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# Involvement of the lateral and dorsolateral amygdala in conditioned stimulus modality dependent two-way avoidance performance in rats

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**Abstract**. Post-lesion learning and performance of shuttle-box avoidance and subsequent transfer to two warning signals (CSs) of different modality were investigated in 27 rats subjected either to a sham lesion (Group NORM), electrolytic injuries of the lateral amygdaloid nucleus (Group LAT), or combined lesions of the amygdalostriatal transition area and dorsolateral amygdala (Group D-LAT). All groups were divided into two subgroups according to warning signal sequences. In the first subgroup (D-DN-N sequence) the subjects were initially trained with the visual CS (darkness - D), then transferred to the more salient visual and auditory compound CS (darkness and noise - DN), and finally to the auditory CS alone (noise - N). The opposite arrangement of the CSs (N-ND-D sequence) was employed in the second subgroup. A small interference with shuttle-box learning, and no transfer deficit were seen in Group LAT, whereas D-LAT rats showed dramatically slow and inconsistent acquisition of avoidance responding followed by rapid weakening of performance during the training. In contrast to controls, in both lesioned groups avoidance and intertrial responding (ITR) were independent of the CS modality changes. The results indicate differential involvement of the lateral, and also of the dorsolateral amygdala, and amygdalostriatal transition area in CS processing, as well as in the mechanisms related to consolidation of the associations created during avoidance training.

**Key words:** amygdala, amygdalostriatal transition area, shuttle-box, stimulus saliency, blocking, transfer, rat

## INTRODUCTION

The amygdaloid complex is the key forebrain structure for recognition and processing of unconditioned reinforcers and primary cues that occur in temporal proximity to the reinforcers (Weiskrantz 1956, Cormier 1981). Moreover, it is involved in the association of sensory information with appropriate emotional and motivational levels (Jones and Mishkin 1972, Werka and Zieliński 1978, Werka et al. 1978, Werka 1980, Cador et al. 1989). Functionally, the amygdala is located at the interface between the sensory systems involved in processing the conditioned fear stimuli, and the brain centers which are directly responsible for execution of appropriate emotional and motor responses (Gloor 1960, LeDoux 1987, Price et al. 1987, Quirk et al. 1995, Maren and Fanselow 1996).

The lateral nucleus of the amygdala (AL) and amygdalostriatal transition area (AST) are the main recipient structures in this interface system (LeDoux et al 1990a, Uwano et al. 1995). They receive direct and indirect auditory, visual and somatosensory afferents from the thalamus and/or the neocortex (Turner 1981, LeDoux et al. 1990b, 1991, Turner and Herkenham 1991, Mascagni et al. 1993). In rats, unimodal neurons responding to auditory or somatosensory stimuli, and also those responding to visual cues were found in the AL and AST (LeDoux et al. 1990b, Bordi and LeDoux 1992, Muramoto et al. 1993, Quirk et al. 1995, Uwano et al. 1995). Multimodal neurons that responded to both auditory and somatosensory stimuli were also found in these structures. These neurons are more frequently distributed in the AST (Uwano et al. 1995), and in contrast to the AL, they do not respond to the conditioned fear stimuli (Romanski et al. 1993, Uwano et al. 1995).

The lateral nucleus of the amygdala is involved in attention or arousal processes (Kaada et al. 1954) associated with biologically and motivationally important signals (Kaada et al. 1954, Brown and Buchwald 1973). Consistent with this, it participates in the formation of associations between neutral and noxious somatosensory stimuli during classical (Romanski et al. 1993) and instrumental conditioning (Pellegrino 1968, Grossman et al. 1975, Zieliński et al. 1983, Coover et al. 1992, Parent et al. 1995). The role of the AST in conditional defensive reactivity, and/or in the CS processing is not properly known. In our recent study (Werka and Zieliński 1997) we showed that the basolateral nucleus (ABL), one of the main targets of AL projections, is involved in transfer of warning signals of different modalities. It processes physical, arousing, and emotional attributes of the primary cues that are associated with noxious stimulation during instrumental conditioning. The focus of the present study is the role of the AST and AL, the first amygdaloid system that receives and transforms sensory information.

To delineate effects of the CS modality on shuttle-box learning and performance, an experimental design similar to that employed in our previous studies (Zieliński et al. 1991, Werka and Zieliński 1997) was used. This design is an efficient tool to explore mechanisms involved in processing and transfer of different physical and arousing properties of the warning signals, and to examine the blocking effect (Kamin 1969). Thus, the shuttle-box training was composed of three stages with the CSs which differed each other not only in modality, but also in discriminability from the background, saliency, and attentional properties (Bolles 1970). There is no single physical scale for comparing the relative intensities and reflexogenic properties of different stimulus modalities (for comments, see Mackintosh 1974). Therefore it was decided to pay more attention to "on line" comparisons related to the instrumental response modifications reflecting the consequent changes of the CS modality, rather than to more direct comparisons of CS modality effects, *per se*.

## METHODS

### Subjects

This experiment was conducted on 27 adult male Möll-Wistar rats, experimentally naive and weighing 300-350 g at the beginning of the experiment. The experimental procedures were done according to the rules established by the Nencki Institute Bioethics Committee. Rats of a given group were housed 4 or 5 *per* homecage (43 cm long, 25 cm wide, 18.5 cm high), containing food and water available *ad libitum*. Animals were trained once a day in the morning or early afternoon, in the same order and about the same time of day.

Rats were randomly assigned to three groups, a control group (Group NORM, 12 subjects) and two lesioned groups. In Group LAT (9 subjects) the lateral nucleus of the amygdala (AL), and in Group D-LAT (6 subjects) dorsal parts of AL and adjacent AST were bilaterally destroyed. Animals were anesthetized by intraperitoneal injections of 360 mg/kg of chloral hydrate (Sigma) dis-

solved in sterile saline (0.9% NaCl). Electrolytic lesions were produced by passing 1.0 mA anodal current for 15 s in Group LAT and 1.3 mA for 15 s in Group D-LAT. The electrode was made of 0.4 mm in diameter tungsten wire insulated except for 0.4 mm of its well-sharpened tip. The stereotaxic coordinates, from skull surface at bregma, for Group LAT were: 1.4 mm posterior, 4.9 mm lateral, and 8.4 mm ventral, and for Group D-LAT: 1.0 mm posterior, 4.6 mm lateral and 8.5 mm ventral. In Group NORM the skin on the head was incised and the bone trephined, but the electrode was not inserted into the brain.

After behavioral testing was completed, the animals were deeply anesthetized with an overdose of Nembutal. They were perfused transcardially with 0.9% saline followed by 10% formalin, and their brains were removed. Frozen brain sections (30 μm) were collected and subjected to Klüver and Nissl's technique. Microscopic inspection was performed to determine the location and the extent of the lesions.

### Apparatus and procedure

After 10 days of recovery from the surgery, habituation sessions and avoidance training in the shuttle-box began. The apparatus consisted of two identical opaque dark acrylic compartments (31 cm long, 18 cm wide, 29 cm high) separated by a wall containing a rectangular (7 cm wide, 10 cm high) opening at the level of the grid-floor. Each compartment was covered by a movable transparent acrylic ceiling and was illuminated by a 5 W lamp mounted centrally just below the ceiling. A 10-cm loudspeaker was mounted on the outside of each end wall 15 cm above the floor. Crossing through the opening was recorded by photocells mounted 4 cm to either side of the central partition, 5 cm above the floor level. The floor of each compartment was made of 16 stainless steel rods, 0.4 cm in diameter, and located parallel to the central partition 1.5 cm apart center to center. The shuttle-box apparatus was in a dark, sound-proof room. The subjects' behavior was watched on a TV monitor in an adjoining room in which equipment for automatic programming of the experiment and recording of data was located.

Prior to avoidance training rats were habituated to the situational cues of the apparatus. During each of two 10 min habituation sessions, the number of crossing through the central opening with the house light on was recorded for each subject. Avoidance training started on the next day. At the beginning of each training session, the rat was placed in the left compartment of the shuttle--box, close to and facing the end wall. After 20 s a trial started with the CS onset and, 5 s later, the scrambled DC shock of 1.6 mA intensity was given *via* the grid-floor (unconditioned stimulus, US). Crossing to the opposite compartment within the 5 s CS-US interval precluded the foot-shock, immediately terminated the CS and was scored as an avoidance response. Crossing after the US onset immediately coterminated the CS and US and was scored as an escape response. The maximal shock duration was 60 s. Each daily training session consisted of 50 trials. The intertrial intervals (ITI) were 15, 20, and 25 s and varied in a semi-random order. During the intertrial intervals subjects were permitted to move between the two compartments, so they could cross away from or back into the compartment in which they had previously been. The next trial always started in the compartment in which the subject was actually located.

### Group treatment

Prior to the two-way avoidance training each group of animals (NORM, LAT and D-LAT) was randomly divided into two subgroups according to CS modality sequences applied in three consecutive training stages. In the first subgroup composed of 4 subjects (Ss) from Group NORM, 5 Ss from Group LAT, and 3 Ss from Group D-LAT, the house-light termination (darkness - D) was used as a less salient CS during Stage 1, consisting of the four initial days of training (Sessions 1-4). During the next stage (Session 5) the darkness CS was given in a compound with a more salient stimulus: 70 dB (re: 20 $\mu N/m^2$) white noise (darkness and noise - DN). During Stage 3 consisting of the last four days (Sessions 6-9), the 70 dB noise CS (noise - N) was presented alone. Hence, in the first subgroup the D-DN-N sequence of CSs was applied. The opposite CSs sequence (N-ND-D) was applied in the second subgroup. It was composed of 8 Ss from Group NORM, 4 Ss from Group LAT, and 3 Ss from Group D-LAT. Each CS was applied in the compartment occupied by the rat, so that subjects moved away from the CS during training.

