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THE EXTRACTION OF FREQUENCY INFORMATION FROM ELECTRICAL STIMULATION OF THE MEDIAL GENICULATE BODY

A Thesis Presented

by

Frederick W. Mis

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July, 1973

Abstract

This study sought to determine if the generalization gradient obtained along the frequency dimension of acoustic clicks would be similar for a group of rabbits simultaneously conditioned to stimuli consisting of 15 pulses of brain stimulation per second and 25 clicks per second, and a group of rabbits conditioned to stimuli consisting of 15 and 25 acoustic clicks per second. A summated generalization gradient along the frequency dimension of acoustic clicks was obtained from rabbits conditioned to ESB and acoustic clicks if the electrode tips were located in the medial geniculate body. If the electrode tips were located in nonauditory brain structures (e.g., optic tract, lateral geniculate body, midbrain reticular formation), the generalization gradient obtained along the frequency dimension of acoustic clicks resembled one obtained from a group of rabbits initially conditioned to a stimulus consisting of 25 acoustic clicks per second. The results are discussed in terms of providing evidence for a frequency theory of learning and questioning the usefulness of a "labeled lines" code for carrying information within the central nervous system.

Acknowlegments

I wish to express my gratitude to Dr. John W. Moore for guidance and continuous assistance in all phases of this experiment. I would also like to thank Dr. John T. Danielson and Dr. Arnold D. Well for their helpful comments and the generousness with which they gave their time helping me prepare this manuscript. My parents also deserve a note of thanks for their continued support in my educational endeavors. In addition, W.R.S. and B.G. deserve thanks for their help during various critical periods in my life. I would also like to thank Nancy L. Zygmont for her expert typing and proofreading of this thesis. Lastly, I would like to thank my rabbits for generating aesthetic data.

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In a simple S-R learning situation an organism extracts or processes information contained within the signal or cue and behaves in some appropriate manner. The attributes or dimensions of the signal that control the behavior of the organism have come under increasing scrutiny by learning psychologists. With peripherally presented stimuli there is little difficulty in determining which attributes (frequency, intensity, etc.) of the stimulus come to control the behavior of the organism. The present investigation sought to determine if the pulse frequency attribute of brain stimulation could come to control the behavior of an organism.

Background:

The literature on electrical stimulation of the brain (ESB) (see Doty, 1969) suggests that ESB can function in most, if not all, of the roles of a peripheral stimulus. That is, ESB can serve as a simple CS, a discriminative stimulus, a conditioned inhibitor, a rewarding or punishing stimulus. Although in the behavioral context it appears that peripheral and central stimuli are functionally alike, it has not yet been determined if the information extracted from ESB is similar to that extracted from a peripheral stimulus.

Both transfer designs and generalization tests have been employed in an effort to determine if an organism can extract the same types of information from a centrally presented stimulus as from a peripherally presented stimulus. If one finds transfer in an organism initially conditioned to an acoustic stimulus to stimulation of the medial geniculate body (MGB) and not in an organism initially conditioned to a flash of light one could infer that there was some system-specific transfer between central and peripheral stimuli. Generalization tests have the added advantage of providing information as to which of the parameters of the stimulation is controlling the conditioned response. Such observations permit inference as to what information is being extracted from the stimulus.

Doty and Rutledge (1959) were the first to attempt to determine the degree of transfer of information between peripheral and central (cortical) stimulation. Using both photic and auditory peripheral stimuli, and a number of cortical CSs, Doty and Rutledge found a great deal of nonspecific transfer between all modalities; that is, transfer between the two peripheral CSs as well as from peripheral to cortical CSs and vice versa.

Neider and Neff (1961) attempted to determine if one could "inject behaviorally meaningful information" into a subcortical nuclei of the auditory system. According to Neider and Neff, "behaviorally meaningful information" refers to the ability of the information contained in a train of 100 pulses per second of ESB presented to the inferior colliculus (IC) to elicit a conditioned response given that the organism had been previously conditioned to respond to a train of acoustic clicks at 100 Hz. Neider and Neff investigated generalization both from central to peripheral stimulation and from peripheral to central stimulation. Their basic procedure involved training cats to avoid a mild shock to the foot by flexing the left hind leg when an auditory signal was presented, or when stimulation was presented to a subcortical structure (MGB, IC, auditory radiations (AR), optic tract (OT)). In some subjects, a shuttle box avoidance task was used to assess the amount of information transferred from central to peripheral stimulation.

In testing for generalization from peripheral to central stimulation, Neider and Neff found that there was immediate generalization to stimulation of the IC (all four animals), but much less to stimulation of the cochlear nucleus (two animals a few CRs and two animals no CRs). For the animals trained to avoid shock when subcortical stimulation served as a CS, only one out of three of the animals who had IC stimulation as a CS showed any generalization to peripheral stimulation at the same frequency; the subject trained to avoid shock to AR stimulation and the subject trained to avoid shock to MGB stimulation showed some nominal generalization to the peripheral stimulus while the subject trained to avoid shock to stimulation of the OT failed to show any generalization to the peripheral auditory stimulus.

Continuing this line of research, Schuckman and Battersby (1966) investigated the generalization of a flicker discrimination to either cortical or subcortical stimulation in the monkey. In two of their four animals (one subject stimulated in the occipital cortex and one subject stimulated in the corpus straitum) there was some transfer of the discrimination, but only at high (10-15mA) intensities of brain stimulation.

Briefly summarizing these investigations, one finds evidence of nonspecific transfer both from peripheral to central and central to peripheral stimulation. There is also evidence of system-specific generalization from central to peripheral stimulation. However, none of these investigations provide sufficient information to determine the specific nature of the relevant stimulus dimensions mediating transfer between peripheral and central stimulation, more precisely the types of information the organism can extract from ESB.

Problem:

One major question that remains unanswered is whether an organism can extract from ESB the necessary information to code the specific parameters of the ESB, particularly the frequency of the stimulation. A recent investigation by Swadlow and Schneiderman (1970) attempted to determine if responding to ESB could come under the dimensional control of the frequency of the ESB. Dimensional control of responding to the frequency of the stimulation refers to the ability of the training frequency to elicit the most responses during a generalization test while either higher or lower frequencies of stimulation elicit fewer responses. Swadlow and Schneiderman conditioned the rabbit's nictitating membrane response to a train of ESB to the lateral geniculate body (LGB) of 21 Hz. After 10 days of acquisition each animal was given a generalization test in which the frequency of the stimulation was varied and the total stimulus energy (TSE) was allowed to vary along with it, or the frequency of the stimulation was varied but the TSE was held constant by covarying the pulse duration or pulse amplitude (intensity). Most responses during the generalization test occurred to the training frequency providing the TSE was held constant, suggesting that the organism may have been coding the ESB according to the frequency of the stimulation. When the TSE was allowed to vary, the number of responses increased as a function of the TSE. Given the necessity of covarying the pulse duration or amplitude in order to establish control of responding by the frequency of the stimulation it cannot be determined that the responding of the organism during the generalization test was, in fact, under the control of the frequency of the stimulation, and not one of the other parameters of the stimulation. What is needed to overcome this obstacle is a test for dimensional control of responding which unequivocally demonstrates that the frequency characteristics of the signal are being extracted.

