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Effects of stimulus omission during habituation of the pupillary dilation reflex

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The pupillary dilation reflex of the paralyzed cat was studied during habituation to an acoustic stimulus. The effect of a scheduled stimulus omission was assessed by examination of pupillary activity during the omission, in the 4-sec intertrial interval, and on the following trial. It was found that dilation responses during the omission were rare. Effects were seen more often in the intertrial interval or on the following trial ("dishabituation"). Responses to an omitted stimulus were related to the dynamics of background ("tonic") pupillary size; specifically, they occurred significantly more often for subjects which exhibited an increase in background pupillary diameter following initial stimuli and then a decrease during the later course of habituation.

Habituation is a ubiquitous behavioral characteristic (e.g., Harris, 1943). At present there are two major theories of the neural bases of habituation. The dual-process theory presented by Groves and Thompson (1970) postulates that behavioral habituation is the net result of interactions between two independent processes, habituation which occurs in the stimulus-response (S-R) pathway and sensitization which occurs in the state or arousal system. The plastic components are thought to be interneurons of two types, either habituation or sensitization neurons. The second theory, Sokolov's (1963, 1975) stimulus model system, proposes a mechanism for habituation specifically for the orienting reflex (OR). The presentation of stimuli initiates the formation of a multidimensional neural representation of the stimulus, inclusive of duration and temporal pattern of the stimulus. This neuronal model is thought to be comprised of a series of neuronal nets each coding a stimulus parameter. These nets are said to be elaborated in the sensory cortex. A comparison of an extent stimulus with the model serves as the basis for control of the orienting reflex: mismatches elicit ORs, whereas matches result in response decrements, i.e., habituation.

While both theories seem to account for many aspects of habituation, the effects of the omission of a scheduled stimulus during habituation are of particular importance because the theories predict opposite results. In the dual process theory, there would be no stimulation of the S-R pathway during omission and thus no behavioral response to the omission (Groves & Thompson, 1970). While questioning the scant evidence for an omission effect, these authors believe that omission effects are due to temporal conditioning. For the neuronal model theory, the omission of a stimulus also would not activate the afferent system. However, the neuronal net coding the stimulus interval would be activated by the extended time interval between stimuli, that is, there would occur a "mismatch," resulting in elicitation of an OR. Davis (1939), Voronin and Sokolov (1960), Voronin, Bonfitto, and Vasilieva (1975), and O'Gorman and Lloyd (1976) have observed effects due to the omission of a scheduled stimulus during habituation of orienting responses (EEG, GSR, EMG). However, little quantitative data are available. The purpose of the present study is to determine the form and relative frequency of occurrence of the effects of an omission of a scheduled acoustic stimulus during habituation of the pupillary dilation response, a behavioral response which is also a component of the orienting response.

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METHODS

Subjects

The subjects were 18 adult cats of either sex weighing 2.3 to 4.5 kg. The animals had previously undergone surgery for placement of recording electrodes. Electrophysiological data will be reported in a separate communication. Surgical procedures are described in Oleson, Ashe, and Weinberger (1975). During surgery, a headholding device was affixed to the skull for atraumatic fixation of the head during the experiment. A postoperative recovery period of at least 3 weeks was allowed.

Experimental Procedures

Paralysis of the subjects was induced with a 10-mg/kg IP injection of gallamine triethiodide (Flaxedil). An endotracheal tube, coated with a local anesthetic (Xylocaine), was inserted into the trachea under laryngoscopic control; artificial respiration was initiated immediately with a Harvard respirator. The animal was placed for the duration of the experiment in a double acoustic room (IAC 1202), the head atraumatically fixed, using the device previously attached to the skull. An acoustic stimulus was delivered to the right ear of the animal via a TDH-39 earphone. The stimulus was a 1-sec pulse of white noise generated by a Grason-Stadler white-noise generator (85-90 dB re: 0.0002 dynes/cm²) The left eyelid was retracted with a pediatric speculum to facilitate the monitoring of pupillary diameter with an infrared pupillometer (Oleson, Westenberg, & Weinberger, 1972). The output of the pupillometer was amplified and written out on a Grass Model 7 polygraph. Dilations to acoustic stimulation were measured in millimeters from baseline level at the onset of the white noise to the peak of the dilation during the 1-sec duration of the stimulus. After the pupillometer was positioned, the animal received a supplemental injection of Flaxedil, and the experiment was begun following a 5-min period of quiet.

