor was there an interaction between the factors treatment and stimulus ($F_{1,22}$ = 0.08, p = 0.78). Both groups treated with KX had higher percent preference scores than the saline-treated groups.

Individual two-tailed t-tests comparing the percent preference scores of the groups with the no-preference level of 50% were performed. The low numbers reaching the activity criterion in each group coupled with the fact that the analysis of variance revealed a significant treatment effect, but no effect of stimulus made it possible to lump the groups without respect to stimulus. As is obvious from the graph, the percent preference scores of the saline-treated group were not different from the no-preference level (t = 0.15, p = 0.88). The percent preference scores of the chicks in the KX-treated group were significantly higher than the no-preference level (t = 2.75, p = 0.02).

8.3 Discussion

The main finding of this experiment was that, when tested 24 h after training on day 8, light-reared chicks treated with KX at 10 h post-hatching showed a preference for the stimulus on which they had been exposed. This occurred regardless of the stimulus used in training and as such is in contrast to the results of Chapters 5 and 6 in which the chicks were reared in the dark. In those experiments, a significant preference for an imprinting stimulus 24 h after training was shown only in those KX-treated chicks that were trained on the hen, but not when they were trained on the box.

Neither of the saline-treated groups displayed an imprinting preference in the test 24 h after training, although the box-trained saline-treated group of chicks did display a significant preference in the test 1 h after training, as did both of the KX-treated groups.

That light-reared chicks treated with KX 10 hours post-hatching could form a preference for an imprinting stimulus, and retain this preference 24 h after training was somewhat unexpected. It is reasonable to suspect that the chicks would have formed

some preference for the walls of their home-cage, considering that they were exposed to these features for 8 days, and one might expect that this would contribute to the ending of the sensitive period for imprinting (Bateson, 1964b).

As suggested in Chapter 6 it must be considered that an action of KX is to allow the chicks to rapidly form other imprinting memories. Viewed in this way, the KX-treated chicks might have imprinted on their home-cage, but were able to form a secondary imprinting memory on the stimulus during the training period (Cook, 1993). Thus, the effect of KX treatment could be to alter the neural systems underlying imprinting so that the sensitive period for imprinting is never able to end. According to this theory the chicks could go on imprinting on one stimulus after another. It would follow that the imprinting memories are retained, and not 'written over' by the formation of the next memory because during the interval between the two testing periods the chicks would have had ample time to establish a memory of the home-cage if it had been lost as a consequence of imprinting in the experiment.

The major difference between this experiment and the experiments in which the chicks were dark-reared is the fact that in the present experiment imprinting occurred regardless of the stimulus on which the KX-treated chicks were trained. In the dark-rearing experiments it was suggested that imprinting did not occur on the box because it was not as effective as an imprinting stimulus as the hen. Clearly some feature of this experiment has enabled KX-treated chicks to imprint equally as well on both stimuli, and the major difference is the light-rearing procedure of the present experiment, which should allow chicks to form a preference for their rearing environment.

If the chicks had learnt the features of their environment, namely their home-cage, it is possible that they were able to generalise some of the features of the box to the home cage. Bolhuis and Horn (1992) have shown that chicks generalise an existing preference for one stimulus to another similarly shaped stimulus of a different colour. The box and the home-cage share some common features such as vertical lines and plain rectangular surfaces, but do have an obvious difference in colour. It is conceivable that the common features of the box and the home-cage were sufficient for the chicks to generalise the

learnt preference for the home-cage to the box. It may be further argued that the red colour of two of the surfaces of the box actually made this a very attractive imprinting stimulus, as it has been shown that red is an effective colour for imprinting (Schaefer and Hess, 1959; de Vos and Bolhuis, 1990).

In the test 1 h after training, both the KX-treated chicks and the saline treated chicks, that were trained on the box, demonstrated a preference for it. The KX-treated chicks were able to retain this attachment, evidenced by their preferences in the test 24 h after training, while saline-treated chicks were not able to retain the attachment.

Cook (1993) has recently shown that primary imprinting preferences are retained after secondary imprinting has occurred. The presence of the primary stimulus may serve to inhibit the formation or consolidation of a secondary imprinting memory. Consolidation of a secondary preference in saline-treated chicks could have been disrupted because the chicks were returned to their home-cages immediately after training. In this context, the home-cage is the primary imprinting stimulus. The KX-treated chicks might be able to form the memory more rapidly than the saline-treated chicks, or as previously proposed, they may have the ability to form multiple imprinting memories.

Despite a clear difference between the treatments with respect to their percent preference scores, there was no significant difference between the two groups in activity during the training session or in either of the testing sessions. Similarly, there was no significant effect of the stimulus used in training. During the training period there was, however, a main effect of the direction that the chicks moved. Significantly more activity was directed towards the imprinting stimulus than away from it. The relative contributions of the groups to this result cannot be ascertained because there was no significant interaction between any of the factors at any of the times tested. However, there was an indication that the saline-treated chicks trained on the hen were less active than the other groups, possibly because they were more fearful of the imprinting stimulus.

8.4 Conclusion

Chicks that were treated with KX 10 h post-hatching and then light reared to day 8 still exhibited a preference for the imprinting stimulus. Saline treated chicks showed no preference for an imprinting stimulus. There was no stimulus specificity in this experiment, as KX-treated chicks showed imprinting on the box and the hen equally as well. There is thus a profound influence of light exposure on the ability of the chick to imprint on day 8 post-hatching in that, in contrast to dark-reared chicks, light-reared chicks also imprint on the box.

Light-reared chicks may already have imprinted on the walls of the home-cage, and could have generalised the preference for the home-cage to the box. The box could have been a more attractive imprinting stimulus because of its colour. Two sides of the box were red, which is a preferred colour to imprint upon. Thus, a chick that is already imprinted on the sides of its home-cage could have generalised this preference to a similar, but slightly more attractive imprinting stimulus.

Chapter 9

Effects of Ketamine-Xylazine treatment on behaviours other than imprinting

Experiment 9-1

An investigation into the effect of ketamine-xylazine treatment on pebble floor visual discrimination learning

Thus far, the effect of KX treatment on the behaviour of chicks has only been investigated with respect to imprinting behaviour. It has been established that treatment with KX alters the response of the chick to the imprinting stimulus so that it will imprint on a hen in the second week of life. One possible explanation for this occurrence is that the KX treatment delays or prevents the maturation of the nervous system. In this manner, the imprinting system of the chick may remain in a state of readiness to form an imprinting memory. Similarly, other behaviours with established developmental time-courses may also be influenced.

The pebble floor task provides a measurement of visual discrimination learning in the chick. In this task, chicks must search for their normal granulated food against a background of small, similarly shaped pebbles glued to a perspex floor (Rogers *et al.*, 1974). After 3-5 h of food deprivation, chicks in their second week of life learn to peck at the grains and avoid the pebbles. Chicks initially peck at random, making approximately an equal number of pecks at pebbles and grains over a trial of 60 pecks. The learning is evidenced by a reduction in pecks at pebbles such that in the last 20 pecks they will only make 2-4 pecks at pebbles. Discriminations are made using texture and brightness cues only (Rogers, 1986). Although the chicks are deprived of food 3-4 h

prior to the task, learning is not necessarily related to a food reward. Frequently a chick will mandibulate a grain without swallowing it (Reymond and Rogers, 1981). Nevertheless, a change in behaviour over the course of the 60 pecks is normally evident suggesting that they have learned to peck at grains in preference to the pebbles.

The pebble floor task can thus be used as a sensitive tool to measure the rate at which chicks can learn the characteristics of objects at which they should or should not peck. This behaviour is of course important to the survival of the chick. In natural broods, learning about food objects normally occurs around day 4-5, after the chick has imprinted. In fact, it is the tidbitting actions of the hen which usually initiate the pecking responses of the chicks (Workman *et al.*, 1991). Initially, young chicks will peck at small objects in an almost reflexive manner. Through experience they learn to recognise stimuli that are to be avoided and stimuli that may be pecked (Andrew, 1991, p. 17).

