Regular interstimulus interval as a critical determinant of short-term "habituation" of the auditory averaged evoked response* **

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In order to delineate the critical condition for the short-term "habituation" of the cortical auditory averaged evoked response, two levels of activation were combined with regular vs irregular interstimulus intervals in a 2 by 2 factorial design. Averages were computed across 24 trains of 10 click stimuli each. It was found that a regular interstimulus interval produced a rapid exponential decreasing function within trains for the N_1 - P_2 component regardless of activation level. High activation, however, resulted in smaller P_2 - N_2 components.

In order to be distinguished from the background electroencephalogram, evoked responses from the scalp in humans need averaging over many individual stimuli. Correct interpretation of these averaged evoked responses (AERs) therefore requires knowledge of the factors governing systematic changes in evoked potentials over successive stimuli. A direct approach to this problem is complicated by the difficulties in observing stimulus-to-stimulus changes in the AER. Ritter et al (1968), however, introduced an indirect technique to study short-term changes in the AER by averaging across stimuli occurring in discretely presented trains. Thus, averages were taken over the first stimuli in all trains, the second stimuli, and so on. These authors found a rapid exponential decrease in AER amplitude over the first few stimuli within trains when the interstimulus interval (ISI) was short (less than 2 sec) but not when it was long (10 sec). Similar results were reported by Fruhstorfer et al (1970) and Roth & Kopell (1969). The interpretation of these findings, however, is open to dispute. While the response decrement fulfills some of the criteria for habituation (Thompson & Spencer, 1966), i.e., exponential decrease (Fruhstorfer et al, 1970), spontaneous

recovery between trains (Cook et al, 1968; Fruhstorfer et al, 1970), potentiation of habituation (Fruhstorfer et al, 1970; Öhman & Lader, 1972; Ritter et al, 1968), and stimulus generalization (Butler, 1968; Butler et al, 1969; Fruhstorfer, 1971), a convincing demonstration of dishabituation is still lacking (Fruhstorfer, 1971; Ritter et al, 1968). Therefore, some authors have adopted an explanation in terms of neuronal refractoriness (Ritter et al, 1968; cf. Davis et al, 1966). It should be pointed out, however, that a demonstration of dishabituation probably is very difficult to achieve, since the averaging procedure requires repeated presentations of the dishabituating stimulus which should drastically reduce its effect. Of the above criteria, the only one besides dishabituation differentiating between the alternative interpretations is potentiation of habituation, since lasting decremental effect could not be expected from refractoriness alone. Therefore, the consistent reports of significant amplitude changes over trains of stimuli (Fruhstorfer et al, 1970; Öhman & Lader, 1972; Ritter et al, 1968) is probably the most crucial evidence for a habituation interpretation and against a mechanism of neuronal recovery.

Before the controversy regarding the nature of the short-term decrement of the AER can be settled, however, a more basic question needs an answer. Although the majority of the studies published so far seem to agree that stimulus-to-stimulus change with short ISI can be described as an exponentially decreasing function that reaches an asymptote after three to four stimuli (Fruhstorfer, 1971; Fruhstorfer et al, 1971; Ritter et al, 1968; Roth & Kopell, 1969), this seems not to be generally the case. Öhman & Lader (1972) measured

AERs to click stimuli occurring in trains of 10 clicks each, while the Ss produced reaction times (RTs) either to the clicks or to visual stimuli presented independent of the clicks. With ISIs of both 3 and 10 sec, they observed a slowly decreasing trend in amplitude which did not reach any asymptote during the 10 stimuli studied. The present study, therefore, was initiated to reconcile the discrepancy in the observed decremental functions.