### Behavioral measures

Three main measures of the animals' behavior were recorded: the frequency of avoidance responses, the number of crossings from one compartment to the other

during habituation, and during pauses between trials (ITRs), as well as the latencies of instrumental responses measured to the nearest 0.01 s. The size of the class interval used for the distribution of latencies of instrumental responses was 0.5 s. For graphical constructions, the percentages (p) of avoidance responses were calculated for each 50 trial session, and for statistical analysis the percentages were transformed to arcsin values according to the formula: $arcsin\sqrt{p}$. For individual rats the run length was used as an index of the consistency of avoidance performance within each session and stage of training. Siegel (1956, p. 52) defines run as "a succession of identical symbols which are followed and preceded by different symbols or no symbols at all". In the present experiment the maximal number of consecutive avoidance responses in a given session was used as the run index.

## RESULTS

### Histology

The anatomical location of lesions (Fig. 1) was established with the aid of the Paxinos and Watson stereotaxic atlas (1997). The injuries in Group LAT bilaterally and symmetrically affected AL, mostly its ventrolateral division. They also invaded the adjacent external capsule, as well as a small medial fragment of the dorsal endopiriform nucleus. Moreover, minute bilateral lesions located in the dorsolateral part of ABL were seen in four rats. The lesions in Group D-LAT were slightly larger. In all subjects they bilaterally affected AST (Uwano et al. 1995), also called the fundus striati (Paxinos and Watson, 1982), close and adjacent to AL and to the central nucleus (AC). Also noted was invasion of the ventral region of the caudate putamen. There were injuries of the dorsolateral (capsular) fragment of AC, the medial division of AL, and in two animals, a small dorsal region of ABL.

### Visual vs. auditory warning signals: reciprocal transfer

The modality arousing properties, and the CS sequence differentially influenced individual measures of behavior in normal and lesioned rats, during consecutive training sessions. This was confirmed by a 2 (the CS sequence) x 3 (group) x 9 (session) ANOVA *for repeated* measures (Table I), that yielded significant group and session effects, as well as significant group x session and group x session x CS sequence interactions. Although there was no significant difference between the compared CS sequences for any of the measures, they were involved in most of double, and all triple factor interactions. Hence, it was decided to analyze more precisely the avoidance and intertrial responding modifications according to the consequent changes of the CS modality, independently for the two CS sequences.

### The D-DN-N sequence

*AVOIDANCE PERFORMANCE*

The acquisition of avoidance responses tended to be faster in Group LAT than in Groups NORM and D-LAT during the two initial sessions of Stage 1 (Fig. 2, upper part). However, in normal animals it was markedly in-

TABLE I

The *F* values of the main behavioral measures in all groups, sessions, and the CS sequences

| Source of variation | *df* | Percentage of avoidance | Rate of ITRs | Run index |
|---|---|---|---|---|
| Group (A) | 2,21 | 39.50*** | 4.86** | 47.20*** |
| Session (B) | 8,168 | 51.36*** | 4.90*** | 20.31*** |
| CS sequence (C) | 1,21 | 3.43 | 0.10 | 0.29 |
| A x B | 16,168 | 3.22*** | 3.03*** | 4.49*** |
| A x C | 2,21 | 3.48* | 2.21 | 4.14* |
| B x C | 8,168 | 7.09*** | 6.10*** | 8.48*** |
| A x B x C | 16,168 | 2.94*** | 5.48*** | 5.65*** |

*$P<0.05$; **$P<0.025$; ***$P<0.001$.

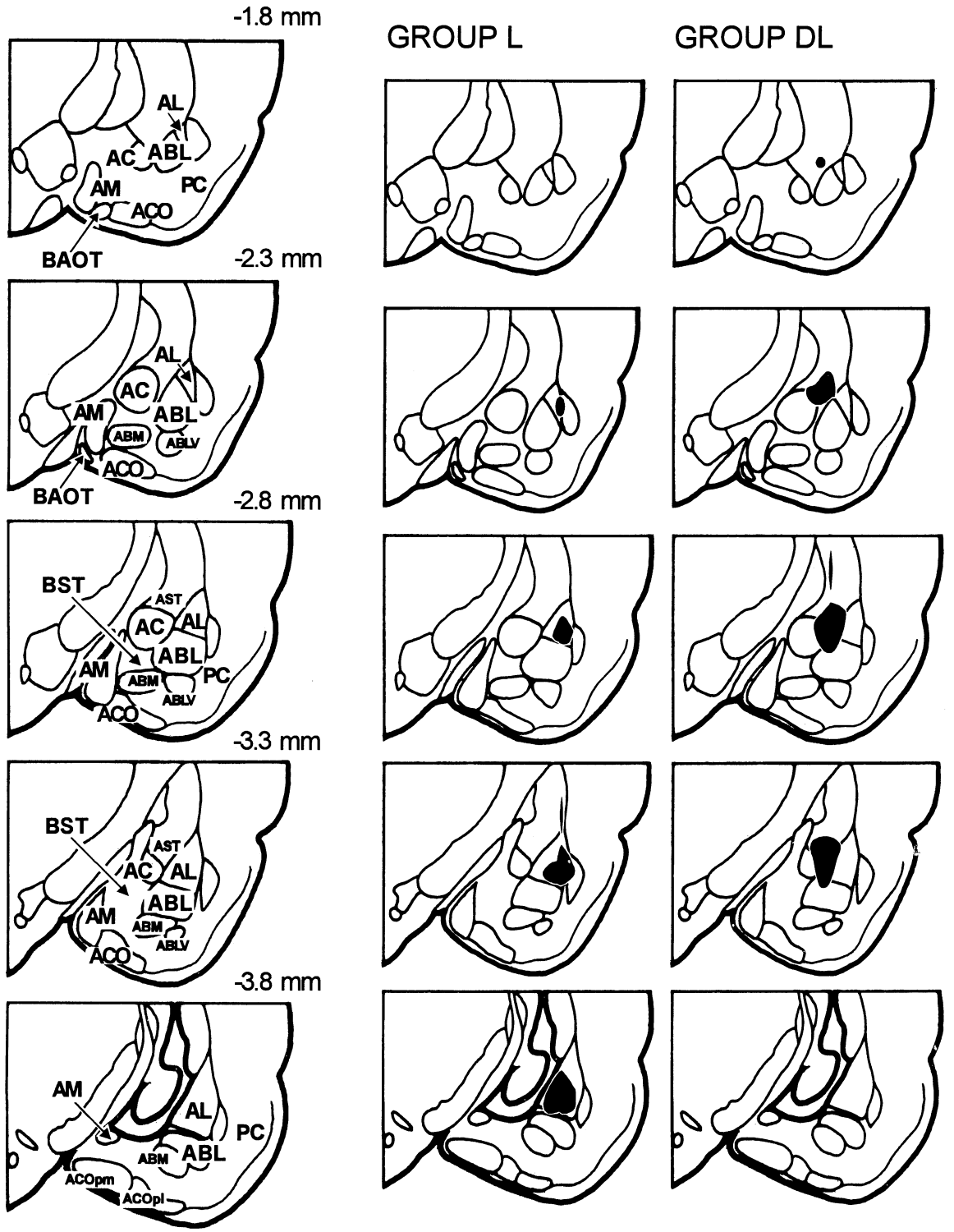


Fig. 1. Depiction of the range of the lesions. Left: schematic drawings of amygdaloid areas adopted from Paxinos and Watson's stereotaxic atlas (1997), showing forebrain coronal sections from rostral (1.8 mm behind bregma) to caudal (3.8 mm behind bregma) regions. Right: reconstruction of typical bilateral lesions for both hemispheres in the adequate areas, in randomly selected rats from groups LAT and D-LAT, one by one. BAOT, bed nucleus of the accessory olfactory tract; ABL, basolateral nucleus; ABLV, basolateral ventral nucleus; ABM, basomedial nucleus; BST, bed nucleus of the stria terminalis; AC, central nucleus; ACO, cortical nucleus; ACOpm, posteromedial cortical nucleus; ACOpl, posterolateral cortical nucleus; AL, lateral nucleus; AM, medial nucleus; PC, piriform cortex; AST, amygdalostriatal transition area.