The pebble floor visual discrimination task is a task on which 2-3 day-old chicks do not perform well (Rogers, 1971). In other words, at an age when chicks will normally imprint, they will perform poorly on the pebble floor task. In this experiment chicks that were treated with KX and which were able to imprint on day 8 post-hatching were tested on the pebble floor visual discrimination task on day 10 post-hatching. This was done to determine if KX treatment also delays the development for the ability to perform on the pebble floor visual discrimination task. Additionally, groups of chicks that were treated with the two components of this mixture, ketamine alone or xylazine alone were also tested.

9-1.1 Methods

Chicks from Experiment 1 of Chapter 6 were tested on the pebble floor visual discrimination task on day 10 post-hatching, which is the day following the last imprinting test. They had been dark-reared to day 9 post-hatching. Immediately after the imprinting test they were transferred to individual cages 21 × 21 × 30 cm (width × depth × height) that were illuminated by 40-W pearl light globes 40 cm overhead. They

thus received approximately 20 h of light exposure prior to the pebble floor test. There were four treatments in this experiment, saline, KX, ketamine itself and xylazine itself. All treatments were given 10 h after hatching. Along with the dark-reared groups, a saline-treated group that was reared in the light was also tested. Chicks in the light-reared group were obtained from two of the same hatches as the chicks in the rest of the groups. The light-reared chicks were reared as a group until day 5 post-hatching, whereupon they were transferred to individual cages.

Food and water were available *ad libitum*. The food was scattered on the floor of the cage, and the water was available from a small-bird waterer. The reservoir was outside the cage and the drinking receptacle protruded through a hole in the side of the cage.

Testing was performed between 9 am and 1 pm only to avoid any diurnal variations in learning (Reymond and Rogers, 1981). The chicks were deprived of food for 3 to 4 h prior to the test. To keep the food deprivation periods approximately uniform, food was taken away from five chicks at a time, starting at 6 am. Every hour a further five chicks were deprived of food. To keep to this schedule a maximum time of ten minutes was allocated for each chick to complete the task. Those chicks that did not complete the task in the specified time were excluded from the analysis.

Parameters measured were the latency to peck, time taken to make 60 pecks and the number of error pecks in the first, second and third blocks of 20 pecks. The decreasing number of error pecks in subsequent blocks is the standard measurement of learning performance on the pebble floor task (Rogers *et al.*, 1974). As mentioned previously, not all grains that are pecked are swallowed. Grains may be pecked at with a closed beak and not picked up; in which case the grain usually shoots off. If the chick directed its next peck(s) towards the same grain, that peck was not counted. Similarly, only the first of a bout of pecks directed at a pebble was scored.

9-1.2 Results

Table 9-1 presents the number of animals trained in each group, the number that completed the task in the allocated 10 minutes, the mean ± SEM of the latency to peck and the time taken to make 60 pecks. The latency to peck and the time taken to complete 60 pecks was analysed using a Kruskall-Wallis test. There was no significant difference between the groups in the latency to peck ($H = 2.62$, $p = 0.45$) or the time taken to make 60 pecks ($H = 5.36$, $p = 0.15$).

Table 9-1. Latency to peck and time taken to make 60 pecks in the pebble floor task

Group	Number trained	Number completed	Latency to peck	Time taken
Saline light-reared	13	9	54 ± 27	224 ± 43
Saline dark-reared	19	16	47 ± 25	316 ± 47
KX	19	15	31 ± 17	262 ± 44
Ketamine	15	10	65 ± 27	159 ± 31
Xylazine	18	14	14 ± 3.7	264 ± 42

Table presents the number of chicks in the experiment, the mean latency to peck and the mean time taken to make 60 pecks in the pebble floor visual discrimination test. There was no significant difference between the groups in either of these measures.

Figure 9-1 presents the number of pecks at pebbles made by the chicks in 20 peck increments. There was no significant difference in the mean number of error pecks that each group made in any block of 20 pecks (Kruskall-Wallis one-way analysis of variance, $p > 0.05$ for each group). Learning performance did, however, differ between the groups. A comparison of the number of pecks at pebbles in the first and last 20 pecks revealed a significant difference only in the two saline-treated groups (Wilcoxon matched-pair rank test, $p < 0.05$). The other groups did not significantly decrease their pecks at pebbles ($p > 0.05$ for each).

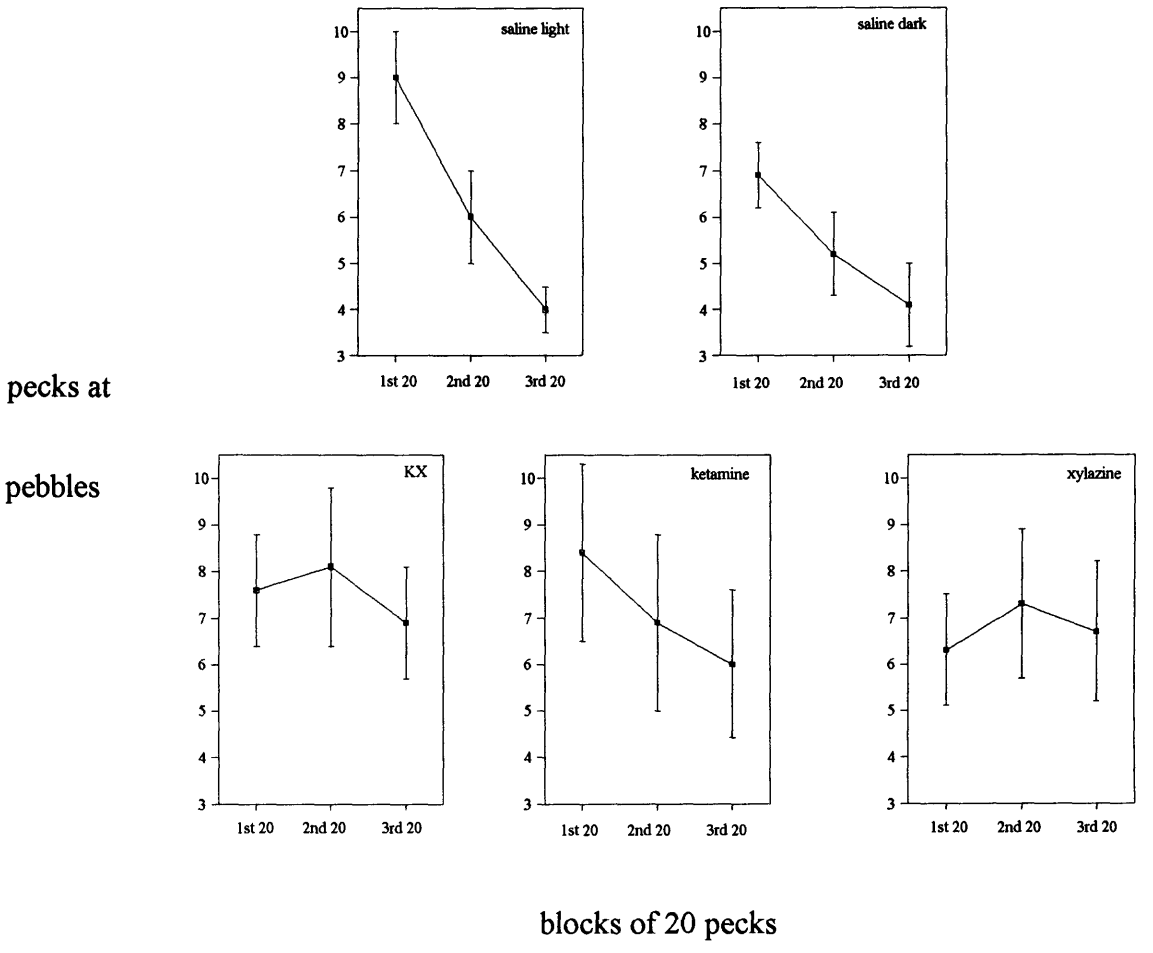

Figure 9-1. Pebble floor test of groups treated with saline, KX, ketamine alone or xylazine alone. One saline-treated group was light-reared; all other groups were dark-reared. Plotted are the mean ± SEM number of pecks in each block of 20 pecks. The number of pecks at pebbles are represented on the y axis. Only the two saline treated groups showed a significant reduction in the number of pebbles pecked.