There are at least two important differences in the experimental conditions used by Öhman and Lader and the previous authors. First, while the earlier studies used regular stimulus presentations, Öhman and Lader used an irregular ISI, which could contribute to slower response decrement (Fox, 1964). Second, the RT task used by Öhman and Lader might be more activating than the reading task used in the previous studies. At least for skin conductance measures, there is an inverse relationship between unspecific background activation and habituation to stimuli (Lader, 1967, 1969). In the present study, two levels of activation were combined with regular vs irregular ISI in an attempt to delineate the critical conditions for the rapid short-term decrement of the AER with repeated stimuli. In order to evaluate the performance level and autonomic activity, RTs and skin conductance level (SCL) were included as dependent variables.

METHODS

Four males and four females from the staff of the Institute of Psychiatry acted as paid volunteer Ss in the experiment. Their ages varied between 22 and 34 years.

The S was seated comfortably in a sound-protected room, the recording equipment being in an adjacent laboratory. The experimental procedure was outlined, and the S was particularly instructed to keep his eyes open and to avoid any movements during the trains of stimuli.

The experiment was carried out on-line under the control of a LINC-8 computer.

The EEG was recorded from bipolar saline pad electrodes (C_z - T_3 on the 10-20 system) by means of a Grass Model 511C amplifier of bandpass 0.3-1,000 Hz, and led into an A-D converter input of the computer. The EEG was sampled every 2 msec starting 20 msec before each stimulus and continuing for a 500-msec epoch. The computer program included tests for overflow in the background EEG and the AER. Skin conductance level was recorded as resistance, using double-element electrodes (Lader & Wing, 1966), the computer sampling

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Fig. 1. Effects of regular interstimulus interval on the mean amplitude of the N_1 - P_2 component of the auditory evoked response for the stimulus-by-stimulus averages ($N = 8$).

the skin resistance immediately prior to each stimulus. EEG epochs, skin resistance, and RTs were stored in digital form on LINC tape for later analysis. In all conditions, auditory evoked responses were measured to clicks of about 70 dB intensity and 1 msec in duration, presented through a loudspeaker behind the S. The stimuli appeared in trains of 10 clicks each, with 24 trains in each experimental condition. The start of a train was heralded by a red lamp 1 m in front of the S, which was switched on before the first stimulus in the train, the interval corresponding to the ISI under study, and which remained on throughout the train. The intertrain interval (ITI) was always irregular, varying between 24 and 36 sec with a rectangular distribution. During the trains, the computer was programmed to start the counter of a digital timer (Venner Model TSA 6614) placed 1 m in front of S 10 times. The counter was not started within 0.5 sec before and 1 sec after a click.

The basic design was a 2 by 2 factorial, with two levels of activation as one factor and regular vs irregular ISIs as the other. Each S was tested on two occasions, two conditions to each occasion. The order of presentation of conditions was counterbalanced, with the restriction that the two ISI conditions on each occasion were either both regular or irregular. The between-occasion interval was at least 3 days.

In the high activation conditions,

the S was instructed to stop the digital timer as fast as he could each time it was started by pressing a microswitch; he could then read off his RT from the counter. He was informed that he would be paid according to performance. In the low activation condition, the S was instructed merely to count the number of times the counter started during each train, because he would be required to tell the E after the experiment the number of trains in which the counter did not start 10 times (occasional trains in which the number of starts did not equal 10 were given). In the regular ISI condition, the interval between successive clicks was always 3 sec; in the irregular condition, the average ISI was also 3 sec, but varied randomly from 2.4 to 3.6 sec with a rectangular distribution. The visual ISI was always irregular, having the same mean ISI as the clicks, but had a greater range (1-5 sec) to prevent alternating presentations of the two types of stimuli.

To study short-term changes in the AER, averages were computed stimulus by stimulus by taking every first stimulus in the trains, every second stimulus, and so on. Long-term or train-by-train changes were studied by averaging over successive stimuli, the stimuli in two trains making up an average. Amplitudes and latencies were measured manually by setting cursors against the peaks of the AERs as displayed on the LINC oscilloscope. Variances were also calculated and

displayed as a check for artifacts. Four components were measured: a positive component with latencies of 50-100 msec (P_1); a negative component with latencies of 80-150 msec (N_1); a positive component with latencies of 150-250 msec (P_2); and a negative component of 250-300 msec latency (N_2). Amplitudes were taken as the difference between negative and positive peaks, i.e., P_1 - N_1 , N_1 - P_2 , and P_2 - N_2 . Latencies were measured separately for each of the four components.