The summated generalization technique employed by Liu (1971) may provide a solution to the problem. Liu, using the rabbit nictitating membrane preparation, demonstrated that nondifferential training to two pure tone CSs of different frequencies resulted in a generalization gradient with a peak lying between the two training CSs. If an organism is able to extract the same kind of information from both ESB and acoustic stimulation, when a train of ESB to the MGB or some other subcortical nuclei of the auditory system is substituted for one of the acoustic CSs, the organism should produce a summated generalization gradient similar to Liu's. Specifically, consider a rabbit conditioned to both a train of ESB at 15 Hz and a train of acoustic clicks at 25 Hz and tested for generalization along the click frequency dimension. In this case, a summated generalization gradient with a peak at 20 Hz would indicate that an organism has the ability to extract frequency information from both the acoustic clicks and the ESB, provided the subjects conditioned to clicks of 15 and 25 Hz produce summated generalization gradients. If the ESB was a more "potent" stimulus and the organism was extracting frequency information from it, the peak of the gradient should be shifted in the direction of the frequency of the ESB, while if the ESB was a less salient stimulus the peak may be closer to the frequency of the acoustic stimulus.

Theoretical Relevance:

The present investigation was designed to provide information about the type of code employed by the CNS in conveying information from the peripheral transducers to the central processing stations. Mountcastle (1967) discussed a variety of available codes. These range from a simple frequency code within a single axon, to a frequency profile within a population of axons or neurons (a group of axons or neurons that are carrying the same frequency coded information), to a coincidence-gating code that serves as a method of informing the organism of the simultaneous or almost simultaneous arrival of two bits of information of the same modality. One finds that most of the codes discussed by Mountcastle as possible means of conveying information within the CNS involve some variation in the frequency of the generated potentials or in the number or temporal characteristics of the potentials. One alternative code, that does not involve modulations of this type, is the "labelled lines" code, in which a particular axon or group of axons always carry the same sensory experience whenever they are activated.

Relating these codes to the auditory system, the "labelled lines" code is the one code that fulfills the requirements for a place theory of hearing, while most other codes would be compatible with some form of a volley or frequency theory of hearing (Wever, 1949). The present experiment should provide information on the place and volley properties of the auditory system. Assuming that MGB stimulation initiates activity in a large collection of labelled lines, each coding a different acoustic frequency, summated generalization gradients along the click frequency dimension would not be expected. Instead, conditioning to ESB would entail simultaneous reinforcement of a broad range of auditory frequencies, each contributing uniformly to the click frequency gradient. In contrast, the volley principle requires that ESB initiates a frequency specific train of impulses independent of which particular acoustic neurons are activated. A summated click gradient with a peak shifted toward the frequency of the ESB would imply successful extraction of the frequency information from the pulse train.

Method

Animals:

The animals were 29 experimentally naive male and female albino rabbits who weighed approximately 3.0 kg and were approximately 100 days old at the time of surgery. At all times the rabbits were maintained in individual cages on ad lib food and water.

Apparatus:

A detailed description of the apparatus and technique for recording from the nictitating membrane (NM) is available elsewhere (Gormezano, 1966). Two rabbits were run concurrently in the upper two drawers of a four drawer fireproofed file cabinet that was ventilated and illuminated. A panel in front of the subjects supported two house lights (28 V dc. behind translucent white plastic) and two impedance matched speakers which were used to present the click CSs. The unconditioned stimulus was administered via stainless steel wound clips attached approximately 1/2 cm below and posterior to the right eye, and consisted of a 2 mA shock of 50 msec. duration presented immediately after the cessation of the conditioned stimulus (CS).

Each rabbit was restrained within a Plexiglas box identical to those described by Gormezano. A rotary minitorque potentiometer coupled to a suture in the right nictitating membrane of the rabbit served to convert any lateral movement of the right nictitating membrane to a dc signal that was recorded on a two channel Beckman RP Dynograph. A conditioned response (CR) was defined as a 1 mm positive deflection of the recording pen and was equal to less than a 1 mm lateral movement of the NM.

The click CSs were generated by a transistorized click generator with a frequency range from 5 to 35 Hz. The ESB CSs were delivered via a Grass Model S-88 stimulator in conjunction with stimulus isolation and constant current units. CS_1 was either a 25 Hz (85 dB) train of clicks lasting 500 msec., or a 500 msec. train of ESB of 25 pulses per second, 6 msec. duration and 0.2 mA intensity monophasic rectangular pulses; while CS_2 was either a 15 Hz (85 dB) train of clicks lasting 500 msec., or a 500 msec. train of ESB of 15 pulses per second, 10 msec. duration and 0.2 mA intensity monophasic rectangular pulses presented bilaterally.

Surgery and Histology:

Each rabbit was implanted with four bipolar electrodes, two of which were aimed at the MGB and the other two which were aimed at the LGB. Stereotaxic placement of the electrodes was based on coordinates from Sawyer, Evert, and Green (1954).

The electrodes were constructed of 00 Clay-Adams insect pins (shaft diameter 0.25 mm; tip diameter 0.03 mm), insulated with insul-X except for an area 0.5 mm from the tip, and bonded together by a bead of epoxy resin at an approximate point on the electrode such that when lowered into the approximate brain structure the bead should be flush with the skull of the animal. Separation between the tips of each electrode pair was no more than 1 mm.

Forty-five minutes prior to surgery each rabbit was injected with 15 mg/kg of Thorazine (IM) to potentiate the effects of Nembutal anesthetic (IV, 15-20 mg/kg cut with physiological saline). Prior to placing the rabbit in a large Kopf stereotaxic frame equipped with a rabbit adapter, the animal was injected with Xylocaine at the base of each ear and then a SC application of Xylocaine with epinephrine to the scalp.

The procedure for implanting electrodes in the rabbit is the same as for the rat (see Miller, Coons, Lewis, & Jensen, 1961). Briefly, a 4 to 5 cm midline incision was made extending caudually from between the eyes. The skull was then exposed by scraping and pushing the tissue and muscle fibers laterally and then cleaned and dried. Two stainless steel jeweler's screws .061 inches in diameter were then inserted into the skull to anchor the dental cement. One was located approximately 6 mm anterior to bregma and 6 mm lateral to the midline while the other was located approximately 12 mm posterior to bregma and 7 mm contralateral.

The skull was then aligned with the stereotaxic instrument such that lambda was 1.5 mm below bregma. Then the placements for the electrodes were marked on the skull with the stereotaxic instrument, and small holes drilled into the bone. The electrodes aimed at the MGB were inserted first.