9-1.3 Discussion

In this experiment those chicks treated with KX did not significantly reduce the number of pebbles that they pecked at over the course of the 60 peck trial. Similarly, the chicks treated with ketamine alone or xylazine alone did not show a decrease in the number of pebbles pecked. Only those groups treated with saline showed a significant reduction in the number of pebbles pecked over the 60 peck trial. Notably, one of the saline-treated groups was reared in the dark and the other group was reared in the light from 10 h post-hatching. Thus, the period of dark-rearing did not have a detrimental

effect on the visual ability of the chicks, at least as measured on the pebble floor task. The deficits in performance on the pebble floor task that were observed in the groups treated with the drugs can thus be attributed to the effects of the drugs themselves and not to a deterioration in visual performance caused by dark-rearing.

There was no significant difference in the latency to begin pecking or in the time taken to make 60 pecks. The mean pecking latency of the xylazine-treated group certainly appears as though it might be significantly different to the other groups, although the high variability of those groups probably accounts for the lack of statistical significance in this measure.

The fact that a detrimental effect on the performance in the pebble floor task was shown for those chicks treated with ketamine alone, xylazine alone or the mixture of the two, indicates that the effect is not specific to an action on either the NMDA receptor system or the noradrenergic system. It is not known if the same systems have been affected by these treatments or if different systems are involved for each drug. This question cannot be definitively answered from this experiment. However, no differences were found between the group treated with ketamine alone and the group treated with xylazine alone, indicating that the two drugs might be acting on the same system, or that the task may be sensitive to alterations in more than one neurotransmitter system during development.

Glutamate and its agonists have been shown to retard visual discrimination learning if injected intracranially from day 2 to day 8 post-hatching (Sdraulig *et al.*, 1980; Rogers and Hambley, 1982). These treatments were effective only if the chicks received normal patterned visual experience following the treatment. Chicks that were deprived of patterned visual input immediately following the treatment showed no deficits. Thus, the deficits produced by glutamate treatment were dependent upon an active visual system. In the present experiment KX, ketamine, or xylazine all acted to retard the performance on the task even though the chicks were reared in the dark.

It is not paradoxical that the same treatment that enhances the ability of chicks to imprint on day 8 post-hatching retards their performance on a visual discrimination task

when tested on day 10 post-hatching. The outcome of the treatment on both behaviours is actually an inappropriate one. Chicks treated with KX perform both tasks with the ability that is expected of chicks aged 2-3 days post-hatching. Thus, it may be argued that the treatment delays brain development in the chick in a non-specific manner. However, unlike the experiments that have shown an effect on the filial behaviour of the chicks, the pebble floor task was affected by xylazine treatment as well as by ketamine treatment. The processes involved in performing the pebble floor task may simply be more sensitive to the effects of the treatments than the systems involved in imprinting behaviour. Indeed, in Experiment 2 of Chapter 6, repeated doses of ketamine, but not xylazine, were shown to extend the sensitive period for imprinting. With a prolonged action of ketamine alone, filial behaviour was significantly affected.

This argues against the notion that the effect of antagonising the NMDA receptor produces a generalised retardation of brain development. Xylazine treatment has been shown to disrupt at least one learning mechanism (that which is involved in the pebble floor task), but does not extend the sensitive period for imprinting. Had xylazine not affected performance in the pebble floor task, one might conclude that antagonism of the NMDA receptor at an early post-hatch age delays brain development in a non-specific manner. This was not the case and it thus is more likely that the respective treatments disrupt normal development for particular functions depending on the physiological relevance that each of the treatments has on the neural systems underlying the relevant function. The systems underlying pebble floor learning may be sensitive to manipulations of the noradrenergic system and the NMDA receptor system, while the systems underlying the sensitive period for imprinting may be sensitive to manipulations of the NMDA receptor system only. The experiment reported in Chapter 5 suggests that only those systems that are at a sensitive period of development will be affected. It is possible that, had the treatments been given at a later age when the systems had already developed, pebble floor learning would not have been affected. Pebble floor learning was, however, affected by the treatments. It is as if the development of the chicks has been limited to the stage at which they received their treatments.

The occurrence of different developmental stages has been a popular idea in developmental psychology (e.g. Flavell, 1963). Each stage may lay the foundation for the following stage or period. The occurrence of different developmental stages in the chick may result from an interaction between systems that need to utilise similar neural functions.

For example, the IMHV has been implicated in both filial learning (Horn, 1985) and in classifying objects that should or should not be pecked, as represented by passive avoidance learning (Rose, 1991, p. 277). (At present it is not known whether the IMHV is used in pebble floor learning.) The involvement of this region in both types of learning may have evolved through pressures put on the developing neural systems of the chick. The chick, being a precocial species is forced to learn about the properties of its environment, and a common mechanism that is involved in recognising various features may serve to conserve developmental resources.

A central recognition component may also serve to direct the attention of the chick to the type of stimulus that is most likely to fulfil its needs at a particular time. For example, during the first few days post-hatching a chick does not need to feed because it has enough residual yolk sac to sustain itself (Schilling and Bleecker, 1928). Instead, its attention needs to be focussed on a stimulus that will provide it with protection and warmth. In practice, the stimulus then provides an example from which the chicks learn to feed. A chick's behavioural development may thus be viewed as a series of functions that have evolved to satisfy the needs of the chick at a particular stage of its life. From the results of this chapter it cannot be inferred whether the disruption of one of these phases disrupts the development of preceding phases because pebble floor learning was impaired in all drug-treated groups.

Experiment 9-2

Open Field Ambulation

Although the percent preference score is designed to express the behaviour of the animal without respect to its activity, it is possible that another action of the treatments is to alter the activity level of the animals. Non-competitive NMDA receptor antagonists produce an acute increase in locomotor activity in mice when injected intraperitoneally (Triklebank *et al.*, 1989; Liljequist *et al.*, 1991). It is possible that treatment with ketamine, xylazine or the combination of the two might produce a long-term effect on the activity of the chicks.

However, in each of the imprinting experiments the total activity in the imprinting wheels did not differ significantly between the groups, indicating that there was no effect of the drugs on the level of activity, at least as measured in the imprinting wheels. It is fair to say, however, that the imprinting situation has some features that could alter the activity of the animals. The imprinting stimulus may significantly influence the normal activity levels of the chicks, in either a positive or a negative way. For example, the level of activity could be masked by the motivation of a chick to follow the imprinting stimulus, or it may act as an aversive stimulus, inhibiting the movement of the chick.

In this experiment, the activity of chicks outside the imprinting apparatus has been examined using an open field arena.

9-2.1 Methods

Sixty one chicks from several different hatches were used in this experiment. These chicks were all from Experiment 2 of Chapter 6. They had been treated 10 h after hatching with either saline, the mixture of ketamine and xylazine, ketamine alone or xylazine alone. The groups that received ketamine or xylazine treatments were given another injection 2 h after the first treatment. Each treatment was delivered

intramuscularly in a volume of 0.1 ml. On day 9, 4-5 h after the imprinting test 24 h after training, the chicks were tested in the open field apparatus.