A habituation session consisted of a 1-sec presentation of white noise given at the rate of one/5 sec for a total of 80-120 trials. During the course of a single habituation session, three scheduled trials were omitted: Trials 30, 60, and 90 or Trials 20, 40, and 60. Of the 18 animals, 4 received the omissions on Trials 30, 60, and 90, 13 received omissions on Trials 20, 40, and 60, and 1 animal received only two omissions on Trials 40 and 60.

RESULTS

Assessment of the effects of stimulus omission requires prior habituation to that stimulus. Accordingly, data were first analyzed to determine which of the subjects exhibited a systematic decrement to the repeated presentation of white noise. The criteria for habituation were (1) a negative coefficient of correlation between magnitude of dilation and serial number of stimulus presentation (trials), and (2) a smaller response on the trial immediately preceding the omission than on Trial 1. Fifteen of 18 animals met these criteria, and their subsequent data were therefore subjected to the analysis of the effects of stimulus omission.

Before proceeding to the effects of stimulus omission, it should be noted that the orienting reflex has two major components, phasic and tonic (Sokolov, 1963). Above, we have considered habituation of the phasic component, i.e., the short-duration response to stimulus presentation itself. Additionally, stimulus repetition has been shown to cause a systematic change in the background activity of response systems, the so-called "tonic component" of the orienting reflex. In the present study, baseline pupillary size was also measured and correlation coefficients were computed to determine the effects of stimulus repetition upon background pupillary size. Initial stimulus presentation usually elicited an increase in dilation which was seen for both the phasic and tonic components of the pupillary response. Thereafter, the background level also decreased, as evidenced by negative correlation coefficients; 12/15 of the subjects had such negative coefficients, 8 of these 12 reaching statistical significance (Table 1B and Figures 1C and 2). Thus, as in the case of response systems such as that of the GSR (Sokolov, 1963), the tonic component of the pupillary response system also exhibits systematic decrement with stimulus repetition.

The effect of stimulus omission is ordinarily indicated by the elicitation of a response in the interval during which the scheduled stimulus is not presented. However, the effect of omission could also be revealed as a response during the intertrial interval immediately following the omission. A third index of the omission would comprise augmentation of the dilation response on the trial immediately following the omission. In this case, the omission would serve as a "dishabituating stimulus." Data were analyzed for all three effects. However, in order to avoid possible complications of habituation of the omission effects, only the first stimulus omission of each habituation series was studied.

Table 1
Summary of the Effects of Stimulus Repetition and Omission

(A) Evoked		(B) Baseline Measures			(C) T + 1 Effects	
Animal Number	Response During T	T − 1 vs. T − 3	T + 1 vs. T − 1	(r) Baseline vs. Trials	T − 1 vs. T − 3	T + 1 vs. T − 1
18	+	–	+	–.538**	+	+
19	0	+	–	–.729**	–	+
23	0	–	+	–.613**	0	–
24	0	0	0	–.314	0	0
25	0	–	0	–.308	+	–
26	0	0	0	.774**	0	–
28	0	0	0	–.713**	0	+
29	0	0	+	–.633**	–	+
31	0	–	–	–.188	–	0
32	0	–	+	–.760**	–	+
33	0	0	0	.484*	0	–
34	0	+	–	–.067	0	+
35	0	0	0	–.552*	0	0
36	0	–	+	.027	+	+
46	+	+	–	–.739**	–	+