Reaction times and skin resistances were read off from the LINC tapes, the former being transformed to a speed measure ($1,000/x$) and the latter to log conductance. Averages were computed stimulus by stimulus and train by train as for the AER.

Trend analyses were used for statistical treatment of the data (Edwards, 1960), trial number being thus a third factor after activation and regularity of the ISI.

RESULTS

The results for P_1 - N_1 and N_1 - P_2 were very similar, and therefore only N_1 - P_2 will be dealt with further. Figure 1 shows the stimulus-by-stimulus averages for the N_1 - P_2 . Since there was no effect of activation on this measure [$F(1,7) = 0.29$], the figure is based on the means from the two activation conditions. The main effect of regularity was not significant [$F(1,63) = 0.08$], but as is apparent in Fig. 1, there was a significant effect of stimulus repetition [$F(9,63) = 5.83$, $p < .001$]. The significant linear trend component of the stimulus repetition mean square [$F(1,63) = 19.74$, $p < .001$] indicates a decrease in amplitude with successive stimuli for the means of the two curves, and the significant quadratic component [$F(1,63) = 27.86$, $p < .001$] indicates that the decreasing function is curved. Furthermore, the decrease in amplitude was both steeper and more curved for the regular ISI, as indicated by the significant components of the Repetition by Regularity interaction [$F(9,63) = 2.56$, $p < .05$, for the overall mean square; and $F(1,63) = 9.44$, $p < .01$, and $F(1,63) = 6.41$, $p < .05$, for the linear and quadratic components, respectively]. For the train-by-train averages, the only significant effect was a slow linear decrease in amplitude over the experimental session [overall $F(11,77) = 8.35$, $p < .001$, and the linear $F(11,77) = 27.62$, $p < .001$].

Figure 2 shows the results for the P_2 - N_2 amplitude in the stimulus-by-stimulus averages.

Also, this measure showed an overall linear, slightly curved decrease with stimulus repetition [$F(9,63) =$

2.81, $p < .01$, $F(1,63) = 4.04$, $p < .05$, and $F(1,63) = 7.30$, $p < .01$, respectively]. There was a significant Repetition by Activation interaction that was due to initially bigger responses in the low activation condition that decreased somewhat more rapidly than those in the high activation condition [$F(1,63) = 8.18$, $p < .01$ for the linear component]. Also, for the P_2 - N_2 , the decrease in amplitude with successive stimuli tended to be more pronounced when the ISI was regular, as indicated by the Repetition by Regularity interaction [$F(1,63) = 8.75$, $p < .01$, for the linear component]. The P_2 - N_2 amplitude did not change significantly with trains, but the low activation condition tended to produce bigger responses than the high activation one, as shown by the significant main effect of activation in the train-by-train analysis [$F(1,7) = 7.22$, $p < .05$].

The N_1 latency had a tendency to be shorter with repetition in both the stimulus-by-stimulus and train-by-train analyses [$F(9,63) = 3.00$, $p < .01$, and $F(11,77) = 2.18$, $p < .05$, respectively]. As attested by the Repetition by Activation interactions, this tendency was more pronounced in the low than in the high activation conditions [$F(9,63) = 3.11$, $p < .01$, and $F(11,77) = 2.06$, $p < .05$, respectively]. In the train-by-train averages also, the P_2 latency had a tendency to become shorter with repetition [$F(11,77) = 1.95$, $p < .05$].