9-2.1.1 Open field apparatus

The open field consisted of a square 90 cm enclosure with sides 35 cm high. The floor of the open field was divided into 10 cm squares. The chicks were placed in the centre square at the start of the test. Each time both feet of a chick crossed a line into another square one movement was scored. Latency to move from the start and the number of squares crossed were recorded over a five minute period.

9-2.2 Results

The mean ± SEM latency of the groups to move are presented in Table 9-2. The latency to move was analysed using a one-way analysis of variance. There was no significant difference between the groups in the latency to move in the open field ($F_{3,58}$ = 0.63, p = 0.60).

Table 9-2. Latency to move in open field

Treatment	Number	Latency to move
Saline	17	63 ± 15
KX	15	64 ± 16
Ketamine × 2	14	44 ± 13
Xylazine × 2	15	56 ± 13

Table presents the mean ± SEM latency to move in the open field test. Also presented is the number of chicks in each group. There was no significant difference in the latency of the chicks to move in the open field.

9-2.2.1 Ambulation in open field

The mean ± SEM activity for each treatment group in the open field is presented in Figure 9-2. The data was analysed using a one-way analysis of variance. There was no significant difference in the activity of the groups ($F_{3,58}$ = 0.55, p = 0.65).

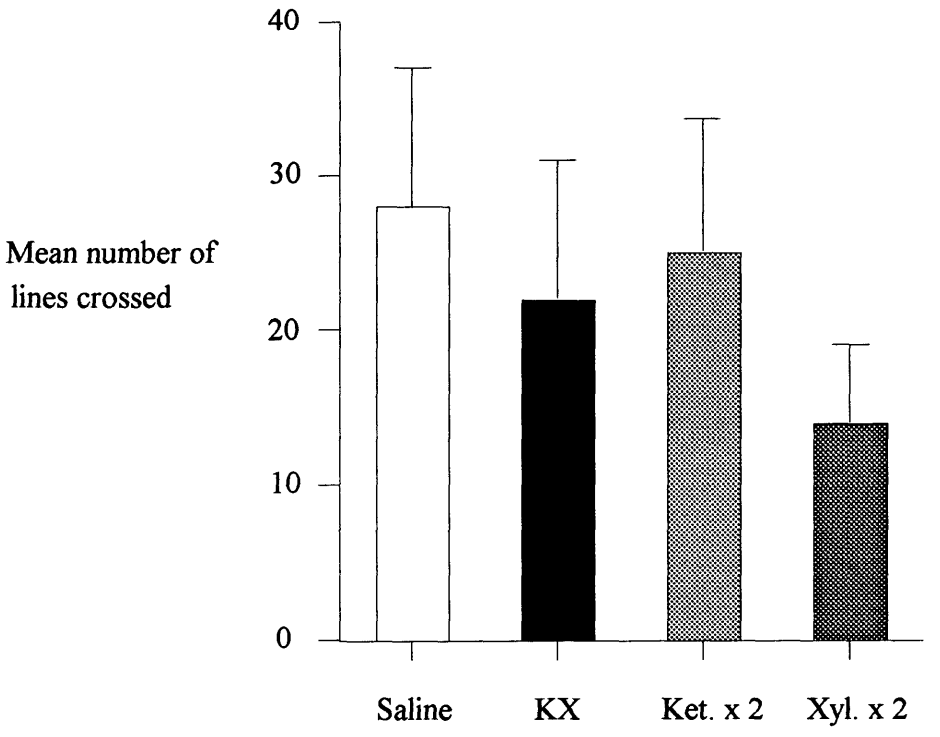

Figure 9-2. Mean ± SEM activity of the chicks in the open field arena.
These animals came from Experiment 2 of Chapter 6. They were treated 10 h after hatching with either saline, KX, two doses of ketamine (ket. × 2) or 2 doses of xylazine (xyl. × 2). There was no significant difference in activity between any of the groups.

9-2.2.2 Correlation between activity in the open field and activity during the imprinting tests

As the chicks had previously been tested in the imprinting apparatus, it was possible to directly compare their activity during the imprinting test with their activity in the open field. Total activity in training and in both of the testing periods was compared to the activity in the open field.

Figure 9-3 presents the correlation between activity in the open field and activity in both preference tests. The data from each group is presented separately for clarity. However, the correlation co-efficients were calculated from the combined results. The correlation co-efficients are presented in Table 9-3.

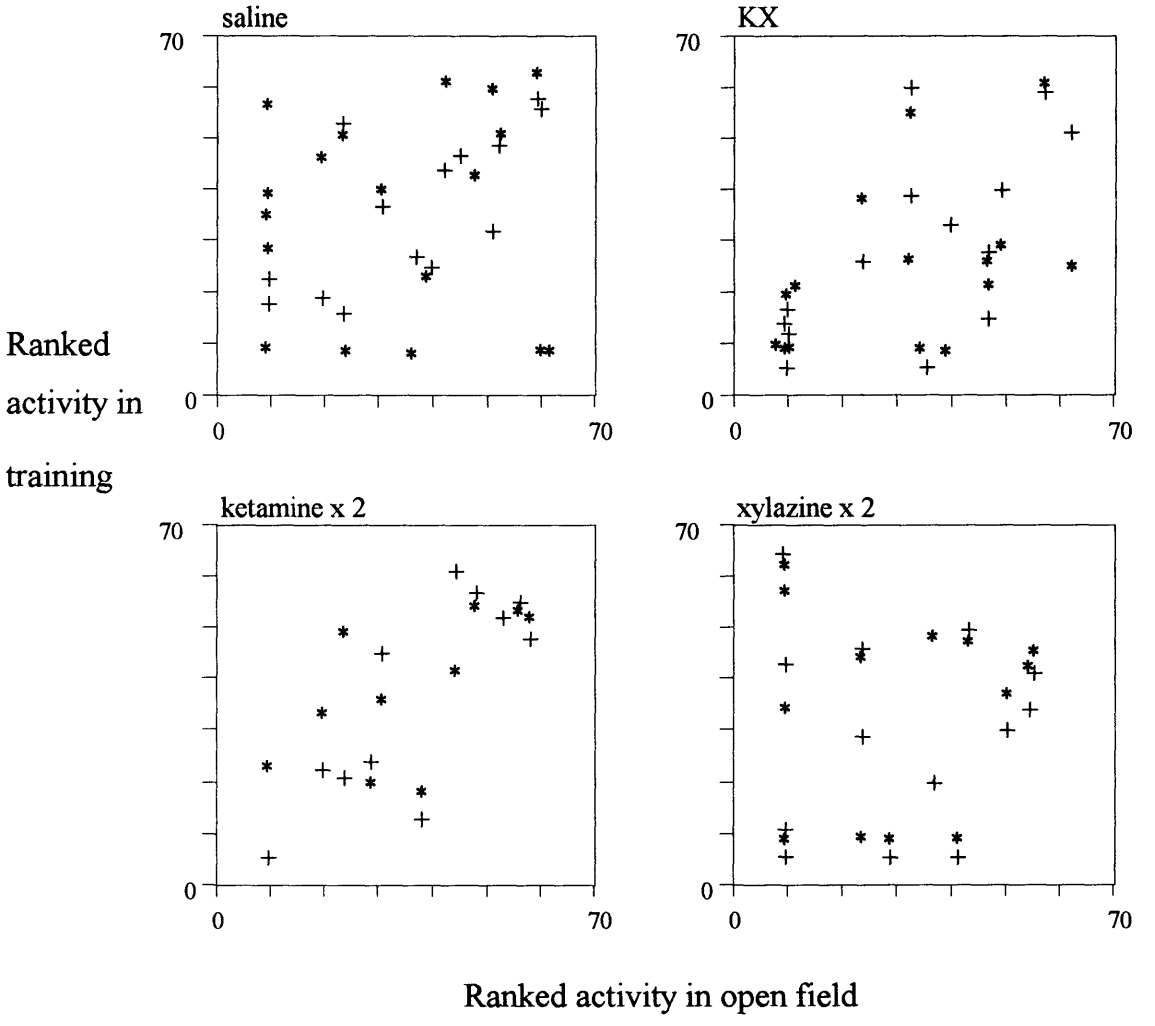

Figure 9-3. Ranked activity in preference tests is plotted against the ranked activity in the open field. Asterisks represent the scores from the 1 h test, the crosses represent the scores from the test 24 h after training.