*$p < .05$
**$p < .01$

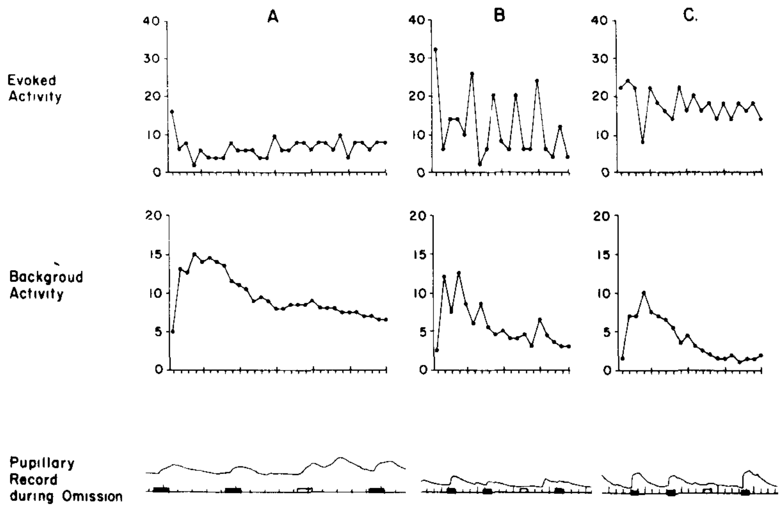

Figure 1. Examples of the three measures of an effect due to the omission of a stimulus. Both the background and evoked activity prior to the omission is shown for each animal. (A) A response during the 1-sec omission period (open box) can be seen in the pupillary records for ACA No. 18. (B) A response during the 4-sec intertrial interval is seen in the pupillary records for ACA No. 23. (C) A dishabituated response to the trial following T can be seen for ACA No. 46. The abscissa is trials; the ordinate is millimeters of pen deflection of the polygraph writeout. Time marks on polygraph records are in 1-sec intervals.

Pupillary dilation responses during the omission period (i.e., the 1-sec period in which the scheduled white noise was omitted) were defined as a change in output of the pupillometer during the omission trial (T) that was visually discernible from the 4-sec intertrial interval immediately preceding T. Such responses were found in two cases; 13 animals failed to demonstrate a response during omission (Table 1A). Figures 1A and 1C illustrate the positive findings.

To test for omission effects during the intertrial interval immediately following T, the level of pupillary size was measured immediately prior to the onset of the next trial, T + 1. An effect of the omission was defined as a higher measure at the end of the intertrial interval following T in comparison with the pupillometer output immediately prior to the onset of the trial preceding the omission (T − 1). However, such a pupillary response could also be the result of a background pupil size which was increasing during the intervals surrounding the period of stimulus omission. The likelihood of this outcome was small because baseline levels generally decreased significantly with repeated trials (Table 1B). Nevertheless, a precautionary measure was instituted; baseline at onset of T − 1 was compared with the same measure for T-3. T-3 was selected because its temporal distance from T − 1 is the same as that for T + 1). For animals in which baseline at T − 3 was less than at T − 1, any rise in baseline at T + 1 would be considered uninterpretable, reflecting either a general rise in baseline or the effect of stimulus omission. Such a situation was found for three subjects, but in each case the baseline at T + 1 was *lower* than at T − 1, and thus failed to reveal an omission effect.

The effects of omission were observed in five instances, i.e., the pupillary record indicated larger pupillary size at the end of the intertrial interval (ITI) immediately following the omission (Figure 1B, T + 1 vs. T − 1). However, this baseline measure is not independent of responses during the omission period; a large response during omission could still be in evidence at the end of the interval. In fact, this did occur for Subject 18 (Figure 1A, lower row). Thus, the baseline effect for this animal was uninterpretable and consequently discounted, reducing the number of omission effects to 4/14 (Table 1B, T + 1 vs. T − 1).

It might be argued that this estimate is too conservative because the baseline measure would not have detected a short-duration dilation which occurred after the period of omission, but terminated prior to the end of the succeeding 4-sec intertrial interval. However, inspection of all records failed to reveal such a response. Rather, all responses occurring after the omission period were still evident at the end of the following intertrial interval (Figure 1B, lower row).

The third and final measure used to determine if stimulus omission had a behavioral effect was based upon comparison of the pupillary response on the trial following the omission with the response on the trial preceding the omission. A larger response following omission could be considered to be evidence of dishabituation by the omission (Figure 1C, lower row). The same control maneuver used on the measure of intertrial responses was also employed in this analysis. Two animals which displayed an apparent omission effect were found to have larger responses on T − 1 than on T − 3, rendering increased responses on T + 1 relative to T − 1 uninterpretable. Accordingly, data from these animals were not considered further. In six other cases, the response on T + 1 was larger than on T − 1, suggesting that omission had a dishabituating effect. There were four instances of decreases and three cases of no change, so that overall the effect of omission was observed in 6/13 of the habituation sessions (Table 1C).