A small amount of dental cement (William Getz Corp.) was placed around the electrode and the posterior anchor screw, and then the liquid fastener was applied to the cement. After the cement had hardened, the stereotaxic arm was removed from the electrode. After all the electrodes had been implanted and the protruding end of each electrode clipped off, the leads from the electrodes were connected to an Amphenol socket and the entire assembly secured to the skull with dental cement. Each rabbit was given a minimum of 10 days to recover from surgery prior to being run in the experiment.

Following training and testing, the animals were given an overdose of Nembutal and perfused with isotonic saline followed by 10% formalin that had potassium ferricyanide dissolved in it. Prior to removing the brains from the animals, a small current was passed through the electrodes used during training and/or testing to mark the cite of the electrode tips. The brains were then removed, stored in formalin, and subsequently frozen sections of the brain were cut at 48 μ. Relevant sections were then floated on to a glass slide and stained with cresyl violet. The location of the electrode tips were determined with the aid of the Sawyer, Evert, and Green (1954), McBride and Klemm (1968) and Gerhard (1968) atlases.

Design and Procedure:

The animals were assigned to one of the four following groups:

1a. Group CLICK (25) Single stimulus training to 25 clicks per second. ($N = 4$)

b. Group ESB (15) Single stimulus training to 15 pulses of ESB per second. ($N = 4$)

2a. Group CLICK (15&25) Nondifferential training to 15 and 25 clicks per second. ($N = 4$)

b. Group ESB (15&25) Nondifferential training to 15 and 25 pulses of ESB per second. ($N = 4$)

3. Group ESB (15) & CLICK (25) Nondifferential training to 15 pulses of ESB per second to non-auditory brain structures and 25 clicks per second ($N = 7$)

4. Group MGB (15) & CLICK (25) Nondifferential training to 15 pulses of ESB per second to the Medial Geniculate Body and 25 clicks per second. ($N = 6$)

On the day before the first conditioning session, the nictitating membrane was sutured, and the animals were habituated to the apparatus by being placed in the restraining box and remaining in the experimental enclosure for at least 45 minutes.

Training was begun on the next day and consisted of 50 presentations of each CS per day, or in the case of the single stimulus conditions, 50 presentations of the CS per day, with reinforcement occurring randomly on half of these presentations. For the groups with two CSs, no more than two trials were of the same type (i.e., there were no more than two presentations of either CS in a row and no more than two reinforcements in a row). All groups were given 8 days of acquisition training followed by at least 2 days of generalization testing. On the first day of generalization testing all the subjects were given an additional 10 presentations of each of the training stimuli, 5 of which were reinforced. Following this additional acquisition training, each subject was presented with 7 nonreinforced presentations in a quasi-random order of each of the following click frequencies: 5, 10, 15, 20, 25, 30, 35 Hz, and 7 presentations of each of the following pulse trains of ESB: 5, 10, 15, 20, 25, 30, 35 pulses per second to either the MGB, or in the case of the subjects in Group ESB (15) & CLICK (25), to non-auditory brain structures. The pulse duration of the ESB was covaried in order to keep the TSE constant. On the second and subsequent days of generalization testing the subjects were not given any additional acquisition training, but received the same sequence of test stimuli they were given on Day 1 of the generalization testing.

For all nondifferential training groups the ITI was a constant 30 seconds, and for the single stimulus training groups the ITI was a constant 60 seconds. During the generalization testing the ITI was a constant 30 seconds.

Results

Histology:

Initially thirteen animals were conditioned to 15 pulses of brain stimulation per second and 25 acoustic clicks per second. For nine of these animals the electrodes selected were aimed at the MGB, while for the four other animals the electrodes were aimed at the LGB. Histological analysis for those animals whose electrodes were aimed at the MGB indicated that in six of these animals both bipolar electrodes were in the MGB. These six animals constitute the Group MGB (15) & CLICK (25). The tips of the electrodes for the other three animals were located in the Midbrain Reticular Formation (MRF). These three animals and the four animals for whom the electrodes were aimed at the LGB have been designated as Group ESB (15) & CLICK (25). For the animals whose electrodes were aimed at the LGB, three animals had both electrodes located primarily in the LGB, while the electrodes for the fourth animal were located in the Optic Tract. In Group ESB (15) three animals had both electrodes located in the MGB while the other animal had one electrode in the MGB and one in the MRF. For the animals in Group ESB (15 & 25), two animals had both electrodes in the MGB while the other two animals had their electrode tips located in the most medial portions of the MGB and in the MRF. For the groups initially conditioned only to acoustic clicks, six animals had the tips of their electrodes located in the MGB, one animal had one electrode located in the MGB while the other electrode was located in the MRF, and the other animal had both his electrode tips located in the MRF. Figure 1 indicates the location of the electrode tips for all animals in this experiment. The reconstructions are based on the Gerhard (1968) atlas.

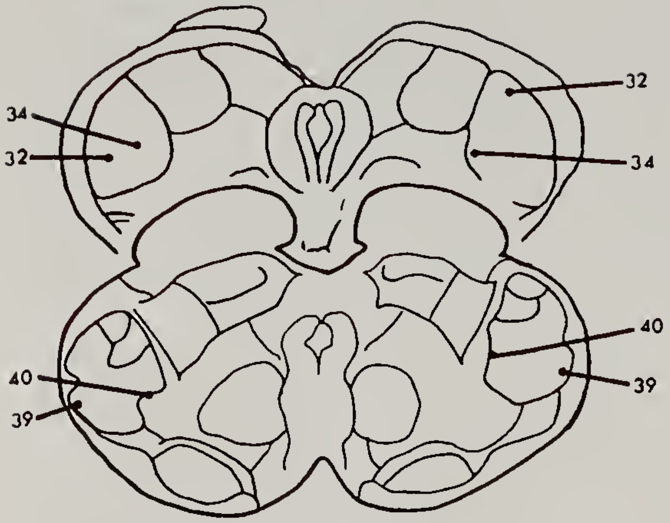
<u>Behavioral Data</u>:

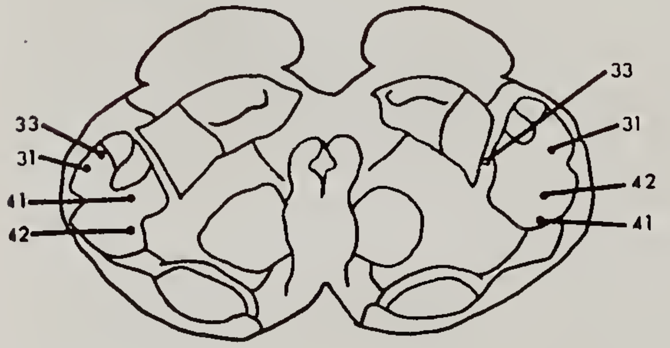
Figure 2 presents the mean absolute generalization gradients along the acoustic click dimension (Panels A & B) and the pulse frequency dimension of brain stimulation (Panels C & D) for the various conditions of this experiment. For those animals initially conditioned to either acoustic clicks or brain stimulation, gradients along the other dimension are not presented because the overall level of responding on the untrained dimension was extremely low. Individual gradients for each animal are presented in Appendix A.