There were no significant main effects in the RTs, but the responses tended to become faster with repetition within train in the regular but not in the irregular ISI condition, as shown by a significant interaction effect for the stimulus-by-stimulus means [$F(9,63) = 2.59$, $p < .01$]. For the SCL, there were no significant effects in the stimulus-by-stimulus measures, but in the train-by-train means, there was a tendency towards a lowering of the SCL as the experiment proceeded [$F(11,77) = 2.03$, $p < .05$]. This tendency, furthermore, was more pronounced in the low than in the high activation condition, as indicated by a significant Repetition by Activation interaction [$F(11,77) = 2.05$, $p < .05$].

DISCUSSION

The present results suggest that a regular ISI is a necessary condition for the observation of a rapid, exponential stimulus-by-stimulus decrease in amplitude for the N_1 - P_2 component of the auditory AER. Thus, with an irregular ISI, the results conformed to the low, almost linear decremental function observed by Öhman & Lader (1972), whereas a regular ISI produced an exponential curve very similar to that reported by Fruhstorfer et al

Fig. 2. Effects of regular interstimulus interval and task-induced activation on the mean amplitude of the P_2 - N_2 component of the auditory evoked response for the stimulus-by-stimulus averages ($N = 8$).

(1970), Ritter et al (1968), and Roth & Kopell (1969).

From these results, it is clear that the dispute regarding the nature of the stimulus-by-stimulus decrement of the AER mainly seems to have dealt with a rather narrowly defined instance of experimental conditions. Both the habituation and the neuronal recovery interpretations have difficulties in accounting for the present results. Although faster decrease in response amplitude with regular than with irregular ISI could be predicted from a habituation point of view, it is difficult to see why an exponential "habituation" curve should occur only in the former condition. From an interpretation in terms of neuronal refractoriness, on the other hand, no effect of regularity could be expected (cf. Rothman et al, 1970).

In view of the difficulties that seem to be inherent in a decision about habituation or refractoriness as the basis for our results, a more fruitful course of action might be to elaborate the type of mechanism that seems necessary to account for them. The fact that the regular ISI affected the stimulus-by-stimulus but not the train-by-train averages seems to call for a two-factor explanation, with one factor accounting for short-term and the other for long-term changes in AER amplitude. The former would be an ephemeral inhibitory process, developing during stimulation,

recovering between trains, and dependent on a regular ISI. The latter would be more general, slower in development, not recovering between trains, independent of ISI, and perhaps corresponding to changes in general activation level. In accordance with the latter suggestion, there was a decline in SCL over the experimental session. From this two-factor model, it would be expected that a regular ISI should result in short-term within-train amplitude attenuation, which recovers between trains and is superimposed on a more slowly developing response decrement over the whole experimental session. For an irregular ISI, the short-term mechanism would be less important, and therefore the second mechanism would determine the course of response decrement both within and between trains. In this way, the two curves in Fig. 1 would be replicated. This model would predict the length of the stimulus trains to be critical for the observation of a main effect of regular ISI on AER amplitude. In agreement with this prediction, Rothman et al (1970) observed larger responses with irregular than with regular ISI when 128 stimuli were continually presented. In the present study, however, where there was time for recovery between trains, no main effect of regularity was observed.

The fact that the P_2 - N_2 amplitude, but neither P_1 - N_1 nor N_1 - P_2 , was

affected by the activation conditions gives further support for the notion of these components as reflecting different processes (Bostock & Jarvis, 1971; Wilkinson & Morlock, 1967). In the earlier study (Ohman & Lader, 1972), P_1-N_1 and N_1-P_2 were affected by different conditions of attention, whereas no effect was observed on the P_2-N_2 . The two former components thus reflect attentional status, whereas the latter seems sensitive to changes in activation level.

It seems that a regular ISI is a necessary condition for rapid short-term decrease in AER amplitude, but it is not clear whether it is also a sufficient one. For instance, we do not know whether similar results would have been obtained with a motor response to the stimuli. This question is at present being examined.

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