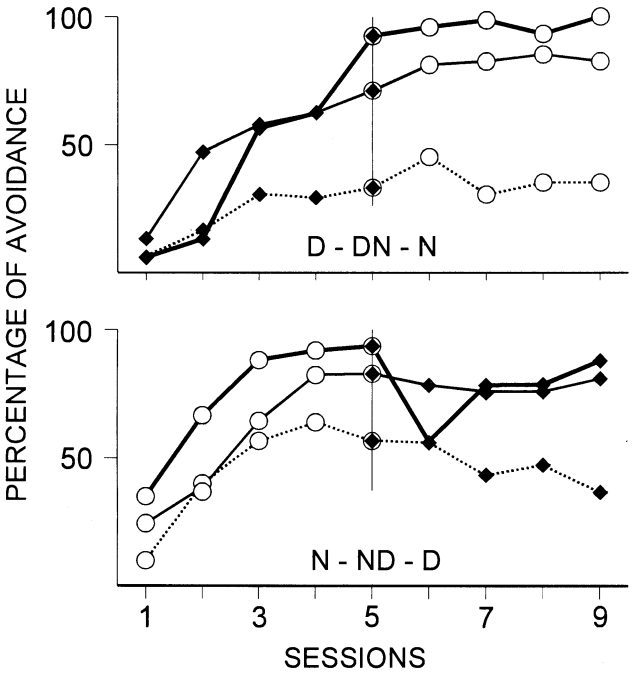


Fig. 2. Change of avoidance response in Groups: NORM (heavy line), LAT (thin line), and D-LAT (dotted line) during consecutive sessions of both CS sequences. Filled diamonds denote the darkness CS, circles denote the 70 dB white noise, filled diamonds in circles denote the compound CS consisting of darkness and 70 dB noise.

creased during Session 3, reaching almost the same level as Group LAT during the two last sessions of this stage. In contrast, the level of avoidance performance in Group D-LAT was low, even at the end of Stage 1. A 3 (group) x 9 (session) ANOVA for repeated measures of the avoidance responding rate in all sessions yielded significant effects of group, $F(2,9) = 17.17$, $P<0.001$; session, $F(8,72) = 32.72$, $P<0.001$; and a group x session interaction, $F(16,72) = 2.90$, $P<0.001$. Duncan tests for this interaction showed that there were no between group differences during Session 1. The avoidance performance of Group D-LAT was slower than in Groups NORM and LAT ($P<0.01$ or better) in Sessions 2, 3, and 4. No significant differences were found between NORM and LAT subjects during the analogous sessions.

In Group NORM introduction of the salient compound CS, the combined visual and auditory stimulus (DN), markedly enhanced avoidance responding during Session 5 (Stage 2), in contrast to Group LAT and D-LAT ($P's<0.001$). Only minor changes in avoidance performance were observed during the subsequent sessions of Stage 3 with the auditory CS alone. In Group LAT, changes of the CS modality did not disturb the slow, progressive increase of avoidance rate. Hence, there were no differences between NORM and LAT rats during the two final sessions of Stage 3. In Group D-LAT, essentially no change in avoidance performance was observed in Session 5 with the compound CS, and during the subsequent sessions with the auditory CS even a decreasing tendency was noted. The level of avoidance performance in Group D-LAT during the last experimental session was half that of Groups NORM and LAT. The Duncan tests showed that D-LAT rats significantly differed from the normal and AL lesioned subjects ($P<0.025$ or better) during all sessions of Stages 2 and 3.

*CONSISTENCY OF AVOIDANCE PERFORMANCE*

The group mean maximum run lengths for each session are presented in the upper part of Fig. 3. This measure was similarly small in Groups NORM and LAT, but gradually increased during the subsequent sessions of Stage 1. In Group NORM the introduction of the salient auditory stimulus in Session 5 (compound CS) rapidly enhanced a value of the index, and that was not disturbed by further transfer to the auditory CS alone during Stage 3.

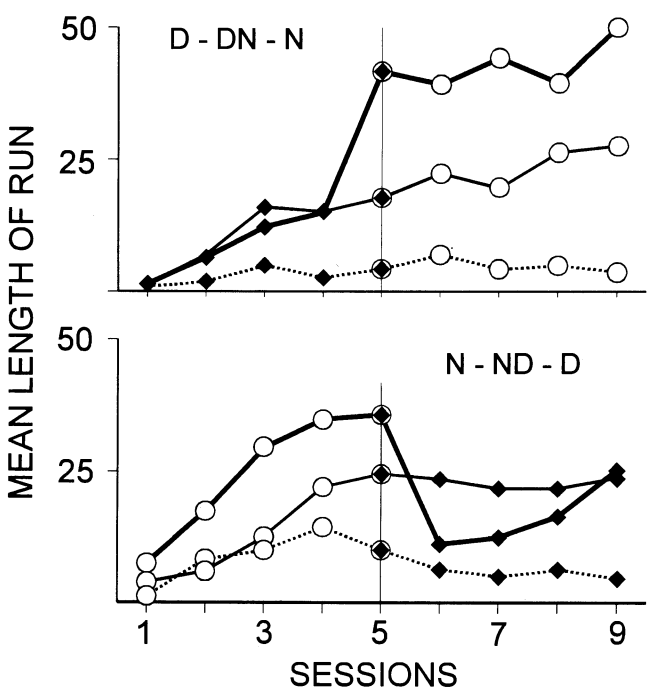


Fig. 3. Change of the run index during consecutive sessions of both CS sequences. Group denotations and symbols as in Fig. 2.

In contrast to normal animals, the consistency of avoidance performance in Group LAT slowly, but systematically increased during the subsequent stages, with the run duration being independent of the changes in saliency of the CS. However, the index did not reach the level of Group NORM during Stage 3. In Group D-LAT very short sequences of consecutive avoidances were observed in all stages of the experiment. A 3 (group) x 9 (session) ANOVA for repeated measures of the run index revealed significant effects of group, $F(2,9) = 32.51$, $P<0.001$; session, $F(8,72) = 28.78$, $P<0.001$; and a group x session interaction, $F(16,72) = 8.86$, $P<0.001$.

*INTERTRIAL RESPONDING*

Mean frequency of crossing between compartments during habituation and ITRs during training sessions for all groups are presented in the upper part of Fig. 4. The comparison of crossing rate during habituation sessions with the frequency of the intertrial responses (ITRs) on the first session of avoidance training showed no between--group differences. A 3 (group) x 3 (session) ANOVA for repeated measures yielded only a significant effect of session, $F(2,18) = 8.87$, $P<0.001$, and further Duncan tests showed ($P<0.025$) that the effect was caused by the decrease of crossing frequency during the second habituation session.

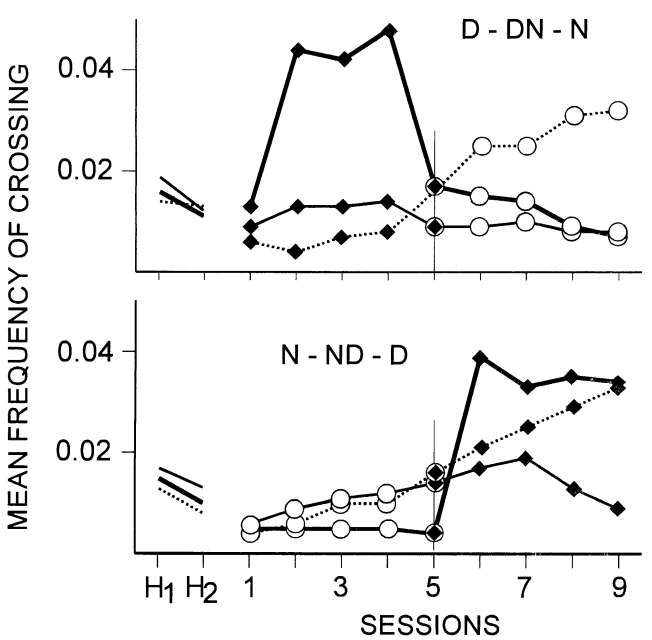


Fig. 4. Change of crossing frequency during habituation ($H_1$ and $H_2$), and training sessions of both CS sequences. Group denotations and symbols as in Fig. 2.

In normal animals, the ITR rate was markedly enhanced by the visual CS during the Stage 1. Introduction of the salient compound stimulus during Session 5, and further training with the auditory CS presented alone clearly decreased intertrial responding. That CS modality dependent ITR rate was not observed in Group LAT, where a relatively low level of responding was maintained during all three stages of training. In Group D-LAT a low ITR frequency was observed during Stage 1, but the compound and auditory CSs presented during Stages 2 and 3, provoked a systematic increase in ITRs toward the end of training. Those between-group differences in the dynamics of ITR responding were corroborated by a 3 (group) x 9 (session) ANOVA, which showed only a significant group x session interaction, $F(16,72) = 4.02$, $P<0.001$.

*RESPONSE LATENCIES*

The CS modality also influenced the latencies of the instrumental responses. These data were analyzed by separate between- and within-group comparisons of the cumulative frequency distributions of avoidance and escape responses in consecutive 0.5-s intervals after the CS onset. Figure 5 (upper part) presents within-group comparison of the distributions for the last session with the visual CS (Session 4), the session with the compound CS (Session 5), the first (Session 6) and the last (Session 9) sessions with the auditory CS. To evaluate for each group the pair-wise changes of response latency between sessions, the magnitudes of the maximum vertical distance ($D_{max}$) between the cumulative distributions were analyzed by the Kolmogorov-Smirnov two-sample test (Table II, left-hand side). In all groups clear acceleration of shuttle-box responding was caused by the introduction of the salient compound CS during Session 5. However, in contrast to rather small and inconsistent changes observed in the lesioned groups during Stage 3, in Group NORM the auditory CS presented in Session 6 decreased responding at the early part of the CS-US interval. That persisted to the end of the training, and was probably related to the inhibition of delay effect.