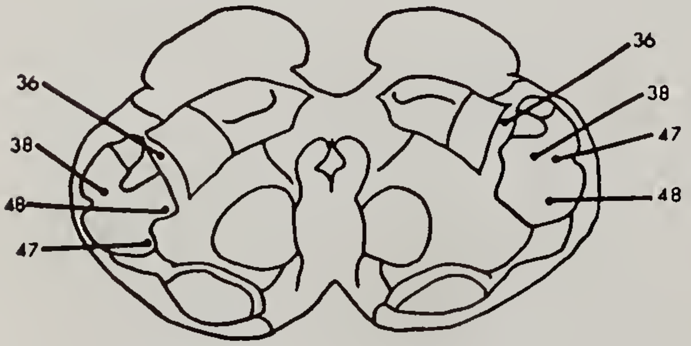
Panel A of Figure 2 depicts the data that is most relevant to the question of whether or not an organism can extract frequency specific information from electrical stimulation of the brain. For the animals in Group MGB (15) &

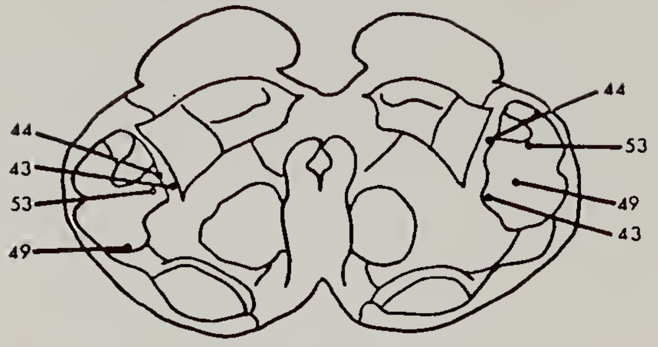
FACE PAGE FOR FIGURE 1

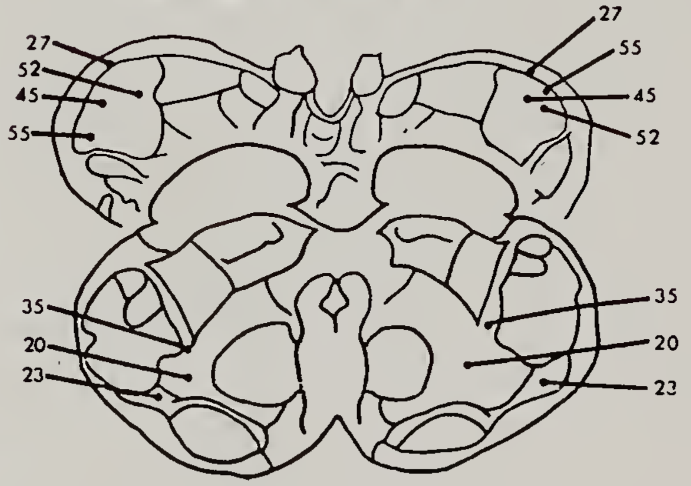
Figure 1. The location of the electrode tips for each rabbit used in this experiment as a function of the experimental group (outlines drawn from Gerhard, 1968 atlas, Plates 28, 31, and 32). The identification number of each rabbit is also given.


Group CLICK (25)


Group ESB (15)


Group CLICK (15 & 25)

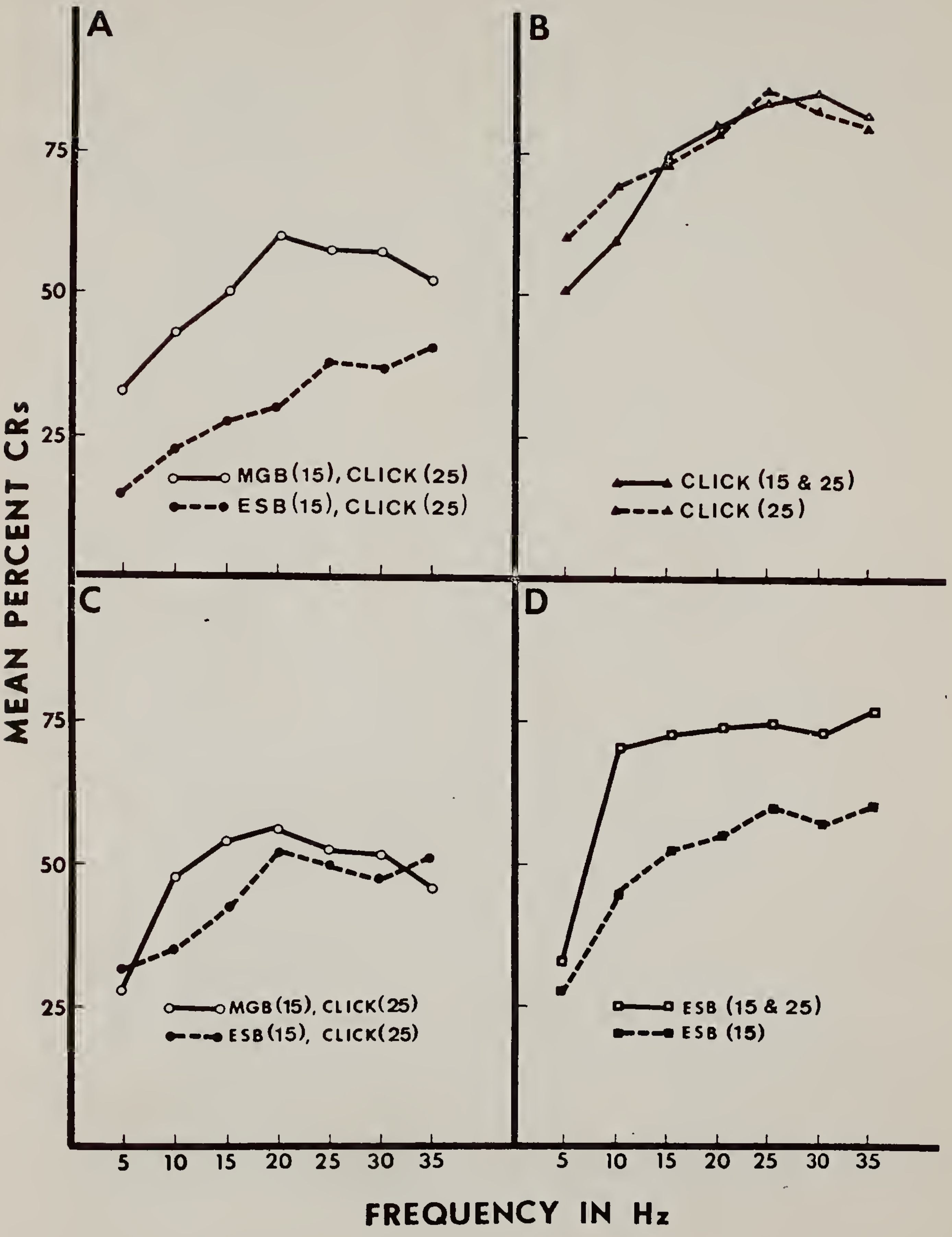

Group ESB (15 & 25)


Group ESB(15) & CLICK(25)


Group MGB(15) & CLICK (25)

FACE PAGE FOR FIGURE 2

Figure 2. Mean per cent conditioned responses made during the generalization test to each frequency of acoustic clicks (Panels A and B) and pulses of brain stimulation (Panels C and D).