The Pearson *r* correlation co-efficients for the open field activity and testing activity are presented in Table 9-3. There was no significant correlation between the activity of the chicks during the training period and their activity in the open field. There was however a significant correlation between the activity in the test 24 h after training and

the activity in the open field ($p < 0.001$). The correlation coefficient for the test 1 h after training and the activity in the open field was just outside the critical value of *r* for statistical significance.

Table 9-3. Correlation between activity in open field and activity in the imprinting wheels.

	Training	Test at 1 hour		Test at 24 hours	
		Total Activity	Percent preference score	Total activity	Percent preference score
Test 1	0.074				
Test 24	0.009	0.651*			
Open field	0.066	0.246	0.021	0.459*	0.077

Pearson r correlation co-efficients are presented for the total activity in training, both testing periods and activity in the open field. The critical value of *r* for 59 df = 0.250. Also presented are the correlation co-efficients of the percent preference scores and the activity in training.

9-2.3 Discussion

In this experiment no significant difference in the mean activity of the groups in the open field was found. There was also no difference between the groups in their latency to move at the start of the test. Treatment at 10 h post-hatch with either the mixture of KX or ketamine or xylazine alone had no effect on the activity of the chicks as measured on day 9 in the open field. This result is similar to that found when examining the level of activity of the same chicks in the imprinting tests in which no significant difference in activity between the groups was found (see Table 6-3, page 112).

In fact, there was a significant correlation between activity in the open field test and activity in the imprinting test 24 h after training. However, the correlation between activity in the open field and activity in the test 1 h after training only just failed to reach significance.

Taken together, these results suggest that the activity of the chicks during the imprinting tests is not especially affected by the imprinting situation as such, but may instead reflect the general activity level of the chick. Those chicks that were more active during the imprinting tests were also more active in the open field test. It is also notable that the closer together in time that the activity measurements were made, the greater was the correlation between the two events. For instance, there was a significant correlation between activity in the open field and activity in the test 24 h after training, but not between open field activity and activity in the test 1 h after training. The fact that a significant correlation was found for two different measures of activity on the same day may merely be a reflection of the physical state of the animal.

It may be argued that an animal that is more active will be better able to express its preference by moving towards the imprinting stimulus. It is thus important to evaluate the imprinting preferences of chicks using a ratio method such as the percent preference score used in this thesis, which controls for differences in the activity of the chicks.

Experiment 9-3

A bias in the turning direction in the imprinting wheels

The dominant eye system of a chick can provide information about the chick's underlying developmental state, especially with regard to the sharply timed lateralised events that occur during the first 2 weeks of a chicks life (Andrew, 1988). The following study was performed to assess the visual dominance of the chicks.

9-3.1 Methods

The chicks in this experiment were derived from the predisposition experiment of Chapter 7 and the pilot experiment. These chicks thus provided a group of chicks that were trained on the hen and a group that were not trained. Behaviour from the test 24 h

after training was scored because in all the previous experiments this is the time at which the differences between the groups become apparent.

As the chicks were relatively active within the wheels, it was not satisfactory to assess monocular viewing of a stimulus as did Andrew and Dharmaretnam (1991). Instead, the direction of turning was scored. A strong bias in turning should indicate which eye-system leads the chick away from one stimulus and towards another. This, however, may be open to interpretation. Each time a chick changed its direction of orientation, from facing one stimulus to facing the next (i.e. 180°) it scored one turn. This data was analysed using a Wilcoxon signed rank test.

9-3.2 Results

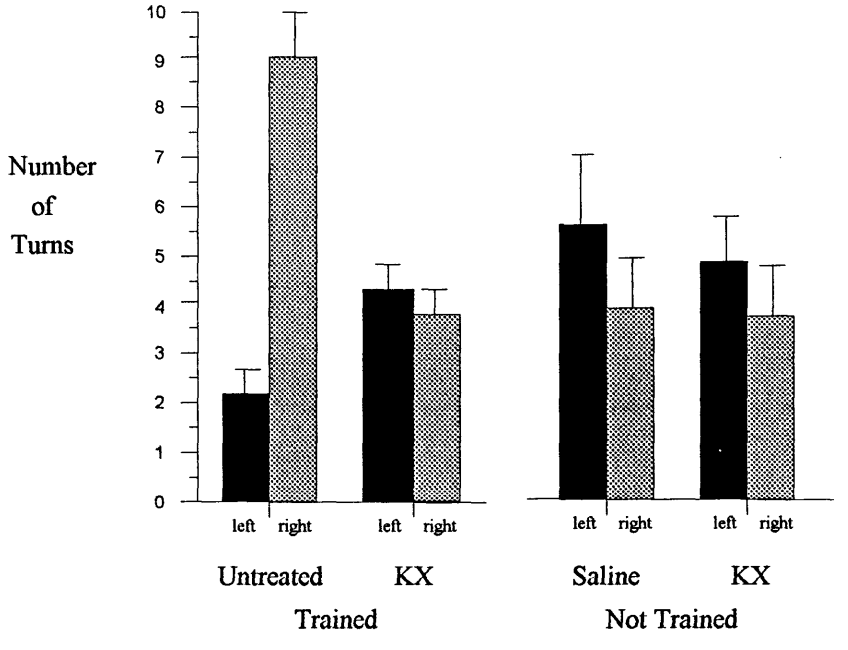

Figure 9-4. Mean ± SEM number of left and right turns in imprinting wheels.
This data was obtained from two experiments, the trained chicks were trained on the hen and were either untreated or treated with KX. The group of chicks that were not trained were from the predisposition experiment, they had been treated with saline or KX. The measurement was the number of complete 180° turns (changes in direction) in the test 24 h after training. Only the untreated group that was trained on the hen exhibited a significant bias in the direction that they turned.

The number of left and right turns of 180° is presented in Figure 9-4. The untreated chicks that were trained exhibited a significant bias in the direction that they turned, making significantly more turns to the right than they did to the left ($W = 102$, $p = 0.002$). There was no significant bias in the direction of turning for any of the other groups: KX-treated and trained ($W = 39$, $p = 0.70$); saline-treated, not trained ($W = 7.0$, $p = 0.14$); KX-treated, not trained ($W = 10.5$, $p = 0.09$).

9-3.3 Discussion

The strong bias to turn towards the right in the untreated, trained chicks may indicate a dominance of the neural systems fed by the right eye. This dominance is absent in all other groups, including the saline-treated group not exposed to the imprinting stimulus.

This turning bias may be related to the fact that when naive day 8 chicks monocularly view a hen they spend significantly more time doing so with their right eye than their left eye (Andrew and Dharmaretnam, 1991). That is, the right eye system is the dominant eye system at this age. The predominance of right turns is probably a result of the systems fed by the right eye dictating which direction to turn. Although it could be argued equally well that while a chick is fixating something in its lateral field of view with its preferred eye, the other eye may be attending to something and directs the chick to that stimulus.

It is interesting that the equivalent group to Andrew and Dharmaretnam's (1991) naive group, the untrained saline-treated group, did not show a turning bias. It is possible that the turning bias developed during exposure to the imprinting stimulus. It is established that day 8 chicks spend more time looking at an imprinting stimulus with the right eye. During the training period dominance may be strengthened because one eye system receives more visual stimulation than the other. In chicks that had been dark-reared to day 8 this may be particularly pronounced. When in a situation during which they are unsure of which stimulus to approach, they may switch from stimulus to stimulus. This may be controlled by the dominant eye system.