The Kolmogorov-Smirnov test for comparing the cumulative latency distributions of the experimental groups showed that in all stages of training the shuttle--box responding in Group NORM was faster than in lesioned groups. Groups LAT and D-LAT also differed

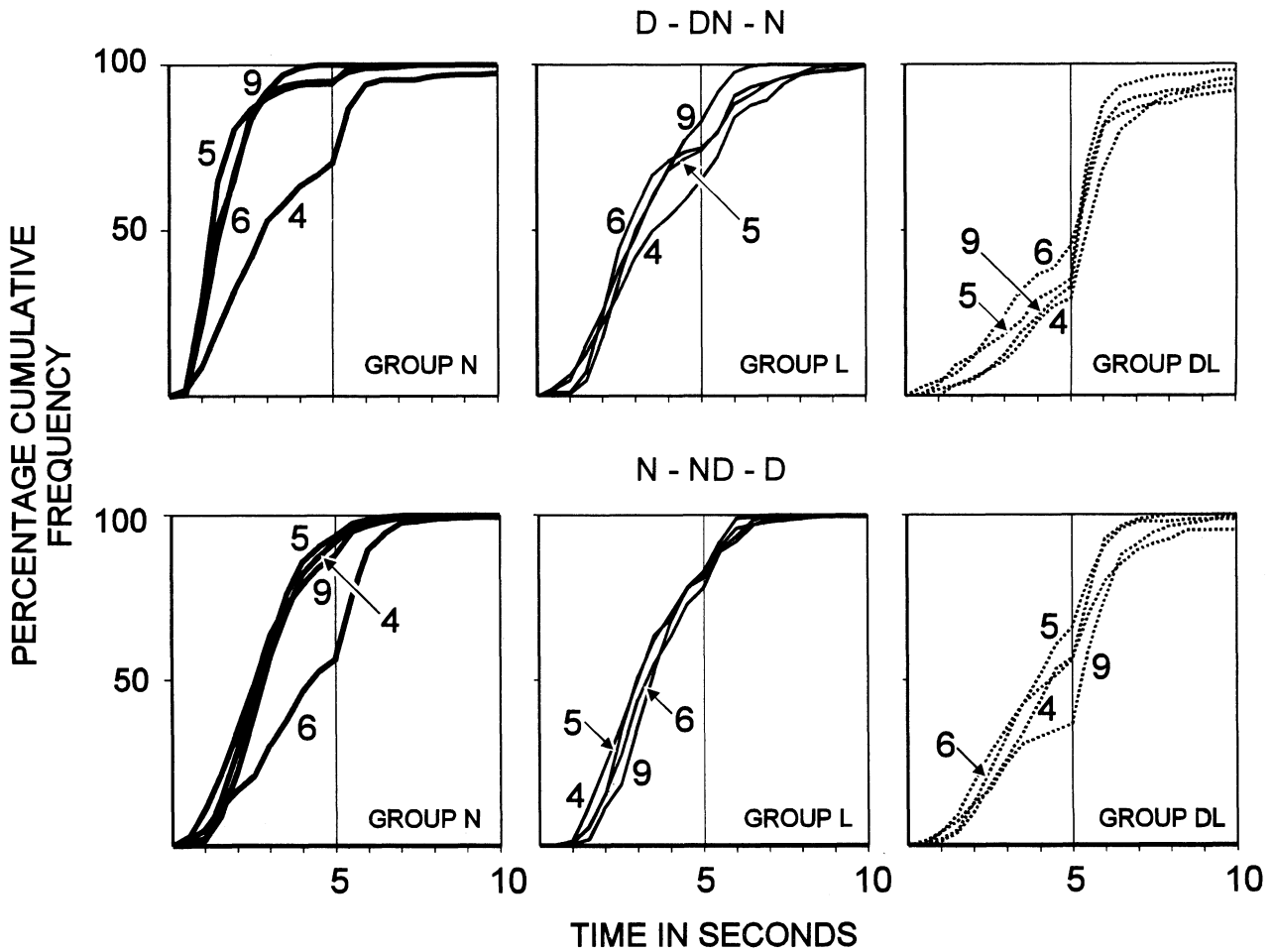


Fig. 5. Cumulative frequency distribution of instrumental response latencies during Sessions 4, 5, 6 and 9 of both CS sequences. Group denotations as in Fig. 2.

throughout training, reflecting the deterioration of responding in Group D-LAT.

### The N-ND-D sequence

*AVOIDANCE PERFORMANCE*

The percentages of avoidance responding for all groups are presented in the bottom part of Fig. 2. During Stage 1 the fastest acquisition was observed in normal rats. A plateau level was reached in this group during Session 3, and remained unchanged during Stage 2, when the auditory CS was presented in compound with the less salient visual CS. The avoidance performance was clearly disturbed in Group NORM early in Session 6 of Stage 3, when less salient visual CS was given alone, but systematically recovered during the subsequent sessions of this stage. In Group LAT acquisition of the two-way avoidance responses was slower in comparison to Group NORM. The LAT rats reached a plateau level of performance during Session 4 of Stage 1, and retained that level almost unchanged to the end of training. In contrast to normal animals, in Group LAT transfer to the less salient visual CS did not disturb avoidance responding, which reached much the same level of performance as Group NORM during the final Sessions 7-9 of Stage 3. The lowest two-way avoidance performance during Stage 1 was revealed in Group D-LAT. In these animals the highest level of the avoidance responding was seen during Session 4, than gradually decreased toward the end of training, reaching in Session 9 almost as low a value as in the analogous session of the D-DN-N sequence.

A 3 (group) x 9 (session) ANOVA for repeated measures of these data yielded significant effects of group, $F(2,12) = 20.20$, $P<0.001$, session, $F(8,96) =$

24.11, $P<0.001$, and group x session interaction, $F(16,96) = 2.77$, $P<0.001$. Duncan tests for this interaction showed that the rate of avoidance responding in NORM rats was similar to LAT rats during Sessions 1 and 4 (Stage 1), Session 5 (Stage 2), and Sessions 7, 8, and 9 (Stage 3). The differences between these groups reached only $P's<0.05$ level during Sessions 3 and 4, they were, however, more marked ($P<0.001$) during Session 6. The avoidance performance in Groups NORM and LAT significantly differed from Group D-LAT ($P's<0.01$ or better) during all sessions, excluding Sessions 2 when no difference was found between LAT and D-LAT rats, and Session 6 when the level of avoidance performance in Group NORM was similar to Group D-LAT.

*CONSISTENCY OF AVOIDANCE PERFORMANCE*

Between-group differences and within-group trends of the run index are presented in the Fig. 3, bottom part. In control animals the salient auditory CS provoked fast enhancement of the index during Stage 1. Introduction of the compound CS in Session 5 (Stage 2) didn't change this consistent avoidance performance, but the less salient visual CS in the Stage 3 resulted in a marked decrease of the length of runs in Group NORM. Group mean value of the index in Session 6 was almost as low as that noted during the first training session. In the subsequent sessions of Stage 3 it increased, but did not reach the level seen in Stage 2.

A much slower improvement in the stability of avoidance performance was observed in lesioned animals during Stage 1. The run index did not differ between Groups LAT and D-LAT during the initial three sessions of Stage 1. However, in Session 4 an increase of the index was seen in Group LAT. Also, some improvement appeared in Session 5, and then the level of the run index remained relatively stable during the subsequent Stage 2 with the salient compound CS, and also during Sessions 5-9 (Stage 3) with the less salient visual stimulus. The length of runs was much the same in Groups LAT and NORM during the last training session. A different tendency was noted in Group D-LAT, where only a small increase in avoidance consistency was seen during Stage 1. Moreover, the value of the index gradually decreased from Session 4, and reached dramatically low levels during Stage 3 .

The between-group differences were clearly confirmed by a 3 (group) x 9 (session) ANOVA. It showed significant effects of group, $F(2,12) = 14.75$, $P<0.001$; session, $F(8,96) = 7.35$, $P<0.001$; and group x session interaction, $F(16,96) = 2.96$, $P<0.001$.

*INTERTRIAL RESPONDING*

The normal and lesioned rats showed a tendency to reduce the frequency of crossing from one compartment to the other within two habituation sessions (bottom part of Fig. 3). The introduction of training with the salient auditory CS caused a further decrease of intertrial responding during the initial session of the Stage 1. This was confirmed by 3 (group) x 3 (session) ANOVA for repeated measures, which yielded a significant effect of session, $F(2,24) = 33.42$, $P<0.001$. Duncan tests showed that the differences in the rate of ITRs in each of the three sessions were significant ($P<0.001$).

In Group NORM a very low ITR rate was observed during Stage 1 which was maintained up to the end of Session 5 (Stage 2) with salient compound CS, whereas the less salient visual CS, presented during Sessions 6-9 (Stage 3), provoked a marked enhancement of intertrial responding. The animals from Group LAT behaved as though embedded CS modality was never changed during the training. A slow but systematic increase in ITR rate in Sessions 1-7, however, collapsed during subsequent sessions. An increase in intertrial responding was also noted in Group D-LAT. In this group ITR rate was almost the same as in Group NORM during the last experimental session. These between-group differences in ITR responding were confirmed by a 3 (group) x 9 (session) ANOVA, which yielded a group x session interaction, $F(16,72) = 4.02$, $P<0.001$, without any other significant effects.

