cagon, secretin, glucose, and bovine serum albumin, similarly administered, did not. Subsequently several groups have shown that intravenous or intraperitoneal administration of purified CCK or CCK-8, or both, can elicit satiety-like behavior in several animal species (*1*). However, the doses administered were so large that they resulted in circulating levels likely to be in excess of those occurring postprandially.

It has long been appreciated that damage to the ventromedial hypothalamus results in hyperphagia and obesity. Thus if CCK were to be involved in control of appetite by the ventromedial hypothalamus one would expect that it would be more effective from intracranial than from peripheral sources. The observations in rats of Stern *et al.* (*3*), that intraventricular caerulein (a sulfated decapeptide with seven amino acids in common with CCK-8) was more effective in limiting eating than was systemic caerulein, and of Maddison (*4*), that the operant response to food was modulated with intracranial doses tenfold smaller than intraperitoneal doses, are consistent with this expectation.

The current study unequivocally demonstrates that *ob/ob* mice who manifest hyperphagia have a strikingly lower cerebral cortical content of CCK than their lean littermates and other normal mice. It suggests, further, that the lower amount of CCK in the brain may be causally related to the unrestrained appetite of these mice. Whether the deficiency of CCK is restricted to the brain or occurs also in the gut of the *ob/ob* mice has yet to be determined.

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Target Range–Sensitive Neurons in the Auditory Cortex of the Mustache Bat

Abstract. *Echolocating bats determine distance to targets by the time delay between their emitted biosonar pulses and the returning echoes. By varying the delay between synthetic pulses and echoes in stimulus pairs at various repetition rates and durations, neurons have been found in the auditory cortex of the mustache bat* (Pteronotus parnellii rubiginosus) *which are sensitive to target range during the search, approach, and terminal phases of prey capture or landing. Two classes of range-sensitive neurons were found: (i) tracking neurons, whose best delay for response to an echo following the emitted pulse becomes shorter and narrower as the bat closes in on the target, and (ii) range-tuned neurons, whose best delay is constant, and which respond to the target only when it is within a certain narrow fixed range. Range-tuned neurons are specialized for processing echoes only during a particular period of the search, approach, or terminal phases of echolocation, and they provide support for a theory of ranging in bats that incorporates groups of neurons with a spectrum of preferred echo delays to detect target distance.*

Using echolocation, insectivorous bats are able to hunt flying insects in total darkness by producing a series of stereotyped biosonar signals and listening to echoes (*1*). In the cochlea of the bat's inner ear, echoes are converted into the activity of spiral ganglion cells (cochlear nerve fibers), whose discharge rates depend on signal amplitude and frequency and whose short recovery cycles enable them to follow acoustic events occurring at a rate of up to 3000 to 4000 per second in stimulus-locked (or phase-locked) fashion (*2*). All the information available for echolocation is contained, therefore, in the activity of these peripheral neurons. Higher auditory nuclei in the brain then process the echo information, sorting out for analysis such parameters as relative target velocity (*3*), size (*4*), and location (*5*).

For target ranging, bats analyze the delay between the emitted pulse and returning echo (*6*), so the responses of neurons to paired stimuli of differing delays (that is, recovery cycles) have been studied to explore neural mechanisms for processing information about target range. Spiral ganglion cells respond to both the emitted pulse and the echo even from a target at a very short range (*2*). In the lateral lemniscus and inferior colliculus, this stimulus-locked response is preserved not only by a group of tonic neurons, but also by a group of phasic neurons, which act essentially as reliable event markers for target ranging (*2, 7–10*). In contrast, many other inferior collicular neurons have significantly different recovery cycles (*2, 7, 8*) and have been categorized into six types: undelayed short and medium suppression, undelayed long inhibition, delayed inhibition, temporary recovery, and facilitation. Any of the first five types were also included in the sixth category when they showed facilitation (*11*). There is thus a broad spectrum of recovery cycles in the population as a whole. On the basis of these neurophysiological data, Suga and Schlegel (*7*) proposed a model for target ranging that consisted of three levels containing (i) tonic on-responding neurons with short recovery cycles, (ii) phasic on-responding neurons with a broad spectrum of recovery cycles, and (iii) neurons tuned to echoes with specific delays. Neurons somewhat comparable to those in the third group, but much more fascinating, have recently been found in the intercollicular nucleus (*12*) and the auditory cortex (*13*). In this report we present some of the extensive data from the mustache bat, *Pteronotus parnellii rubiginosus* (*14*), demonstrating neural mechanisms for encoding or processing range information.