Inspection of the functions for background pupillary size indicate that, for seven of the nine subjects exhibiting an omission effect, the background pupillary size was characterized by a very large increment following Trial 1, followed by a more or less exponential decrease up to the period of omission. Such functions were not found for any of the subjects which failed to exhibit an omission effect (Figures 1 and 2).

A summary of the effects of stimulus omission indicates that overall, 9 of the 15 subjects exhibited one or more of the omission indices (Table 1). When one considers the generally low probability of obtaining any one of these indices, together with the fact that only 60% of the cats displayed an omission effect, it is clear that the omission effect is not particularly robust. It is even tempting to dismiss the positive findings as reflecting chance phenomena. Considering three measures per subject (with deletions for cases of uninterpretability noted above) and 15 subjects, there was a total of 39 measures; 14 of these indicated an omission effect, i.e., the probability of obtaining an omission effect was .31. This figure is certainly uncomfortably low for those supporting a "neural model" theory, but at the same time is too high to be attributable to chance alone.

Some clarification of the matter may be provided by considering factors that may predict whether or not an omission effect occurs. In the present case, we considered the relationships between omission effects and two measures of prior habituation, decrements in responses and decrements in baseline pupil size. Subjects were divided into two groups, those which exhibited an omission effect (N = 9) and those which did not (N = 6). A Mann-Whitney test was performed on the magnitude of correlation coefficients for both evoked and baseline measures; all correlation coefficients for the evoked responses were negative and 12/15 of the baseline measures were also negative. The relationship between the magnitude of decrement of evoked responses and the presence of an omission effect was not significant ($U = 21$, $p > .05$, two-tailed). However, the magnitude of the correlation of decreasing background pupil size was significantly greater for animals exhibiting an omission effect than for animals in which no index of an omission effect was obtained ($U = 10$, $p < .05$, two-tailed). In other words, larger decrements in the tonic component of the pupillary orienting reflex are predictive of omission effects.

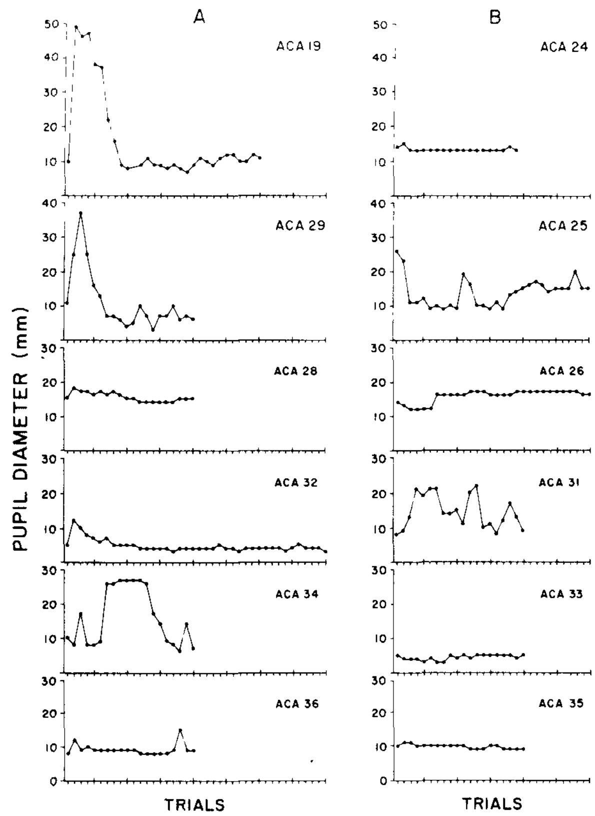

Figure 2. Background pupillary size during the course of the habituation series for individual subjects. (A) Records for animals which demonstrated an effect of stimulus omission. Note that all subjects displayed an increase in background pupillary size during initial trials and five of the six thereafter displayed a decrement preceding the omission trial (Nos. 19, 29, 28, 32, and 34). See also Figure 1, which shows the same type of dynamics for background size in three additional subjects which exhibited effects of stimulus omission. (B) Records for animals which did not demonstrate an effect of stimulus omission. Note that in no case did the same type of charge in tonic pupillary level occur as for the other group; subject No. 31 exhibited an initial increase which was not followed by a more or less exponential decrease. See text for further details. Calibrations are as in Figure 1.