*RESPONSE LATENCIES*

The bottom part of Fig. 5 presents within-group cumulative relative frequency distributions of response latencies emitted in the last session with the auditory CS (Session 4), Session 5 with the compound CS, the first (Session 6) and the last (Session 9) sessions with the visual CS. The magnitudes of the maximum vertical distance ($D_{max}$) between cumulative distributions, and results of the Kolmogorov-Smirnov two-sample tests for each group are presented in Table II (right-hand side). The results showed that the change from the salient compound to the less salient visual CSs markedly prolonged shuttle-box responding in Group NORM, which clearly

TABLE II

Within group comparisons of changes in the cumulative distribution of response latencies emitted during the last session with the visual CS (Session 4), in Session 5 with compound CS, the first (Session 6) and the last session (Session 9) with the auditory CS (Session 6). S4<S5 for example, denotes that the proportion of responses emitted with latencies shorter than the point of Dmax was greater in Session 5 than in Session 4. Size of samples compared were: in D-DN-N sequence - 200 in Group NORM, 250 in Group LAT, and 150 in Group D-LAT, in N-ND-N sequence - 400 in Group NORM, 200 in Group LAT, and 150 in Group D-LAT

| | D-DN-N sequence | | | N-ND-D sequence | | |
|---|---|---|---|---|---|---|
| Group | Change | Dmax | s | Change | Dmax | s |
| NORM | S4<S5 | 48.5**** | 2.0 | S4<S5 | 6.5 | 2.0 |
| | S5>S6 | 17.5*** | 1.5 | S5>S6 | 39.2**** | 4.0 |
| | S6<S9 | 5.0 | 4.5 | S6<S9 | 34.5**** | 3.5 |
| LAT | S4<S5 | 12.4** | 4.5 | S4<S5 | 4.6 | 2.0 |
| | S5<S6 | 8.4 | 1.5 | S5>S6 | 7.0 | 2.5 |
| | S6>S9 | 9.2 | 2.5 | S6>S9 | 9.0 | 2.5 |
| D-LAT | S4<S5 | 15.3* | 5.5 | S4<S5 | 10.7 | 5.5 |
| | S5<S6 | 12.7 | 3.5 | S5>S6 | 9.3 | 4.5 |
| | S6>S9 | 9.3 | 3.5 | S6>S9 | 19.3*** | 5.0 |

*$P$<0.05; **$P$<0.025; ***$P$<0.01; ****$P$<0.001.

recovered toward the last experimental Session 9. Changing the modality of the CS had negligible effect on the latency distributions in Groups LAT and D-LAT. However, D-LAT rats showed pronounced prolongation of the shuttle-box responding during Session 9, especially in latencies located in the second half of the CS-US interval.

The Kolmogorov-Smirnov test for comparisons of between-group cumulative latency distributions revealed that in all stages the responding in Group NORM was faster than in both lesioned groups, except in Session 6 when no difference between Groups NORM and D-LAT was seen. On the other hand, faster instrumental responding was also observed in Group LAT in comparison to Group D-LAT, throughout the training.

## DISCUSSION

The main result of the study was almost total behavioral insensitivity to the CS salience during the transfer of the warning signal in the lesioned groups, contrary to normal animals. Learning of the avoidance response, especially to the salient auditory CS, tended to be slightly slower and less consistent in Group LAT in comparison to normal subjects, as shown by the run index. However, all measures of behavior for LAT rats improved toward the end of training. The avoidance acquisition was dramatically impaired in AST injured subjects, and no improvement was seen during the subsequent stages of the training.

A discussion of the results for both lesioned groups requires previous consideration of some hypotheses regarding learning mechanisms and stimulus processing in normal animals. According to Rescorla and Wagner (1972) the "salience" is the parameter of the stimulus, which determines the rate of conditioning to that stimulus. In an aversive experimental context the salient stimulus can provoke unconditioned fear because of its intrinsic fear-eliciting properties (Walker and Davis 1997). Several theories of conditioning assume that different CSs (Kamin 1968, 1969, Perce and Hall 1980), USs (Rescorla and Wagner 1972) or both CSs and USs (Wagner 1978) may command different initial probabilities of attention (Zeaman and House 1963). Perkins

(1953) and Logan (1954) pointed out that more intense or salient CSs enhance conditioning because they are better discriminated from the never reinforced background stimuli. The results of NORM rats are consistent with this assumption. The salient auditory CS provoked rapid and more consistent avoidance acquisition and decreased ITR rate, contrary to the less salient visual CS. Moreover, the auditory CS overshadowed the visual CS in Stage 2 (Pavlov 1927, Kamin 1969, Mackintosh 1971), because the associative strength (Rescorla and Wagner 1972) of the auditory CS was driven close to asymptote either during the preceding Stage 1, or in the trials with the compound CS.

During Stage 3 Kamin's blocking effect (Kamin 1969) was either observed or not in normal rats, depending on the CSs sequence employed in the preceding stages. Some problems arise in explaining this result on the basis of most contemporary stimuli processing theories (see Mackintosh 1974, Dickinson 1980, for review). Several CS- and US-processing approaches (Kamin 1968, 1969, Rescorla and Wagner 1972, Wagner 1978, Pierce and Hall 1980) have been successful in accounting for mechanisms of blocking and unblocking in the classical conditioning procedures. They were especially satisfactory for interpretation of the effects caused by changes of the US number and/or US magnitude (Holland 1984, 1988, Galagher and Holland 1992). However, these theories have not been able to explain unblocking of the avoidance performance, when only the stimulus modality (from visual to auditory CS) was changed.

A response-contingent reinforcement is supposed to be an important feedback stimulus in instrumental learning (Brener and Hothersall 1966, Taub and Berman 1969, Bolles 1979), especially during the early trials. Since fast and consistent avoidance responding is evoked by the salient CS during the very early period of training, the instrumental response acquires strong reinforcing properties, and increases the associative strength of this CS. This effect occurs whenever the salient CS is given. Therefore in the present study the unblocking effect was observed when D-DN-N sequence of stimuli was applied. The less salient CS exerted an opposite effect, the more so as it was poorly discriminated from the background stimuli, reflecting the marked increase of ITR rate. This interpretation is compatible with many earlier findings which showed that blocking was readily seen if subjects were pretrained with a more salient CS than the new or redundant signals (Mackintosh 1965, Chase 1968). According to some hypotheses, the animals responding reveals a decision criterion appropriate to the CS intensity (Green et al. 1957, Swets et al. 1961, Dember and Warm 1979).

Rats with the AL lesion were almost totally insensitive to any change of the CS modality and behaved as if no transfer of the warning signal occurred. In other words, these animals behaved as though they were unable to utilize subtle physical and arousing properties (saliency) of signals that become the CSs during conditioning of the instrumental defensive response. The avoidance performance and its consistency were not affected by the CS transfer. Hence, in Group LAT the blocking effect was neither observed when the less salient CS was followed by the more salient one (D-DN-N sequence), nor appeared when the more salient CS was changed to the less salient signal (N-ND-D sequence). Only the level of the intertrial responding tended to be slightly increased by the less salient visual signals but it was still rather low, and never exceeded the level of crossings during the habituation sessions.

Because the AL lesioned rats were not able to utilize reflexogenic properties of the CSs, there were no differences in the associative strength related to the stimuli of different saliency. Long latency avoidance responses were insufficient feedback stimuli to modulate the conditioning strength of the particular CS. On the other hand, motivational significance of the CSs was not profoundly affected, since AL injured rats were able to improve the avoidance performance toward the end of training. The escape response latencies in AL lesioned rats were slightly prolonged, in comparison to normal subjects. This would suggest that processing of the US was affected, and the strength of the US expectation was diminished (Rescorla and Wagner 1972), resulting in decrement of the CS-fear associations. Consistently, it was demonstrated that the AL lesion interfered with the acquisition or expression of conditioned fear (Campeau et al. 1992, Sananes and Davis 1992, Davis at al. 1993 and for review, see Davies 1992, LeDoux 1992). However, postlesion reduction of fear should be rejected, since decrease of ITR rate was seen in LAT rats. Moreover, changes neither in the orienting responses, nor in expression of the unconditioned reactions related to fear and pain were observed after AL lesion in others studies (LeDoux et al. 1990a, Romanski and LeDoux 1992, Miscerendino et al. 1990, Werka 1994).

It is unreasonable to entirely ignore a possibility that the AL lesion affected the US processing and US related

associations. However, it might also be possible that the lesion effects were due to a failure of the retrieval process. In spite of an existing CS-US association, the CS might no longer be capable of arousing the short-term memory of the US, or some of its aversive properties (for comments, see Bolles 1979, Bolles and Fanselow 1980). Moreover, this might also be true for the contextual cues. These hypotheses are compatible with the existence of amygdalo-hippocampal and amygdalo-entorhinal cortex circuities involved in memory, acquisition and expression of context fear (Teyler and DiScenna 1985, Zola-Morgan and Squire 1990, Zola-Morgan et al. 1991, Izquierdo and Medina 1997, McNish et al. 1997, Winocur 1997).