The mustache bat produces biosonar signals (called pulses), each consisting of a long constant-frequency (CF) component followed by a short frequency-modulated (FM) component (Fig. 1A). Each component often contains four harmonics (H_{1-4}). Therefore, in total there are eight definable components in each pulse (CF_{1-4}; FM_{1-4}). When the bat is not compensating for a Doppler shift, the CF_1 of the first harmonic (H_1) is 30 to 31 kHz, and its FM_1 sweeps down from the CF frequency by 5 to 6 kHz. The second harmonic (H_2) is always predominant in the orientation sound (*3, 15–18*) and is used for an acoustic behavior called Doppler shift compensation (*18*). The duration and repetition rate of sound emission systematically vary in a target-oriented flight. When the mustache bat is hunting but has not detected a target (search phase), pulses are about 20 to 30 msec in duration and are repeated roughly five to ten times per second. When the bat detects a target and approaches it,

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the pulse duration initially increases by about 10 msec, then decreases roughly linearly with distance. During this approach phase, the repetition rate increases to 30 to 40 per second. Just before the bat intercepts the target (terminal phase), the repetition rate increases dramatically to 90 to 100 per second and the pulses shorten to 5 to 7 msec (*16-18*).

The peripheral and central auditory systems of the mustache bat are remarkably specialized for the detection and fine frequency analysis of the CF_2 component of the pulses and echoes. About 30 percent of the primary auditory cortex in the cerebrum contains neurons sharply tuned to 61- to 63-kHz sounds and is both tonotopically and amplitopically organized. This area is especially suited for processing velocity information carried by the CF_2 component of Doppler-shifted echoes returning from a moving target. Accordingly, it is called the Doppler-shifted-CF processing area (*3, 4*).

Anterodorsal to this is the FM processing area, which shows only a vague tonotopic representation and no clear amplitopic representation. A majority of neurons in this area are sensitive to particular combinations of the 16 components of the pulses and Doppler-shifted echoes. Many of these combination-sensitive neurons show poor or no response to a single CF or FM component presented alone, regardless of frequency and amplitude, but show a vigorous response to one or two of the nonfundamental FM components (FM_{2-4}) when it is preceded by the fundamental (H_1). That is, neural processing of the FM component of the second sound (simulated echo) is facilitated by the fundamental of the first sound (simulated vocal self-stimulation by the emitted pulse), or it is performed in relation to the first sound, or both. The maximum excitation of these neurons by paired stimuli is dependent on their relationship in (i) amplitude spectrum, (ii) overall intensity, (iii) time, and also (iv) repetition rate (*13*). To extend these earlier observations, we used synthetic pulses and echoes containing some or all of the harmonic components of the biosonar signals of the mustache bat and studied the response properties of these combination-sensitive neurons in relation to target detection and ranging.

Eleven mustache bats from Panama were prepared for recording of action potentials from single neurons in the FM processing area. Some experiments were performed on unanesthetized bats (only local anesthetic was applied to surgical wounds) and some on lightly anesthetized bats, as described in previous reports (*13, 19*). Except for a pair of harmonic generators, the instruments used for delivering acoustic stimuli and recording neural responses were the same as before (*13*).

The first harmonic (H_1) of a simulated pulse or echo was generated from a sine wave tone burst near 30 kHz by using a Wavetek voltage-controlled oscillator and electronic switch (rise-decay time, 0.2 or 0.5 msec). Its FM portion was produced by frequency-modulating the oscillator with a linearly decreasing ramp voltage. The FM_1 swept to 6 kHz below the frequency of CF_1. The second and third harmonics (H_2 and H_3) were then generated algebraically by a harmonic generator. Thus, all the CF and FM components of the first three harmonics could be produced with a single CF-FM signal. The fourth harmonic (H_4) was separately produced, if necessary, and delivered together with any of the lower harmonics. The intensity relationship among the harmonics could be varied at will, and any of the CF or FM components could be delivered alone. With a pair of these instruments, we could mimic all or part of both the pulse and the Doppler-shifted echo. This allowed us to