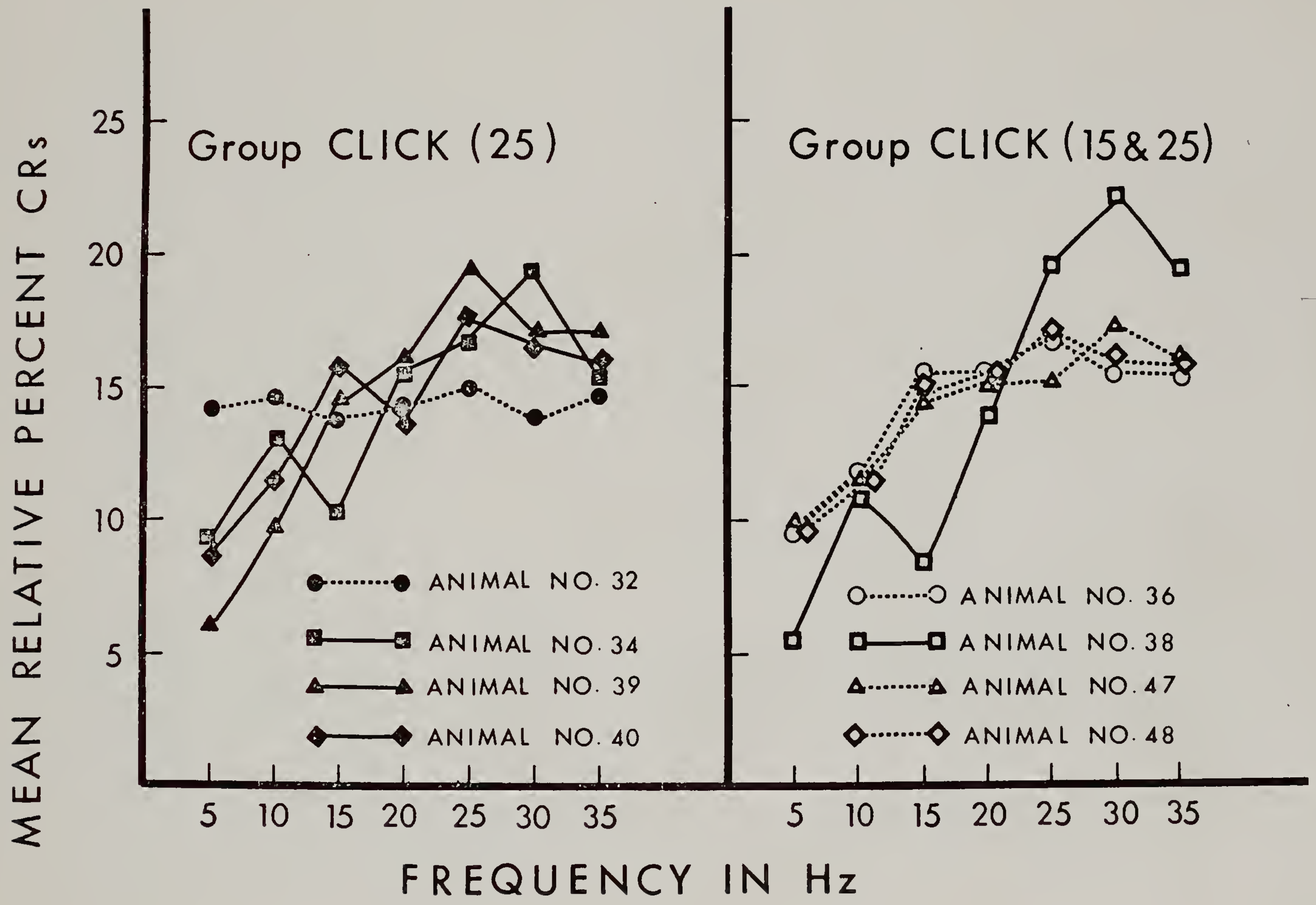

A
B
C
D
MEAN PERCENT CRs
75
50
25
FREQUENCY IN Hz
5
10
15
20
25
30
35
MGB (15), CLICK (25)
ESB (15), CLICK (25)
CLICK (15 & 25)
CLICK (25)
MGB (15), CLICK (25)
ESB (15), CLICK (25)
ESB (15 & 25)
ESB (15)

CLICK (25) one observes a summated generalization gradient with a peak at 20 acoustic clicks per second, while for those subjects in Group ESB (15) & CLICK (25) no summated generalization gradient was evident. A summated generalization gradient along the acoustic click dimension as found in Group MGB (15) & CLICK (25) would only come about if the animals extracted information regarding the pulse frequency of brain stimulation as well as information about the frequency of acoustic clicks. The failure to find a summated generalization gradient in the animals in Group ESB (15) & CLICK (25) indicates that this frequency extraction was limited to information presented to the auditory system.

In Panel B of Figure 2 the generalization gradients for the animals in Group CLICK (25) and Group CLICK (15 & 25) are presented. In both cases no summated generalization gradient was observed. Although the mean absolute generalization gradient for Group CLICK (15 & 25) does not indicate excitatory summation, when one scrutinizes the gradients for individual animals, three of the animals demonstrated excitatory summation. The gradient of the fourth rabbit in this group (Animal no. 38) had the form of a single stimulus excitatory gradient. Also, examination of the individual gradients for Group CLICK (25) indicates that the flattening of this group's gradient was due primarily to one animal (Animal no. 32), which gave a CR to 95% of all the acoustic click stimuli presented during generalization tests. The relative generalization gradients for individual animals in these two groups are presented in Figure 3. (The relative generalization gradient for an individual animal was computed by dividing the number of responses emitted to each test frequency of stimulation by the total number of responses emitted during the generalization test to all the stimulation of that dimension.) Therefore, even though the mean absolute gradient of Group CLICK (15 & 25) does not indicate excitatory summation, and the mean absolute gradient of Group CLICK (15) does not demonstrate good dimensional stimulus control, inspection of the individual gradients indicates that excitatory summation occurs for most animals in Group CLICK (15 & 25) as was found in Group MGB (15) & CLICK (25), and most animals in Group CLICK (25) demonstrated good dimensional stimulus control. It should also be noted that in comparing Group MGB (15) & CLICK (25) to Group CLICK (15 & 25), the shape of the generalization gradient is similar; this similarity is especially noticeable when the individual generalization gradients are compared. In addition, the slope of the generalization gradient along the acoustic click dimension for Group ESB (15) & CLICK (25) and Group CLICK (25) is similar from 5 Hz to 25 Hz, indicating that the animals in Group ESB (15) & CLICK (25) were behaving in a manner similar to a group of animals conditioned to 25 acoustic clicks per second.