9-4 Conclusion

This chapter has provided some evidence that KX treatment may retard the development of the brain of the chick. KX-treated chicks performed poorly on the visual discrimination task, much as would be expected of chicks aged 2-3 days post-hatching. KX-treated chicks performed at the same level as chicks treated with ketamine or xylazine alone. Thus, all of these treatments may delay brain development, either through the same mechanism or through different mechanisms. At this stage it is tempting to postulate that the extension of the sensitive period for imprinting is also due to delaying the development of the systems underlying imprinting.

The ambulation of the chicks in the open field was not affected by the treatments. Instead, open field ambulation was positively correlated with the total activity in the test 24 h after training, indicating that the level of activity of the chicks during the imprinting tests is not especially related to the imprinting experience, rather it may reflect the level of activity of the animal itself. Therefore, measures of imprinting should control for the activity of the animal, as does the percent preference score, which has been used as the main measure of imprinting throughout this thesis.

Chapter 10

General Discussion

In Chapter 3 it was demonstrated that the ability of a chick to acquire a significant filial preference, using the imprinting method of this thesis, ended sometime between days 2 and 4 post-hatching. The preliminary experiment reported in the introductory chapter indicated that this sensitive period could be extended by treatment with a mixture of ketamine and xylazine. The extension of this sensitive period was replicated in subsequent chapters, and it was also shown that the treatment was only effective 10 or 20 h post-hatching (Chapter 5). In Chapter 6 it was shown that ketamine can act alone to extend the sensitive period for imprinting, thus implicating the NMDA receptor. Further evidence for the involvement of the NMDA receptor was that chicks treated with MK-801 were also able to imprint on day 8 post-hatching. Thus, antagonism of the NMDA receptor 10 or 20 h after hatching enables chicks to imprint on day 8 post-hatching. However, in the dark-reared chicks, imprinting, as evidenced by a significant preference for the imprinting stimulus in the test 24 h after training, occurred only in chicks that had been trained on the hen. The exception to this was the experiment reported in Chapter 8 in which the chicks were reared in the light. In that experiment KX-treated chicks demonstrated a significant preference for the imprinting stimulus regardless of whether it was the hen or the box.

Two sub-systems of filial behaviour are recognised (Horn, 1985). One system involves a learning process in which a chick recognises stimuli that it has been exposed to. The other system involves a predisposition of a chick to preferentially approach a particular class of stimuli, most commonly represented by objects resembling members of its own species (Horn and McCabe, 1984; Horn, 1985; Horn and Johnson, 1989; Bolhuis, 1991; Johnson and Bolhuis, 1991). The predisposition is not immediately

evident, but emerges 24 h after training. In this thesis, notwithstanding the results of the light-rearing experiment (Chapter 8), there were initially good reasons to suspect that the developing predisposition mechanism had been affected in the experiments which showed an extended sensitive period. The results were very similar to those that would be expected had a predisposition developed, as only those chicks that were trained on the hen imprinted. Additionally, the clearest results were obtained when the chicks were tested 24 h after training, rather than 1 h after training. At 24 h after training, chicks treated with KX at 10 h, 20 or 40 h post-hatching (Chapters 5 and 6) or treated with ket. × 2 or MK-801 at 10 h post-hatching (Chapter 6) showed a strong filial preference for the hen.

While the age of the chicks (day 8 at training) was clearly outside of the sensitive period for the development of the predisposition, which is between 12 and 42 h post-hatching (Johnson *et al.*, 1989), it was conceivable that the period during which the predisposition could develop had been extended by KX treatment. However, the results presented in Chapter 7 proved that a predisposition had not occurred. Chicks treated with KX 10 h post-hatching and placed in the imprinting wheels on day 8, without exposure to the imprinting stimulus, showed no preference for the hen or the box when tested 24 h after this experience. The filial behaviour that is exhibited by the chicks treated with KX can thus be attributed to a learning effect and not to a developing predisposition. It is probable that the preference for the hen shown by those chicks treated with ket. × 2 or MK-801 at 10 h post-hatching was also the result of learning and not due to a predisposition to approach a hen.

In the absence of a predisposition, it must be concluded that some property of the hen makes it a more effective imprinting stimulus than the box on day 8, so that chicks imprint on the hen and not the box.

According to Bateson (1966) the effectiveness of an imprinting stimulus is related to its conspicuousness to the human eye. Given a choice, day-old chicks will preferentially approach a more conspicuous stimulus (Bateson, 1964a). However, in Chapter 3 there were indications that for day 2 and 4 chicks, the box, a less conspicuous object than the

hen, was the preferred imprinting stimulus. On day 8, the groups that did show a preference for the imprinting stimulus were trained on the hen which is a more conspicuous imprinting stimulus. In the experiments of this thesis it appears that (for the chicks which did show a preference for an imprinting stimulus) there is a shift with age in the effectiveness of the imprinting stimuli.

A number of studies have indicated that the preferences of chicks for imprinting stimuli change with age, both on the basis of colour and in visual complexity. Gray (1961) reported that there was a shift in the colour preferences of chicks with maturity, although the only increase in the imprinting score occurred between days 1 and 2 post-hatching. Red was reported to be the most effective colour for eliciting the following response. In Chapter 3 preferences for the box (coloured red and black) were high on day 2 post-hatching, which may be accounted for by the effectiveness of a red colour in inducing the imprinting response. Berryman *et al.* (1971) reported that 5-6 day old chicks preferred a complex stimulus to a simple one, while no such preference was shown by day 2 chicks. One might argue that as chicks grow older they need a more complex stimulus in order to form a ffilial attachment. To some degree, this could provide an explanation for the fact that on day 8, dark-reared KX-treated chicks imprinted only if they were exposed to the hen. The box may not have been an adequate imprinting stimulus for the chicks at this age.

If one wished to extrapolate this idea, it could be argued that as a chick matures it progresses through different phases of filial attachment. Each phase could be characterised by the type of stimulation needed for an effective attachment to be made. Initially, a chick may become visually attached to a stimulus, but with continued exposure it learns other properties of the stimulus, for example its auditory characteristics and perhaps its smell. Although this can be regarded as a naturally occurring series of events, it is possible that there is a temporally arranged requirement for each relevant sensory system to contribute to the overall imprinting memory. As a chick grows older it may require a greater number of senses to be activated in order for imprinting to occur. In fact, many studies that have demonstrated imprinting in older

chicks or ducklings have manipulated the properties of the stimuli in order to make them more attractive as imprinting stimuli (e.g. Case and Graves, 1978). Auditory stimulation is most frequently used in this manner (e.g. Gottlieb, 1963; Smith and Bird, 1963; Smith and Nott, 1970), although other sensory modalities have also been shown to be effective in contributing to filial imprinting. These include olfactory (Burne, 1992) and tactile senses (Eiserer, 1978). Eiserer (1978) has shown that stroking a duckling during exposure to an imprinting stimulus facilitates its attachment to that stimulus. Perhaps the best example of combined stimulus properties that enhance the attractiveness of an imprinting stimulus is that provided by a live hen. ten Cate (1989) showed that in Japanese quail chicks the strongest attachment was towards a live hen, followed by a moving stuffed hen, while a non-moving stuffed hen failed to induce imprinting. Furthermore, there was a positive correlation between the amount that the hen interacted with the chicks and the subsequent preference shown by the chick towards the hen, supporting the idea that the more sensory modalities that are involved, the greater is the attachment of the chick for the hen. It could be argued that these other procedures serve to enhance the arousal of the chick, and this promotes the memory formation.