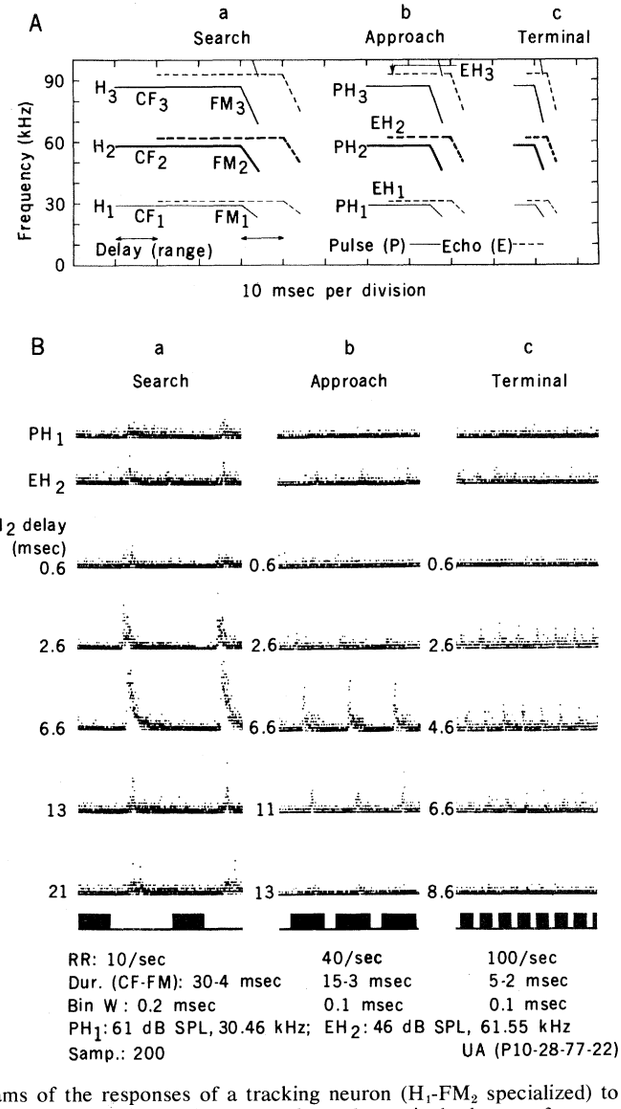

Fig. 1. (A) Schematized sonagrams of synthesized mustache bat biosonar pulses (P; solid lines) and echoes (E; dashed lines) mimicking three phases of target-oriented flight. The three harmonics of both the pulses (PH_{1-3}) and the echoes (EH_{1-3}) each contain a long CF component (CF_{1-3}) followed by a short FM component (FM_{1-3}). The fourth harmonic (H_4) is not shown here. (a) Search phase: CF and FM durations are 30 and 4 msec, respectively. (b) Approach phase: CF and FM durations are 15 and 3 msec. (c) Terminal phase: CF and FM durations are 5 and 2 msec. Repetition rates for (a), (b), and (c) were 10, 40, and 100 pairs per second, respectively. The thickness of the line indicates the relative amplitudes of each harmonic in the pulses and echoes: H_2 is strongest, followed by H_3 (−6 dB), and H_1 (−12 dB). Echo delay is measured as the time interval between the onsets of corresponding components of the pulse and the echo in a stimulus pair. (B) Peristimulus-time histograms of the responses of a tracking neuron (H_1-FM_2 specialized) to different echo delays during simulated search, approach, and terminal phases of target-oriented flight. The essential harmonics for facilitation of this neuron were H_1 of the pulse (CF_1, 30.46 kHz) and H_2 of the echo (CF_2, 61.55 kHz). The amplitudes of PH_1 and EH_2 for these responses were 61 and 46 dB SPL, respectively. The upper two histograms in each column show the poor response or lack of response of the neuron to PH_1 or EH_2 delivered alone at each repetition rate. The five histograms below them show the facilitation at various echo delays when PH_1 and EH_2 were delivered in a pair. Notice the decrease in the range of delays over which the neuron followed the stimulus pair, and also the shortening of the best delay as the repetition rate increased from 10 to 100 pairs per second (corresponding to a change in distance from 114 to 55 cm). Stimulus event markers beneath the histograms indicate the pulse of the stimulus pair only.