FACE PAGE FOR FIGURE 3

Figure 3. Mean relative per cent conditioned responses made during the generalization test to the various frequencies of acoustic clicks for the individual animals in Group CLICK (25) and Group CLICK (15 & 25).


Group CLICK (25)
Group CLICK (15&25)
MEAN RELATIVE PERCENT CRs
25
20
15
10
5
ANIMAL NO. 32
ANIMAL NO. 34
ANIMAL NO. 39
ANIMAL NO. 40
ANIMAL NO. 36
ANIMAL NO. 38
ANIMAL NO. 47
ANIMAL NO. 48
5
10
15
20
25
30
35
FREQUENCY IN Hz

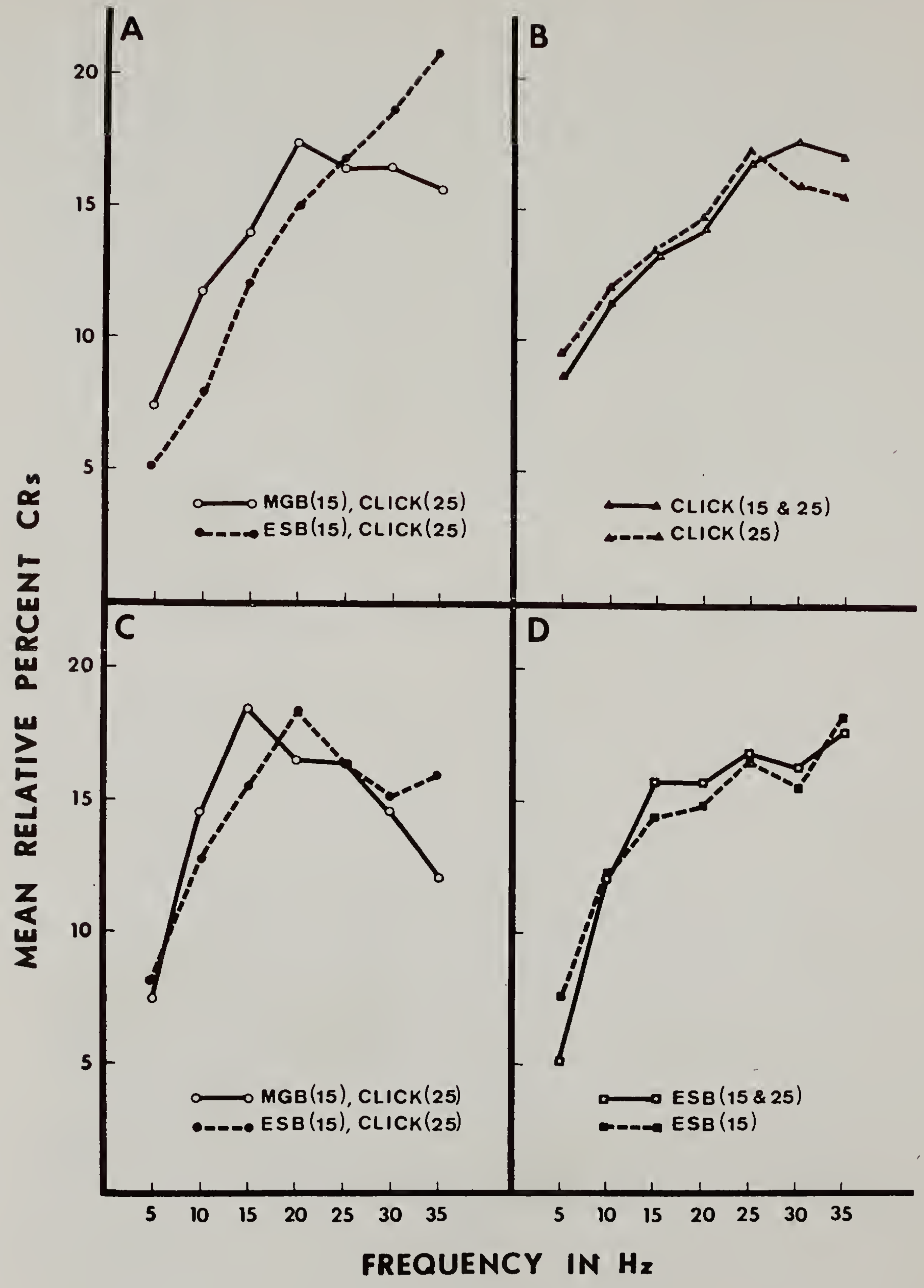
Panel C of Figure 2 presents the generalization gradients along the pulse frequency dimension of brain stimulation for the same animals as in Panel A. For both groups of animals the gradients indicate little stimulus control by the training frequency. Panel D of Figure 2 presents the generalization gradients for those animals in Group ESB (15) and Group ESB (15 & 25). For the animals conditioned to two frequencies of brain stimulation one observes what appears to be a summated generalization gradient, while for those animals in Group ESB (15), however, conditioned responding appeared to be an increasing function of the frequency of the brain stimulation; that is, the higher the frequency of the brain stimulation the more responding that was elicited.

Figure 4 presents the mean relative generalization gradients for the same animals as in Figure 2. Generally, these gradients provide further support for the inferences obtained from the absolute generalization gradients. The inference that Group MGB (15) & CLICK (25) was able to extract frequency specific information from the brain stimulation was supported by the fact that the relative overall level of responding to 20 acoustic clicks per second during the generalization test for this group was significantly higher than for Group ESB (15) & CLICK (25), (Mann-Whitney $\underline{U}$ (7,6) = 7; $\underline{p}$ = .026). (See Panel A of Figure 4.)

Examination of responding of animals conditioned to

FACE PAGE FOR FIGURE 4

Figure 4. Mean relative per cent conditioned responses made during the generalization test to each frequency of acoustic clicks (Panels A and B) and pulses of brain stimulation (Panels C and D).


A
B
C
D
MEAN RELATIVE PERCENT CRs
20
15
10
5
MGB(15), CLICK(25)
ESB(15), CLICK(25)
CLICK(15 & 25)
CLICK(25)
ESB(15 & 25)
ESB(15)
5
10
15
20
25
30
35
FREQUENCY IN Hz

either acoustic clicks or ESB indicated that for those animals initially conditioned only to click stimuli, five out of eight of these animals responded one or more times to ESB during the generalization tests. Also, four out of eight of the animals initially conditioned only to ESB responded one or more times to acoustic clicks during the generalization tests. The stimulating electrodes for all these animals were located in the MGB. In general, there was no tendency for these animals to respond to a particular frequency of stimulation.