Thus, the failure of the box-trained chicks to imprint may be explained by the lack of strength that the box has as an imprinting stimulus on day 8. The box may lack certain features that are attractive to chicks at this age (day 8). The relative attractiveness of a stimulus may determine the attention or arousal of the chick. van Kampen (1993) suggests that a conspicuous object will attract the attention of a chick and may evoke the release of catecholamines, increasing the arousal level of the chick. Catecholamines, such as noradrenaline, may positively affect learning of the imprinting stimulus through an acceleration of synaptic consolidation processes involving adenosine 3',5'-cyclic monophosphate (cAMP) mediated events which can also modify the levels of NMDA or metabotropic receptors (Rauschecker, 1991). There is also evidence for cAMP-dependent protein kinase systems modifying the receptor level. As a further point, the light-reared chicks (of Chapter 8) were reported to have a higher level of arousal

compared to dark-reared chicks, and this could possibly account for the fact that both box and hen trained KX-treated chicks formed an imprinting preference.

Throughout the experiments of the thesis the results obtained in the tests 1 h after training have not always been reflected by the results in the test 24 h after training. In many instances, saline-treated chicks have shown a preference for the imprinting stimulus 1 h after training but not 24 h after training. This is reminiscent of other results in which the effects observed after imprinting have not always been evident immediately after training, but emerged sometime later. As an example, consider multiple unit activity that was studied by Payne and Horn (1984) who reported that spontaneous discharge of units in the IMHV, recorded 1 h after training, was negatively correlated with the approach counts during the 3 h exposure period, while Bradford and McCabe (1992) recorded at least 20 h after training and found a positive correlation between spontaneous multiple-unit activity and the percent preference scores of the chicks. Additionally, McCabe and Horn (1991) demonstrated that the increase in NMDA receptor binding in the left IMHV of chicks did not occur before 6-8½ h after training. McCabe and Horn (1991) suggest that the NMDA binding changes that they observed are not involved in the retention immediately following training, but may play a role in a later stage of memory formation that may involve an alteration in an activity-dependent gene expression. It is quite possible that the results from the test 1 h after training are a reflection of a stage of memory not associated with NMDA-mediated events.

Perhaps the NMDA receptor-mediated events are crucial to the elicitation of a filial response. It is accepted that the ability to learn about objects is not lost after the sensitive period has ended; chicks can go on learning the properties of different stimuli, but do not form filial attachments to them (Bateson, 1979a). Thus, the results from the test 1 h after training may not reflect a permanent imprinting memory. This is not to say that 24 h after training the chicks do not remember the stimulus on which they had been exposed. Indeed, the control chicks of the preliminary experiment showed a significant bias in the direction that they turned. No such bias was shown by the KX-treated chicks of that experiment, or the untrained chicks from Chapter 7. In other words, the

behaviour of the untreated chicks was altered by the presence of the training stimulus, but not in a filial manner.

Chapter 6 has demonstrated that the effect of extending the sensitive period for imprinting is mediated through the NMDA receptor. In many ways the effect of antagonising the NMDA receptor 10, 20 or 40 h post-hatching may be viewed as one of retarding the normal neural development of the chick so that it behaves as if it is a much younger animal, thus allowing the treated chicks (KX, ket. × 2 and MK-801) to imprint on day 8 post-hatching. In the treated chicks, the imprinting that occurs on day 8 is not identical to that of day 2 chicks in that only the chicks that were trained on the hen imprinted. Otherwise it is remarkably similar, even to the extent that an increase in NMDA receptor binding occurs in the left IMHV of imprinted chicks. Further evidence of a retardation of brain development is provided by the poor performance for all treated chicks (KX, ketamine alone, xylazine alone) on the pebble floor visual discrimination task. The treated chicks performed as might have been expected of day 1-2 chicks. This may also be attributed to a general retardation effect of treatment with KX, ketamine alone or in this case, even xylazine treatment. The retardation effect on the pebble floor is thus not specific to the NMDA receptor.

The fact that the treatments had such a profound effect on the normal functioning of the nervous system is not difficult to reconcile with present knowledge given that the time that the treatment was effective was a period during which the developmental organisation of the brain was probably proceeding at a very rapid pace. In fact, 14-17 h post-hatching was traditionally thought of as being the most sensitive period for imprinting (Ramsay and Hess, 1954; Hess, 1959b). The sensitive period for imprinting probably possesses many of the same cellular characteristics of many other developing systems that are regulated in an experience-dependent manner. In numerous systems it is apparent that periods of synaptic plasticity and consolidation of synaptic connections coincide with an increase in excitatory amino acid receptors (Bode-Gruel and Singer, 1989; McCabe and Horn, 1991; Fox *et al.*, 1992).

In the chick, there is evidence of an increased function of the NMDA receptor during the first few days after hatching. Bradley *et al.* (1991b and see page 35) demonstrated that the probability of producing a potentiated synaptic response in the left IMHV peaks at around the time normally associated with the sensitive period for imprinting. The potentiated response is thought to be a form of LTP and is prevented by antagonists of the NMDA receptor (Bradley *et al.*, 1990). With reference to the results of Chapter 5 in which it was shown that KX treatment was only effective in extending the sensitive period when administered at 10, 20 or 40 h after hatching, it may be postulated that the treatment is acting on the NMDA receptor system during a particularly sensitive period of the development of this receptor system in the IMHV. The fact that the effect is shown over a week after the treatment was administered may be due to a modulation of the expression of the NMDA receptor when its endogenous expression is changing.

One theory for the regulation of synaptic plasticity in developing nervous systems involves the differential expression of NMDA receptor subtypes during development (Carmignoto and Vicini, 1992). In the visual system of the rat and cat, the duration of NMDA stimulated excitatory postsynaptic currents (EPSC) is longer in younger animals than it is in older animals (Carmignoto and Vicini, 1992; Hestrin, 1992). The EPSC is caused by an influx of Ca^{2+} into the cell. Thus a longer EPSC will promote the initiation of Ca^{2+} dependent synaptic changes. The change in duration of the EPSC provides a possible mechanism for the termination of the sensitive period for plasticity in the visual cortex.

There is good evidence for such a mechanism in the visual cortex of the cat. Carmignoto and Vicini (1992) demonstrated that the shortening of the EPSC was delayed by dark-rearing or application of tetrodotoxin; both of these procedures reduce the activity of the visual cortex, thus preventing activity dependent synaptic changes from occurring (Swindale, 1988; Reiter *et al.*, 1986). The evidence of Carmignoto and Vicini (1992) and Hestrin (1992) provides a cellular mechanism for an experience-dependent decline in the plasticity of a neural system. Both of these authors suggest that an

activity-dependent mechanism controls the expression of different subunits of the NMDA receptor.

The characteristics of the NMDA receptor (a hetero-oligomeric complex) is thought to be determined by the composition of homo-oligomeric subunits, of which two families (NR1 and NR2) have been identified (Moriyoshi, *et al.*, 1991; Monyer *et al.*, 1992). Up to five subunits combine to form an NMDA receptor complex, and the formulation of the sub-units determines the functional properties of the NMDA receptor. The presence of pharmacologically distinct NMDA receptors (e.g. Maragos *et al.*, 1988; Monaghan *et al.*, 1988; Monyer *et al.*, 1992; Kutsuwada *et al.*, 1992) is probably a reflection of the subunit composition. It has been proposed that throughout development different mRNA species coding for NMDA receptor subunits are present (Williams *et al.*, 1993). When expressed in *Xenopus* oocytes it has been demonstrated that the kinetics of the NMDA channel differ according to the composition of subunits. The differential expression of the subunits at different developmental periods thus provides a mechanism for the regulation of plasticity.