DISCUSSION

This study addressed the issue of whether or not the omission of an acoustic stimulus following habituation produces a response in the pupillomotor system. The results indicate that actual pupillary dilations during the period of omission are extremely rare (2/15 cases) but that increases in pupillary background size and potentiation of pupillary responses on the subsequent trial have a higher probability of occurrence. In short, the "stimulus omission" phenomenon, as generally defined, seldom occurs, but effects due to stimulus omission can be detected at a level greater than would be expected by chance.

These findings pose a problem for Sokolov's neural model theory. Presumably, stimulus omission following habituation causes a mismatch between the model and extent environmental conditions, resulting in evocation of an orienting response. The present findings indicate that such a process might occur but apparently often does not.

It might be argued that failures to obtain an omission effect are due to insufficient habituation and thus insufficient formation of the neural model. However, subjects did meet criteria for habituation, and many animals yielded small or no responses prior to stimulus omission (Figure 1). Also, we found no significant relationship between obtaining an omission effect and the degree of habituation as indicated by the magnitude of the negative correlation between evoked pupillary response size and serial trial number. On the other hand, we did find a significant relationship between decrement in the tonic or background level of the pupil and the occurrence of an omission effect. The decrement in background pupillary size would seem to be more indicative of the general functional state or arousal level of the subjects than of formation of the neural model.

Failure to obtain an omission response has been reported by Voronin et al. (1975) for the EEG and GSR of humans. Interestingly, although responses to omitted stimuli were not obtained for interstimulus intervals of 5 sec and also 30 sec, such responses were found for ITI of 12-15 sec. Like Voronin et al. (1975), we also "failed" to find responses during the omission period (2/15), using an ITI of 4 sec. Previous authors have evidently not measured the other indices of stimulus omission effects that we employed, so their estimates of failures may be too liberal. Nonetheless, the probability of obtaining an omission effect may be critically related to ITI, because O'Gorman and Lloyd (1976) reported positive findings for alpha blocking using an interval of 20 sec, close to the interval that yielded omission responses in the experiments of Voronin and his associates. Additional parametric studies would be desirable.

The present results are not better explained by the dual-process theory of Groves and Thompson than by Sokolov's theory. Stimulus omission caused apparent dishabituation in several cases. This outcome is not predicted by temporal conditioning explanations. A second consideration which is not consonent with temporal conditioning is provided by data of Voronon et al. (1975). These workers specifically studied temporal conditioning, as well as habituation, by requiring a response to each stimulus. Under this condition, stimulus omission was accompanied by definite EEG and motor (EMG) responses, even for short ITI. Thus, it would seem that temporal conditioning using short ITI requires, or at least is greatly enhanced by, imparting some signal importance to the repeated stimulus.

In the present study, background pupillary size decreased with repeated stimulus presentation. This apparent habituation of the "tonic" orienting reflex replicates and extends the findings of Weinberger, Oleson, and Ashe (1975), who obtained this effect with regular presentation (1/3 sec) of tactile stimuli.

It is noteworthy that the degree of decrement of the background or tonic pupillary level was positively related to elicitation of an effect following stimulus omission. If one regards the background level as an index of general organismic excitability, then omission effects are best seen when excitability has undergone a relatively large systematic decrement following the first trial, to the period of stimulus omission. Such decrements could occur two ways: an initially large pupillary diameter which decremented over trials or an initially small pupil size which was greatly increased by the first habituation trial, thereafter decrementing over trials. In fact, the latter type of function was found for subjects for whom the omission produced a perturbation in the pupillomotor system (e.g., Figure 2). Thus, a stimulus omission appears to be effective when subjects undergo an initial large increase in general excitability or arousal, followed by a systematic decrease in this state. Interestingly, this pattern of state change is the same as that which Groves and Thompson (1970) obtained for "sensitization" type interneurons in the spinal cord during habituation of the flexion reflex.

The present results are accounted for neither by the neural model nor the two-process theory of habituation. One major aspect of the "omitted stimulus problem" appears to have been uncovered in this experiment. Evidently, the elicitation of an omission effect is likely to occur when initial trials cause a pronounced increase in tonic pupillary size which then decrements in approximately an exponential manner. It seems that obtaining an effect due to stimulus omission is dependent upon the nature of the state or general arousal changes which an animal has undergone prior to the time of omission. Revisions of current theories or formulations of new theories of habituation must be able to account for this relationship.

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