During the acquisition phase of the experiment in those animals conditioned to both brain stimulation and acoustic clicks there was more responding to brain stimulation, the lower frequency stimulus ($\underline{t} = 2.669$, $\underline{df} = 12$, $\underline{p} < .05$). Also, for those animals conditioned to two frequencies of either brain stimulation or acoustic clicks there was a slight but nonsignificant tendency for these animals to respond more to the higher frequency of stimulation during acquisition ($\underline{t} = 1.99$, $\underline{df} = 7$, $\underline{p} < .10$).

Discussion

The major findings of this investigation are: (a) rabbits were able to extract pulse frequency information from electrical stimulation of the brain. (b) This extraction of the frequency information was system-specific; that is, it was restricted to the sensory system (the auditory system in this case) that was activated by the brain stimulation. (*c*) Some generalization to acoustic clicks was found in those animals initially conditioned to stimulation of the MGB, and some generalization to electrical stimulation of the MGB was found in those animals initially conditioned only to acoustic clicks. (*d*) During the acquisition phase of the experiment there was a tendency for the animals conditioned to both brain stimulation and acoustic clicks to respond more to the brain stimulation than to the acoustic click stimulus.

The finding that an organism can extract frequency information from low frequency stimulation of the MGB, and the recent findings of Clark, Nathar, Kranz, and Maritz (1972) that electrical stimulation of the cochlea in cats up to 200 pulses per second produces pitch sensations demonstrates the importance of a frequency theory (Wever, 1949) in the coding of low frequency acoustic stimuli. In addition to demonstrating the importance of a frequency theory in the coding of low frequency acoustic stimuli, the data obtained from this investigation call into question the usefulness of a "labelled lines" code for conveying low frequency auditory information within the CNS. If the CNS employed "labelled lines" to encode low frequency auditory stimuli one might expect an elevation of the gradient for Group MGB (15) & CLICK (25) as compared to Group CLICK (25). This elevation of the gradient would have occurred because acquisition to ESB would have presumably entailed simultaneous conditioning to a broad range of frequencies (i.e., many "labelled lines") each contributing uniformly to each point along the test dimension. In contrast, the gradients obtained from the animals in Group MGB (15) & CLICK (25) differed in shape from that of the animals in Group CLICK (25) (the former showing summation, the latter not). In addition, as seen in Figure 2, the generalization gradient obtained from animals in Group MGB (15) & CLICK (25) was below that of the animals in Group CLICK (25) indicating that excitatory summation probably did not occur at each point along the acoustic click dimension.

The findings that summation was obtained in Group MGB (15) & CLICK (25) and not in Group ESB (15) & CLICK (25) implies that not only is it possible to extract frequency specific information from brain stimulation, but that the nature of the responding of the organism is governed by the functional system activated by the brain stimulation. This system specificity is in some respects similar to the findings that little generalization occurs between electrode loci unless the electrodes are in the same area within a neural structure (Manning & Schneiderman, 1970; Nielson, Knight, & Porter, 1962; Swadlow & Schneiderman, 1970). Doty (1965) suggests that generalization between electrode loci also may indicate that the stimulation of these electrodes produces equivalent sensory experience within the organism. In the present experiment, stimulation of the MGB at 15 pulses per second appears to have been producing the same sensory experience as a stimulus consisting of 15 acoustic clicks per second.

The finding that there was some generalization from stimulation of the MGB to acoustic clicks and some generalization from acoustic clicks to MGB stimulation in essence replicates the findings of Neider and Neff (1961). As in the Neider and Neff study, the amount of generalization obtained in this case was weak. Given that little generalization is observed between the two dimensions when the animals are conditioned only to one dimension and tested on the other, the question arises as to the origin of the summation effect observed in Group MGB (15) & CLICK (25). Evidently it is essential that animals in this group compare the neural activity initiated by the two training stimuli over a series of acquisition trials. The subjects in Group ESB (15) & CLICK (25) may also have made this comparison, but given that the two stimuli were activating different neuronal pools, the two CSs did not acquire sufficient excitatory strength along the same dimension.

The results of the generalization tests along the pulse frequency dimension of brain stimulation holding the TSE constant partially replicates the findings of Swadlow & Schneiderman (1970). Of the seventeen animals who had one frequency of brain stimulation as a CS, seven animals produced a generalization gradient with a peak at or near the training frequency (15 pulses per second). In general the gradients for the other ten animals demonstrated either an increasing function of the frequency of the brain stimulation or an almost equal responding to all frequencies of brain stimulation. The fact that the majority of the animals conditioned to one frequency of brain stimulation failed to show good dimensional control along the ESB frequency dimension raises some question about the effectiveness of holding the TSE constant in order to observe dimensional stimulus control along the pulse frequency dimension of brain stimulation. Variations in the threshold energy to elicit a CR might account for this poor dimensional control. However, ancillary data gathered in this investigation indicates that the threshold for responding to ESB was solely a function of the TSE of the brain stimulation and essentially constant over the various frequencies. For example, when the frequency of the ESB was 5 Hz and the pulse amplitude was 200 μA the pulse duration had to be at least .468 msec. in order to reliably elicit a CR; while if the frequency of the ESB was 40 Hz and the pulse amplitude was 200 μA then the pulse duration had to be at least .058 msec. in order to reliably elicit a CR. Data relevant to the question of ESB thresholds are presented in Appendix B. It should be noted that the pulse durations of brain stimulation used in this experiment were approximately ten times as great as those used in the Swadlow and Schneiderman study, raising the possibility that the inability to replicate the findings of Swadlow and Schneiderman may have been a function of this difference in pulse duration.

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Appendix A

The individual relative generalization gradients along the click frequency and pulse frequency dimensions for all the animals in this experiment as a function of experimental condition.