It is significant for our understanding of sensitive period phenomena, that changes in NMDA receptor subtypes occur throughout normal development, and that these changes can be modulated by activity-dependent processes (Carmignoto and Vicini, 1992; Hestrin, 1992). The sensitive period for imprinting may be viewed as an analogous process. Bateson (1991) believes that the limiting factor in the ability to imprint lies at the interface between the recognition or memory component and the executive component of the imprinting system. Here, the number of neurones accessing the executive system is thought to be limited and the ability to change the connections is also restricted. At the cellular level, the restriction of synaptic plasticity may be accounted for by a change in NMDA receptor subtype. Delaying the change in NMDA receptor subtype or promoting the expression of a subtype which is associated with synaptic plasticity would extend the sensitive period for imprinting.

Analogous to sensitive periods in the mammalian visual system, the sensitive period for imprinting may be extended by reducing the activity of the visual system (Moltz and

Stettner, 1961; Case and Graves, 1978). Carmignoto and Vicini (1992) have shown that dark rearing delays the developmental change in the EPSC associated with the NMDA receptor, and the inference is that there is continued expression of a developmentally young subtype of NMDA receptor. Treatment with KX, ket. × 2 or MK-801 may have promoted the expression of a developmentally young subtype of NMDA receptor, thus allowing chicks to imprint on day 8 post-hatching.

An up-regulation of NMDA receptors has been shown to occur in cultured cortical neurones after exposure to NMDA receptor antagonists (Williams *et al.*, 1992). Therefore, it is possible that an up-regulation of a subtype of NMDA receptors in the treated chicks could account for the extended sensitive period, although in Chapter 4 it was shown that the density of NMDA receptors in the IMHV of chicks that received no light exposure was lower in KX treated chicks compared to saline treated chicks. However, the density of NMDA receptors in the left IMHV of KX-treated chicks increased significantly compared to the KX-treated chicks that were left in the dark. Instead of increasing the number of NMDA receptors it must be postulated that treatment with KX at a time normally associated with experience dependent synaptic changes prevents a change in the subtype of NMDA receptor that is expressed. According to this hypothesis the ability to express a subtype of NMDA receptor that is sensitive to activity dependent events is preserved.

It is perhaps relevant that the increase in density of NMDA receptors in the left IMHV occurs in day 2 chicks between 6 and 8½ h after training (McCabe and Horn, 1991). The latency for the increase in NMDA receptor density could represent a period during which the expression of NMDA receptors is increasing. Johnston *et al.* (1993) demonstrated that a change in affinity of the glutamate receptor occurred in the left hyperstriatum ventrale of imprinted chicks. A significant advancement in our understanding of the factors controlling the sensitive period for imprinting would be achieved by characterising the subtypes of NMDA receptors present in the chick brain before and after imprinting.

Kavanagh *et al.* (1991) measured the affinity of [^{3}H]-MK-801 binding in the forebrain of young (11 days) and mature chickens. They found evidence for two populations of NMDA receptors based on the affinity of [^{3}H]-MK-801 binding. However, the relative distributions of the populations did not differ between the two ages. For the purposes of this discussion, the study by Kavanagh *et al.* (1991) is not ideal because they obtained their tissue from chicks much older than would be required in the investigation of experience-dependent receptor changes, and the tissue was also obtained from the whole forebrain. Nevertheless, there is evidence of two populations of NMDA receptors in the chick forebrain which deserves further investigation in the context of experience-dependent changes.

The proliferation of NMDA receptors in the nervous system leads one to suspect that they are generally involved in many forms of developmental plasticity. The results of the present study suggests that the sensitive period for imprinting may also be regulated by the development of the NMDA receptor system.

Another way of interpreting the results is to consider that antagonism of the NMDA receptor exerts a neuroprotective effect over the systems that underlie imprinting. An overproduction of neurones is a characteristic of vertebrate systems (Oppenheim, 1991). The ending of the sensitive period could be interpreted as a result of trimming inactive neurones or alternatively, their competing for neural space, which could arise, for example, by representations of different stimuli competing for limited access to the executive system (Bateson, 1981, 1991). The potential of the IMHV to fulfil an integrative role in information processing (Bradley *et al.*, 1985; Brown and Horn, 1992) suggests that other sensory systems may have the capacity to compete for control over the imprinting system. Although filial imprinting is largely considered to be controlled by visual stimuli there is ample evidence of at least a minor involvement of other systems, particularly the auditory system (van Kampen and Bolhuis, 1991; Bolhuis and van Kampen, 1992). The involvement of other systems may be enhanced if the visual system is relatively inactive. Indeed, this could have occurred in the present study where it was

shown that untreated dark-reared chicks lost the ability to visually imprint between days 2 and 4 post-hatching.

NMDA receptor activation has been shown to support neural growth (Pearch *et al.*, 1987; McDonald and Johnston, 1990). In the present study, the role of antagonists of NMDA receptors could be one of preventing the growth of neural connections, thereby reducing competition and extending the sensitive period for visual imprinting. However, this explanation fails to account for the fact that the treatment is maximally effective 10-40 h after hatching, and that imprinting is manifest on day 8. As such, the downfall of this type of explanation is similar to the explanation that the effect of extending the sensitive period is due to preventing an imprinting memory from forming (see page 126). Both of these explanations would be more plausible if the extended sensitive period was for a lesser time or if it resulted from a more prolonged treatment. This not being the case, the explanation that a modulation in the type of NMDA receptors that are expressed is the preferred explanation.

Another explanation to consider is that the treatments produced a reduction in visual learning ability of the chicks. If chicks have a reduced visual learning ability, it is possible that they are capable of forming an attachment on the most effective imprinting stimuli only. A deficit of this type may favour a chick forming an attachment at a later age than normal, if in the interim period it is not exposed to an effective imprinting stimulus. The dark-rearing period could be viewed as a time during which the chicks were exposed to sub-optimal imprinting stimuli. In the case of the treated animals, these sub-optimal imprinting stimuli may not have been sufficient for the chicks to form an attachment. In contrast, the sub-optimal stimuli may have been sufficient for the control chicks to form an attachment during the period of dark-rearing. On day 8 the treated chicks, which did not imprint during the dark-rearing period were able to imprint if they were exposed to a suitable imprinting stimulus. The control chicks may have already imprinted and thus were not able to form an attachment on day 8. The fact that the treated chicks will imprint on day 8 if they are exposed to the hen, but not the box, strengthens the argument that a functional lesion was created by the treatment. The box,

which possesses fewer arousing features than the hen may not be an efficacious imprinting stimuli to the treated chicks. On the other hand, the hen possesses visual qualities such as depth and texture and features such as the head and neck region which may make it a more powerful imprinting stimulus. Thus, the effect of the treatment may be to limit the stimuli that chicks will imprint upon; in other words the treatment may raise the threshold level of stimuli that chicks will respond to in a filial manner. Further strengthening the idea that the treatment produces a generalised deficit in visual learning is that the treated chicks were slower to learn on the pebble floor visual discrimination task. A deficit in visual and auditory learning has previously been shown to occur in chicks that have been treated with CXM or glutamate (Rogers et al., 1974, Rogers and Hambley, 1982). If the treatment did in fact limit the stimuli that chicks were able to imprint on, this effect should also be present in younger chicks. It would be interesting to determine if separate groups of day 2 chicks that had been treated at 10 h post-hatching could imprint on the box or the hen or if they, like the day 8 dark-reared chicks, were able to imprint on the hen only.

The identification of mechanisms underlying sensitive periods in neural development is not only important for our understanding of the ethological implications, but also shows that the chick continues to be a relevant model in the elucidation of these mechanisms. In the future, molecular neuroscience technology may develop to the stage where it might be possible to demonstrate the reinstatement of plasticity. For example in the chick, if the appropriate mRNA that promotes the expression of a subtype of NMDA receptor that is putatively associated with imprinting can be identified, it may be possible to induce the expression of this type of NMDA receptor in vivo and so allow imprinting after the sensitive period. In doing so the understanding of the mechanisms underlying the control of synaptic plasticity will be greatly enhanced.

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