The AL is assumed to be one of the main structures involved in the CS discrimination and differentiation functions, as well as in the mechanisms of transfer and blocking effects. In other words, it plays a significant role in the mechanisms of selective attention and formation of associations between emotional properties of the particular CS and the adequate instrumental responding. Consistently, in our earlier study (Zieliński et al. 1983) we showed that cats with a lesion of AL were more resistant than the normal animals to the change of the instrumental responses (avoidance and/or escape), according to contingencies used in different stages of the experiment. Lesioned subjects were able to learn, extinguish and to retrieve the responding which was previously acquired, but any change in the experimental procedure did not cause as fast modification of behavior, as observed in normal animals. A function of the AL seems to be very similar to that of the adjacent basolateral group of neurons. This has been corroborated by the results of our recent study (Werka and Zieliński 1997) which showed similar effects of ABL injury on shuttle-box performance, two-way avoidance transfer, and on the blocking phenomenon. Sananes and Davis (1992) revealed that lesions restricted to AL produced as severe deficits as joint impairment of the AL and ABL. This is not surprising, considering the close anatomic relations of these structures (Savander 1997), and a large number of neurochemical and functional similarities (Muramoto et al. 1993, Romanski et al. 1993, Uwano et al. 1995, and for review see: LeDoux 1992, McDonald 1992, Davis 1992, 1994, Roberts 1992).

Particularly dramatic effects were seen after AST lesions. Learning and performance of the shuttle-box responding were worse in Group D-LAT than in other groups. No blocking effect was observed when the D-DN-N sequence of the CSs was applied. It was also unclear whether a slight decrease in the avoidance performance after the transfer to the less salient visual CS (N-ND-D sequence) might be recognized as the blocking effect, since very poor conditioning was conducted by the salient CS during the previous Stage 1. Hence, the behavior of D-LAT rats did not seem to be influenced by the CS changes and/or by the specific modality and saliency of the CS.

Somatosensory and visceral information reaching to the hypothalamus and other limbic structures is integrated and modulated in the ventral striatum (VS) (Krettek and Price 1978, Turner and Zimmer 1984, Kita and Kitai 1990, LeDoux et al. 1991, Turner and Herkenham 1991, Mascagni et al. 1993, Uwano et al. 1995, Burstein 1996). Many neurons in AST respond to one particular or to many stimulus modalities, including pain (Uwano et al. 1995). Consistently, VS structures and the ventrolateral periaqueductal gray (PAG) seem to be especially important in the processing of noxious stimuli and in coordinating the emotional reaction to these events (Bandler and Keay 1996). The central and basolateral amygdala, as well as the hippocampus, which evaluate the biological and motivational relevance of various CSs, USs and contextual cues (Phillips and LeDoux 1992, and for review, see LeDoux 1991, 1996), exert their influence on VS (Dafny et al. 1975, Russchen and Price 1984, Alheid and Heimer 1988, Kita and Kitai 1990, Everitt and Robbins 1992), by fibers traveling through AST, among other regions (Bernard et al. 1996). The connections between the amygdala and ventral striatum are critical for processes whereby cues acquire reinforcing value (Rolls 1994). In addition, the connections between the basolateral amygdala and ventral striatum is important for the evaluation of the CSs emotional significance in associative learning, independent of the central amygdala involvement. It was supposed that the AST lesion impaired some of these fibers, and therefore it interfered with the processes integrating somatosensory information with fear.

Consistently, the results of the AST lesion resembled some effects of the AL lesion, and/or the effects of ABL or AC injuries, which we recently reported (for comparison see Werka and Zieliński 1997). In fact, the lesion in Group D-LAT included adjacent fragments of AL, AC and the dorsomedial fragment of ABL. Most probably, they impaired reciprocal connections between the medial division of AL and capsular division of AC (Pitkänen et al. 1995, Savander 1997). However, Group

D-LAT seemed to be slightly more sensitive to any change of the CS modality and saliency than animals with AL or ABL lesions, in spite of its unquestionably decreased reactivity. Learning and performance of the avoidance and escape responses were more profoundly and persistently disturbed in D-LAT rats in comparison to rats with the AC lesion.

The striatum is claimed to be a "limbic-motor interface" (Mogenson et al. 1984). The amygdala - ventral striatum circuit is supposed to be involved in the voluntary control of instrumental actions related to fear and pain, although the specific mechanisms do not seem to be clear (Everitt et al. 1989, Everitt and Robbins 1992, LeDoux 1996, Shapovalova 1997). It was found that AST lesioned animals were unable to acquire and to maintain two-way avoidance responding throughout training. The latencies of the instrumental responses were prolonged, especially during the final experimental sessions. Moreover, an increase of the ITR rate in Stages 2 and 3 might be explained as a cumulated effect of difficulty in retaining the attained instrumental responding. Two related mechanisms might contribute to these effects. First, the avoidance and escape responses lost their feed-back reinforcing properties in AST lesioned rats. Consistently, the caudate-putamen, VS and AST are involved in the control of the stimulus-reward or stimulus--punishment related processes (Mogenson et al. 1980, 1984, Cador et al. 1989, Everitt et al. 1989, Everitt and Robbins 1992, Packard and McGaugh 1992, Heimer et al. 1995, Izquierdo and Medina 1997). The VS is suggested to be a site at which affective processes controlled by the central and basolateral amygdala may gain access to subcortical centers of the motor system (for review, see Alheid and Heimer 1996, Groenewegen et al. 1991, 1996, Nieuwenhuys 1996). Thereby they influence actions of several midbrain structures, especially the ventrolateral PAG (Bandler and Keay 1996, Groenewegen et al. 1996), which are involved in passive emotional coping (Bohus et al. 1996, Bandler and Keay 1996) and voluntary control of instrumental responding related to fear and pain (Everitt and Robbins 1992, LeDoux 1996).

Second, AST lesion impaired the ability of an emotional state evoked by the fear and pain producing stimuli to continue over a long period of time, therefore it affected the instrumental performance and the response consolidation processes. This momentum effect may be based upon the projections from the limbic structures to the VS (Saper 1996) or the spino-parabrachio-amygdaloid pathway, passing by AST (Bernard et al. 1996). The striatal involvement in memory mechanisms and postacquisitional consolidation (see Ferreira et al. 1992) of the aversively-motivated motor behavior has been discussed by many authors (Prado-Alcalá et al. 1975, Prado-Alcalá and Cobos-Zapiain 1979, Polgar et al. 1981, Prado-Alcalá 1985, Pérez-Ruiz and Prado-Alcalá 1989). This complex structure seems to play an important role during relatively short training of the instrumental response, especially in the early stages of learning. However, after an overtraining the memory functions of the striatum are relayed to other neural structures (Pérez-Ruiz and Prado--Alcalá 1989), possibly to cortical areas located in the entorhinal, parietal, frontal, and occipital cortex (Izquierdo and Medina 1997). Overtraining was not involved in the experimental procedure applied in the present study. Moreover, the present results are not enough to state that AST is directly engaged in the storage of emotional events. However, it should be realized that the emotional significance of sensory stimuli and reinforcing properties of the acquired instrumental action depends on past experience. Hence, animals compare them with information stored in memory, before an appropriate responding. It is assumed that the damage to this structure prevents the expression of the memory related to reinforcing properties of the avoidance reaction, thereby interfering with mechanisms of instrumental response consolidation.

The amygdaloid complex, the hippocampal formation, ventral striatum, and areas of transition between these structures form an important part of the "emotional motor system" (for review, see Alheid and Heimer 1996, Nieuwenhuys 1996). A precise segregation of functions within this system is regarded as one of its main heuristic goals. The emotional evaluation of visceral and somatosensory information, the autonomic, endocrine, and memory functions, as well as the mechanisms controlling a voluntary motor behavior are not only elaborated, but they are also integrated in the system. It is concluded that the lateral and basolateral amygdala are involved in processes which imply the evaluation of emotionally significant external stimuli. On the other hand, the AC and the dorsolateral amygdala including the AST are mostly involved in the execution and consolidation mechanisms of instrumental goal directed defensive behaviors.

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## REFERENCES

Alheid G.F., Heimer L. (1988) New perspectives in basal forebrain organization of special relevance for neuropsychiatric disorders: the striatopallidal, amygdaloid and corticopetal components of the substantia innominata. Neuroscience 27: 1-39.

Alheid G.F., Heimer L. (1996) Theories of basal forebrain organization and the "emotional motor system". In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 461-484.

Bandler R., Keay K.A. (1996) Columnar organization in the midbrain periaqueductal gray and the integration of emotional expression. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 286-300.

Bernard J.F, Bester H., Besson J.M. (1996) Involvement of the spino-parabrachio-amygdaloid and -hypothalamic pathways in the autonomic and affective emotional aspects of pain. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 243-255.

Bohus B., Koolhaas J.M., Luiten P.G.M., Korte S.M., Roozendaal B., Wiersma A. (1996) The neurobiology of the central nucleus of the amygdala in relation to neuroendocrine and autonomic outflow. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 447-460.

Bolles R.C. (1970) Species-specific defense reactions and avoidance learning. Psychol. Rev. 77: 32-48.

Bolles R.C. (1979) Learning theory. 2nd ed. Holt, Rinehart and Winston, New York, p. 192-212.

Bolles R.C., Fanselow M.S. (1980) A perceptual-defensive-recuperative model of fear and pain. Behav. Brain Sci. 3: 291-323.

Bordi F., LeDoux J.E. (1992) Sensory tuning beyond the sensory system: an initial analysis of auditory responses properties of neurons in the lateral amygdaloid nucleus and overlying areas of the striatum. J. Neurosci. 12: 2493-2503.