Table 1

Relative percent responding to each frequency of acoustic click for the animals in Group CLICK (25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
32	14.1	14.4	13.8	14.1	15.0	13.8	14.7	326
34	9.1	13.0	10.4	15.6	16.9	19.5	15.6	77
39	6.1	9.8	14.6	15.9	19.5	17.1	17.1	82
40	8.8	11.4	15.8	14.0	17.5	16.7	15.8	144

Relative percent responding to each frequency of brain stimulation for the animals in Group CLICK (25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
32	9.7	16.4	19.4	12.9	14.0	11.8	16.1	93
34	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
39	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
40	50.0	50.0	0.0	0.0	0.0	0.0	0.0	6

Table 2

Relative percent responding to each frequency of acoustic click for the animals in Group ESB (15).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
31	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
33	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
41	0.0	28.6	14.3	0.0	28.6	0.0	28.6	7
42	12.5	12.5	18.8	18.8	12.5	12.5	12.5	16

Relative percent responding for each frequency of brain stimulation for the animals in Group ESB (15).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
31	7.3	13.8	13.8	16.3	16.3	16.3	16.3	123
33	2.3	15.9	18.2	13.6	18.2	13.6	18.2	44
41	7.1	10.7	10.7	14.3	14.3	17.9	25.0	28
42	13.8	8.6	15.5	15.5	17.2	15.2	13.8	58

Table 3

Relative percent responding to each frequency of acoustic click for the animals in Group CLICK (15 & 25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
36	9.5	11.9	15.5	15.5	16.7	15.5	15.5	84
38	5.6	11.1	8.3	13.9	19.4	22.2	19.4	36
47	9.9	11.6	14.6	15.3	15.3	17.3	16.0	294
48	9.7	11.7	14.9	15.2	16.8	15.9	15.9	309

Relative percent responding to each frequency of brain stimulation for the animals in Group CLICK (15 & 25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
36	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
38	50.0	50.0	0.0	0.0	0.0	0.0	0.0	2
47	33.3	0.0	0.0	0.0	0.0	33.3	33.3	3
48	0.0	0.0	0.0	100.0	0.0	0.0	0.0	2

Table 4

Relative percent responding to each frequency of acoustic click for the animals in Group ESB (15 & 25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
43	0.0	0.0	0.0	100.0	0.0	0.0	0.0	1
44	5.6	11.1	5.6	27.8	22.2	11.1	11.1	18
49	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0
53	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0

Relative percent responding to each frequency of brain stimulation for the animals in Group ESB (15 & 25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
43	5.3	14.4	15.7	15.7	16.5	15.4	17.0	395
44	10.1	17.0	14.8	15.1	14.2	14.8	14.2	318
49	0.0	4.5	11.9	16.7	21.4	23.8	21.4	42
53	5.1	12.8	20.5	15.4	15.4	12.8	17.9	39

Table 5

Relative percent responding to each frequency of acoustic click for the animals in Group ESB(15) & CLICK(25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
20	7.8	6.9	11.8	15.7	16.7	20.6	20.6	102
23	3.3	6.7	10.0	13.3	13.3	26.7	26.7	30
27	13.5	14.9	13.5	12.2	16.2	14.9	14.9	74
35	11.3	13.2	13.2	15.1	20.8	13.2	13.2	53
45	0.0	6.7	13.3	13.3	26.7	13.3	26.7	15
52	0.0	7.1	14.3	21.4	21.4	14.3	21.4	14
55	0.0	0.0	9.5	14.3	23.8	28.6	23.8	21

Relative percent responding to each frequency of brain stimulation for the animals in Group ESB(15) & CLICK(25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
20	0.0	5.9	8.8	8.8	17.6	17.6	41.2	34
23	3.3	7.6	12.0	20.7	20.7	18.5	17.4	92
27	14.8	13.6	14.8	16.0	13.6	12.3	14.8	81
35	14.6	14.6	13.5	14.6	13.5	14.6	14.6	96
45	18.5	14.8	13.0	16.7	14.8	13.0	9.3	54
52	5.9	17.6	23.5	29.4	11.8	11.8	0.0	17
55	0.0	0.0	22.7	22.7	22.7	18.2	13.6	22

Table 6

Relative percent responding to each frequency of acoustic click for the animals in Group MGB(15) & CLICK(25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
21	11.3	11.3	15.1	16.4	17.0	16.4	12.6	159
22	8.3	10.8	14.2	19.2	16.7	16.7	14.2	120
26	7.5	14.0	13.1	15.9	16.8	16.8	15.9	107
37	0.0	12.5	12.5	18.8	18.8	18.8	18.8	16
46	11.3	14.5	13.8	15.7	14.5	14.5	15.7	159
56	6.7	8.0	16.0	18.7	16.0	17.3	17.3	75

Relative percent responding to each frequency of brain stimulation for the animals in Group MGB(15) & CLICK(25).

	Frequency in Hz							
Animal No.	5	10	15	20	25	30	35	Total No. Responses
21	10.0	16.7	20.0	13.3	23.3	10.0	6.7	30
22	9.5	12.7	19.0	15.9	12.7	15.9	14.3	63
26	8.3	15.6	15.9	16.7	14.9	14.5	14.1	276
37	0.0	18.2	27.3	18.2	13.6	13.6	9.1	22
46	8.1	11.5	13.5	16.9	16.2	17.6	16.2	148
56	9.5	12.2	14.9	17.6	17.6	16.2	12.2	74

Appendix B

Procedure and results of the brain stimulation threshold test.

PROCEDURE AND RESULTS

One to three weeks after the completion of the main experiment 10 animals were given 100 additional conditioning trials to 15 pulses of brain stimulation per second to the training loci. The pulse duration of the ESB was 10 msec. and the pulse amplitude was 200 µA. On the next day each rabbit was given 5 reinforced presentations of the pulse frequency and pulse duration combinations presented in Table 1. (Using two other rabbits, it was determined that the TSE values used in the experiment were at least 4 times above threshold; therefore, highest TSE used in this experiment was much lower than that used in the main experiment.) The five presentations of each combination of pulse frequency and pulse duration were presented successively, but the various combinations of pulse frequency and pulse duration were randomized within the session. At each frequency there were eight TSE values which were the same for all frequencies of brain stimulation. The ITI was a constant 30 sec. during both sessions and the ISI was 500 msec. The US was a 2 mA shock of 50 msec. duration.

The total number of conditioned responses elicited by each combination of pulse frequency and pulse duration for all animals is presented in Table 2. As seen in Table 2, the fifth highest TSE values used in this threshold test reliably elicited a conditioned response while lower TSE values elicited fewer responses. The trend in responding that is seen in Table 2 accurately describes the responding of each rabbit during the threshold test.

Table 1

The eight pulse durations used in combination with the various frequencies to determine the lowest TSE value that would reliably elicit a conditioned response. (Expressed in msec.)

	Frequency in Hz				
Ranked TSE	5	10	15	20	40
1	7.500	3.750	2.500	1.870	.937
2	3.750	1.875	1.250	.937	.468
3	1.875	.937	.625	.468	.234
4	.937	.468	.312	.234	.117
5	.468	.234	.156	.117	.058
6	.234	.117	.078	.058	.029
7	.117	.058	.039	.029	.014
8	.058	.029	.018	.014	.007

Table 2

Total number of conditioned responses elicited by each combination of pulse frequency and pulse duration for all the animals tested.

	Frequency in Hz				
Ranked TSE	5	10	15	20	40
1	47	50	50	49	47
2	45	47	49	50	45
3	43	46	42	43	36
4	45	42	34	32	30
5	41	30	30	21	38
6	28	14	25	27	28
7	12	18	12	13	11
8	17	11	4	7	5