Brener J., Hothersall D. (1966) Heart rate control under conditions of augmented sensory feedback. Psychophysiology 3: 23-29.

Brown K.A., Buchwald J.S. (1973) Acoustic responses and plasticity of limbic units in cats. Exp. Neurol. 40: 608-631.

Burstein R. (1996) Somatosensory and visceral input to the hypothalamus and limbic system. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 257-267.

Cador M., Robbins T.W., Everitt B.J. (1989) Involvement of the amygdala in stimulus-reward associations: interactions with the ventral striatum. Neurosci. 30: 77-86.

Campeau S., Miserendino M.J.D., Davis M. (1992) Intra-amygdala infusion of the *N*-Metyl-D-aspartate receptor antagonist AP5 blocks acquisition but not expression of fear-potentiated startle to an auditory conditioned stimulus. Behav. Neurosci. 106: 569-574.

Chase S. (1968) Selectivity in multidimensional stimulus control. J. Comp. Physiol. Psychol. 66: 787-792.

Coover G.D., Murison R., Jellestad F.K. (1992) Subtotal lesions of the amygdala: The rostral central nucleus in passive avoidance and ulceration. Physiol. Behav. 51: 795-803.

Cormier S.M. (1981) A match-mismatch theory of limbic system function. Physiol. Psychol. 1: 3-36.

Dafny N., Dauth G., Gilman S. (1975) A direct input from amygdaloid complex to caudate nucleus of the rat. Exp. Brain Res. 23: 203-210.

Davis M. (1992) The role of the amygdala in conditioned fear. In: The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction (Ed. J.P Aggleton). Wiley-Liss, New York, p. 255-305.

Davis M. (1994) The role of the amygdala in emotional learning. Int. Rev. Neurobiol. 36: 225-266.

Davis M., Falls W.A., Campeau S., Kim M. (1993) Fear-potentiated startle: a neural and pharmacological analysis. Behav. Brain Res. 58: 175-198.

Dember W.N., Warm J.S. (1979) Psychology of perception. 2nd ed. Holt, Rinehart and Winston, New York, p. 55-81.

Dickinson A. (1980) Contemporary animal learning theory. In: Problems in the behavioral sciences (Ed. J. Gray). Cambridge Univ. Press, Cambridge, p. 177.

Everitt B.J., Cador M., Robbins T.W. (1989) Interactions between the amygdala and ventral striatum in stimulus-reward associations: studies using a second order schedule of reinforcement. Neuroscience 30: 63-75.

Everitt B.J. and Robbins T.W. (1992) Amygdala-ventral striatal interactions and reward-related processes. In: The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction (Ed. J.P. Aggleton). Wiley-Liss, New York, p. 401-429.

Ferreira M.B.C., Da Silva R.C., Medina J.H., Izquierdo I. (1992) Late posttraining memory processing by entorhinal cortex: involvement of NMDA and GABAergic receptors. Pharmacol. Biochem. Behav. 41: 767-771.

Gallagher M., Holland P.C. (1992) Understanding the function of the central nucleus: is simple conditioning enough? In: The amygdala: Neurobiological aspects of emotion, memory, and mental dysfunction (Ed. J.P. Aggleton). Wiley-Liss, New York, p. 307-321.

Gloor P. (1960) Amygdala. In Handbook of physiology, Neurophysiology (Ed. J. Field). Vol 2. Am. Physiol. Soc., Bethesda, p. 1395-1420.

Green D.M., Birdsall T.G., Tanner W.P., Jr. (1957) Signal detection as a function of signal intensity and duration. J. Acoustic. Soc. Am. 29: 523-531.

Groenewegen H.J., Berendse H.W., Meredith G.E., Haben S.N., Voorn P., Wolters J.G., Lohman A.H.M. (1991) Functional anatomy of the ventral, limbic system-innervated striatum. In: The mesolimbic dopamine system: From motivation to action (Eds. P. Willner, J. Scheel-Kruger). Wiley-Liss, Chichester, p. 19-60.

Groenewegen H.J., Wright C.I., Beijer A.V.J. (1996) The nucleus accumbens: gateway for limbic structures to reach the motor system? In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 485-511.

Grossman S.P., Grossman L., Walsh L. (1975) Functional organization of the rat amygdala with respect to avoidance behavior. J. Comp. Physiol. Psychol. 88: 829-850.

Heimer L., Zahm D.S., Alheid G.F. (1995) Basal ganglia. In: The rat nervous system (Ed. G. Paxinos). San Diego, Acad. Press, p. 579-628.

Holland P.C. (1984) Unblocking in Pavlovian appetitive conditioning. J. Exp. Psychol.: Animal Behav. Proc. 10: 476-497.

Holland P.C. (1988) Extinction and inhibition in unblocking. J. Exp. Psychol.: Animal Behav. Proc. 14: 261-279.

Izquierdo I., Medina J. (1997) Memory formation: the sequence of biochemical events in the hippocampus and its connection to activity in other brain structures. Neurobiol. Learn. Memory 68: 285-316.

Jones B., Mishkin M. (1972) Limbic lesions and the problem of stimulus-reinforcement associations. Expl. Neurol. 36: 362-377.

Kaada B.R., Andersen P., Jansen J., Jr. (1954) Stimulation of the amygdaloid nuclear complex in unanesthetized cats. Neurology 4: 48-64.

Kamin L.J. (1968) Attention-like processes in classical conditioning. In: Miami Symposium on the prediction of behavior: aversive stimulation (Ed. M.R Jones). University of Miami Press, Coral Gables, p. 9-32.

Kamin L.J. (1969) Selective association and conditioning. In: Fundamental issues in associative learning (Eds. N.J. Mackintosh and W.K. Honig). Dalhousie Univ. Press, Halifax, p. 42-64.

Kita H., Kitai S.T. (1990) Amygdaloid projections to the frontal cortex and the striatum in the rat. J. Comp. Neurol. 298: 40-49.

Krettek J.E., Price J.L. (1978) Amygdaloid projections to subcortical structures within the basal forebrain and brainstem in rat and cat. J. Comp. Neurol. 178: 225-254.

LeDoux J.E. (1987) Emotion. In: Handbook of physiology. The nervous system (Ed. V.B. Mountcastle). Vol. 5. Am. Physiol. Soc., Bethesda, p. 419-459.

LeDoux J.E. (1991) Emotion and the limbic system concept. Concepts Neurosci. 2: 169-199.

LeDoux J.E. (1992) Emotion and the amygdala. In: The amygdala: neurobiological aspects of emotion, memory, and mental dysfunction (Ed. J.P. Aggleton). Wiley-Liss, New York, p. 339-351.

LeDoux J.E. (1996) Emotional networks and motor control: a fearful view. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 437-446.

LeDoux J.E., Cicchetti P, Xagoraris A., Romanski L.M. (1990a) The lateral amygdaloid nucleus: sensory interface of the amygdala in fear conditioning. J. Neurosci. 10: 1062-1069.

LeDoux J.E., Farb C., Ruggiero D.A. (1990b) Topographic organization of neurons in the acoustic thalamus that project to the amygdala. J. Neurosci. 10: 1043-1054.

LeDoux J.E., Farb C.R. and Romanski L.M. (1991) Overlapping projections to the amygdala and striatum from auditory processing areas of the thalamus and cortex. Neurosci. Lett. 134: 139-144.

Logan F.A. (1954) A note on stimulus intensity dynamism (V). Rsychol. Rev. 61: 77-80.

Mackintosh N.J. (1965) Incidental cue learning in rats. Q. J. Exp. Psychol. 17: 292-300.

Mackintosh N.J. (1971) An analysis of overshadowing and blocking. Q. J. Exp. Psychol. 23: 118-125.

Mackintosh N.J. (1974) The psychology of animal learning. Acad. Press, London, p. 730.

Maren S., Fanselow M.S. (1996) The amygdala and fear conditioning: has the nut been cracked? Neuron 16: 237-240.

Mascagni F., McDonald A.J., Coleman J.R. (1993) Corticoamygdaloid and corticocortical projections of the rat temporal cortex: a Phaseolus vulgaris leucoagglutinin study. Neuroscience 57: 697-715.

McDonald, A.J. (1992) Cell types and intrinsic connections of the amygdala. In: The amygdala: neurobiological aspects of emotion, memory, and mental disfunction (Ed. J. P. Aggleton). Wiley-Liss Inc., New York. p. 67-69.

McNish K.A., Gewirtz J.C., Davis M. (1997) Evidence of contextual fear after lesions of the hippocampus: a disruption of freezing but not fear-potentiated startle. J. Neurosci. 17: 9353-9360.

Miscerendino M.J.D., Sananes C.B. Melia K.R., Davis M. (1990) Blocking of acquisition but not expression of conditioned fear-potentiated startle by NMDA antagonists in the amygdala. Nature 345: 716-718.

Mogenson G.J., Jones D.L., Yim C.Y. (1980) From motivation to action: functional interface between the limbic system and the motor system. Prog. Neurobiol. 14: 69-97.

Mogenson G., Jones D.L., Yim C.Y. (1984) From motivation to action: functional interface between the limbic system and the motor system. Prog. Neurobiol. 14: 69-97.

Muramoto K., Ono T., Nishijo H., Fukuda M. (1993) Rat amygdaloid neuron responses during auditory discrimination. Neuroscience 52: 621-636.

Nieuwenhuys R. (1996) The greater limbic system, the emotional motor system and the brain. In: The emotional motor system (Eds. G. Holstege, R. Bandler and C.B. Saper). Prog. Brain Res. 107: 552-580.

Packard M.G., McGaugh J.L. (1992) Double dissociation of fornix and caudate nucleus lesions on acquisition of two water maze tasks: Further evidence for multiple memory systems. Behav. Neurosci. 106: 439-446.

Parent M.B., Avila E., McGaugh J.L. (1995) Footshock facilitates the expression of aversively motivated memory in rats given post-training amygdala basolateral complex lesions. Brain Res. 676: 235-244.

Pavlov I.P. (1927) Conditioned reflexes. Oxford, Oxford University Press, 430 p.

Paxinos G., Watson C. (1982) The rat brain in stereotaxic coordinates. Acad. Press, Sydney.

Paxinos G., Watson C. (1997) The rat brain in stereotaxic coordinates. Acad. Press, San Diego.

Pellegrino L. (1968) The effects of amygdaloid stimulation on passive avoidance. Psychon. Sci. 2: 189-190.

Pérez-Ruiz C., Prado-Alcalá R.A. (1989) Retrograde amnesia induced by lidocaine injection into the striatum: protective effect of the negative reinforcer. Brain Res. Bull. 22: 599-603.

Pearce J.M., Hall G. (1980) A model for Pavlovian learning: Variations in the effectiveness of conditioned but not of unconditioned stimuli. Psychol. Rev. 106: 532-552.

Perkins C.C., Jr. (1953) The relation between conditioned stimulus intensity and response strength. J. Exp. Psychol. 46: 225-231.

Phillips R.G., LeDoux J.E. (1994) Lesions of the dorsal hippocampal formation interfere with background but not foreground contextual fear conditioning. Learn. Memory 1: 34-44.

Pitkänen A., Stefanacci L., Farb C.R., Go G.-G., LeDoux J., Amaral D.G. (1995) Intrinsic connections of the rat amygdaloid complex: projections originating in the lateral nucleus. J. Comp. Neurol. 356: 288-310.

Polgar S., Sanberg P.R., Kirkby R.J. (1981) Is the striatum involved in passive-avoidance behavior? A commentary. Physiol. Psychol. 9: 354-358.

Prado-Alcalá R.A. (1985) Is cholinergic activity of the caudate nucleus involved in memory? Life Sci. 37: 2135-2142.

Prado-Alcalá R.A., Grinberg Z.J., Arditti Z.L., Garcia M.M., Prieto H.G., Brust-Carmona H. (1975) Learning deficits produced by chronic and reversible lesions of the corpus striatum in rats. Physiol. Behav. 15: 283-287.

Prado-Alcalá R.A., Cobos-Zapiain G.G. (1979) Interference with caudate nucleus activity by potassium chloride. Evidence for a "moving" engram. Brain. Res. 172: 577-583.

Price J.L., Russchen F.T., Amaral D.G. (1987) The limbic region. II: The amygdaloid complex. In: Handbook of chemical neuroanatomy (Eds. A. Björklund and T. Hökfelt). Vol. 5. Elsevier, Amsterdam, p. 279-388.

Quirk G.J., Repa J.C., LeDoux J.E. (1995) Fear conditioning enhances short-latency auditory responses of lateral amygdala neurons: parallel recordings in the freely behaving rat. Neuron 15:1029-1039.

Rescorla R.A., Wagner A.R. (1972) A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement. In: Classical conditioning II (Eds. A.H. Black and W.F. Prokasy). Appleton-Century--Crofts, New York, p. 64-99.

Roberts, G.W. (1992) Neuropeptides: cellular morphology, major pathways, and functional considerations. In: The Amygdala: Neurobiological aspects of emotion, memory, and mental disfunction (Ed. J. P. Aggleton). Wiley-Liss Inc., New York. p. 229-254.

Rolls E.T. (1994) Neurophysiology and cognitive functions of the striatum. Rev. Neurol. (Paris), 150: 648-660.

Romanski L.M., LeDoux J.E. (1992) Equipotentiality of thalamo-amygdala and thalamo-cortico-amygdala circuits in auditory fear conditioning. J. Neurosci. 12: 4501-4509.

Romanski L.M., Clugnet M.-C., Bordi F., LeDoux J.E. (1993) Somatosensory and auditory convergence in the lateral nucleus of the amygdala. Behav. Neurosci. 107: 444-450.

Russchen F.T., Price J.L. (1984) Amygdalostriatal projections in the rat: topographical organization and fiber morphology shown using the lectin PHA-L as an anterograde tracer. Neurosci. Lett. 47: 15-22.

Sananes C.B., Davis M. (1992) *N*-metyl-D-aspartate lesions of the lateral and basolateral nuclei of the amygdala block fear-potentiated startle and shock sensitization of startle. Behav. Neurosci. 106: 72-80.

Savander V. (1997) Organization of intrinsic connections in the rat amygdaloid complex: with special emphasis on the lateral, basal and accessory basal nuclei. Kuopio University Printing Office, Kuopio, 95 p., thesis.

Shapovalova K.B. (1997) Striatal cholinergic system: participation in motor and sensory components of the motor behavior. J. High Nerv. Activ. 47: 123-134.

Siegel S. (1956) Nonparametric statistics for the behavioral sciences. McGraw-Hill/Kogakusha, Tokyo, p. 312.

Swets J.A., Tanner W.P., Birdsall T.G. (1961) Decision processes in perception. Psychol. Rev. 68: 301-340.

Taub E., Berman A.J. (1968) Movement and learning in the absence of sensory feedback. In: The Neuropsychology of spatially oriented behavior (Ed. S.J. Freedman). The Dorsey Press, Homewood, Illinois, p. 173-192.

Teyler T.J., DiScenna P. (1985) The role of hippocampus in memory: A hypothesis. Neurosci. Biobehav. Rev. 9: 377-389.

Turner B.H. (1981) The cortical sequence and terminal distribution of sensory related afferents to the amygdaloid complex of the rat and monkey. In: The amygdaloid complex (Ed. Y. Ben-Ari). Elsevier/North-Holland, Amsterdam, p. 51-62.

Turner B.H., Herkenham M. (1991) Thalamoamygdaloid projections in the rat: a test of the amygdala's role in sensory processing. J. Comp. Neurol. 313: 295-325.

Turner B.H., Zimmer J. (1984) The architecture and some of the interconnections of the rat's amygdala and lateral periallocortex. J. Comp. Neurol. 227: 540-557.

Uwano T., Nishijo H., Ono T., Tamura R. (1995) Neuronal responsiveness to various sensory stimuli, and associative learning in the rat amygdala. Neurosci. 68: 339-361.

Wagner A.R. (1978) Expectancies and the priming of STM. In: Cognitive processes in animal behavior (Eds. S.H. Hulse, H. Fowler and W.K. Honig). Lawrence Erlbaum Associates, Hillsdale, N.Y., p. 177-210.

Walker D.L., Davis M. (1997) Double dissociation between the involvement of the bed nucleus of the stria terminalis and the central nucleus of the amygdala in startle increases produced by conditioned versus unconditioned fear. J. Neurosci. 17: 9375-9383.

Weiskrantz L. (1956) Behavioral changes associated with ablation of the amygdaloid complex in monkeys. J. Comp. Physiol. Psychol. 49: 381-391.

Werka T. (1980) Acquisition of the escape reflex in cats after the nucleus centralis of the amygdala lesions. Acta Neurobiol. Exp. 40: 433-449.

Werka T. (1994) Post-stress analgesia in rats with partial amygdala lesions. Acta Neurobiol. Exp. 54: 127-132.

Werka T., Skr J., Ursin H. (1978) Exploration and avoidance in rats with lesions in amygdala and piriform cortex. J. Comp. Physiol. Psychol. 4: 672-681.

Werka T., Zieliński K. (1978) Effects of lesions in the amygdaloid nucleus centralis on acquisition and retention of avoidance reflexes in cats. Acta Neurobiol. Exp. 38: 247-270.

Werka T., Zieliński K. (1998) CS modality transfer of two-way avoidance in rats with central and basolateral amygdala lesions. Behav. Brain Res. (in press).

Winocur G. (1997) Hippocampal lesions alter conditioning to conditional and contextual stimuli. Behav. Brain Res. 88: 219-229.

Zeaman D., House B.J. (1963) The role of attention in retardate discrimination learning. In: Handbook of mental deficiency: Psychological theory and research (Ed. N.R. Ellis). McGraw-Hill, New York, p. 159-223.

Zieliński K., Werka T., Naneishvili T. (1983) Do amygdaloid nucleus centralis and nucleus lateralis serve similar functions in defensive responding in cats? Acta Neurobiol. Exp. 51: 71-88.

Zieliński K., Werka T., Nikolaev (1991) Intertrial responses of rats in two-way avoidance learning to visual and auditory stimuli. Acta Neurobiol. Exp. 51: 71-88.

Zola-Morgan S., Squire L.R. (1990) The primate hippocampal formation: Evidence for a time-limited role in memory storage. Science 250: 288-290.

Zola-Morgan S., Squire L.R., Alvarez-Royo P., Clower R.P. (1991) Independence of memory functions and emotional behavior: Separate contributions of the hippocampal formation and the amygdala. Hippocampus 1: 207-220.

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