determine the essential components needed to excite combination-sensitive neurons. Echo delay from the onset of the pulse and the repetition rate of the stimulus pair were varied, mimicking the different phases of echolocation (Fig. 1A). Stimuli 34 msec in duration (CF, 30 msec; FM, 4 msec) were usually delivered in pairs at ten per second (search phase); 18 msec in duration (CF, 15 msec; FM, 3 msec) at 40 per second (middle approach phase); and 7 msec in duration (CF, 5 msec; FM, 2 msec) at 100 per second (terminal phase). Since the approach and terminal phases of echolocation last 300 to 600 and 180 to 190 msec, respectively (*17*), pulse-echo pairs were usually delivered in trains for the repetition rates of 40 and 100 per second. The train was, however, 500 msec in duration and was repeated once per second to facilitate the evaluation of neural responses to the stimuli. The stimuli were presented from an electrostatic loudspeaker 66 cm in front of the bat's head in a soundproofed anechoic room.

For recording neural activity, a tungsten-wire electrode (7- to 15-μm tip) was inserted into the FM processing area obliquely through a small hole in the skull. When the response of a single neuron or a cluster of a few neurons was recorded, we first determined which component or components of the pulse-echo pair were essential for excitation. The best frequency of a CF component or best frequency sweep of an FM component for facilitation was measured. Then the echo delay was systematically varied, and the facilitation threshold (*20*) and magnitude of response to the echo were studied at the three repetition rates and corresponding stimulus durations (Fig. 1A). Responses were expressed by their peristimulus-time (PST) histograms (Fig. 1B). Threshold was measured by an audiovisual method (*13*).

The 14 types of combination-sensitive neurons thus far found may be divided into three major categories according to their essential components for facilitation and are referred to as CF_1/CF, H_1-FM, and FM_1-FM facilitation (or specialized) neurons (*13, 21*). The H_1-FM and FM_1-FM facilitation neurons were found to be delay-sensitive (range-sensitive). They process Doppler-shifted echo FM components in relation to the pulse FM_1; facilitation was poor or absent when the pulse and echo were exact harmonics, but was strong when the echo was slightly higher in frequency than the pulse. The latency of the response to the echo FM when facilitation occurs is only 5 to 8 msec, so that these cortical neurons can be involved in echo processing even during the terminal phase of echolocation. We thus focused our studies on the range sensitivity of FM_1-FM and H_1-FM facilitation neurons.

In terms of range sensitivity, the 39 FM_1-FM and H_1-FM facilitation neurons studied may be dividied into two types: tracking neurons and range-tuned neurons. Tracking neurons are able to track a target during target-oriented flight, and range-tuned neurons are able to detect a target at a particular range. Figure 1B shows the PST histograms of responses of one tracking neuron that showed remarkable facilitation for a certain combination of pulse H_1 (or FM_1) and echo H_2 (or FM_2). At ten pairs per second (search phase), this neuron responded very poorly to either the pulse H_1 or echo H_2 alone, but responded vigorously to the echo H_2 when combined with the pulse H_1 at delays between 2 and 18 msec. The delay at the minimum facilitation threshold (hereafter called the best delay) was about 7 msec. At 40 pairs per second (middle approach phase), facilitation of the response was also evident for echo H_2 delays between 3 and 11 msec. The best delay was 6.4 msec. At 100 pairs per second (terminal phase), the neuron responded to the stimulus pair only if the echo H_2 was delayed by 2 to 6 msec. The best delay was 3.2 msec, which corresponded to a target range of 55 cm. At this best delay, the response appeared clearly to each stimulus pair, although its magnitude was smaller than that for lower repetition rates mimicking the search and approach phases. Such data demonstrate that a relatively loud conditioning sound, such as vocal self-stimulation by the H_1 of the emitted pulse, clearly facilitates the response of this type of neuron to the FM component of a weak echo from a target at a distance that depends on the repetition rate of the stimuli. This type of neuron is sensitive to an echo from a target over a wide range during searching flight; during pursuit, the neuron tracks or focuses on the echo source right up to the final instants before interception, rejecting echoes from farther away. As demonstrated in Fig.

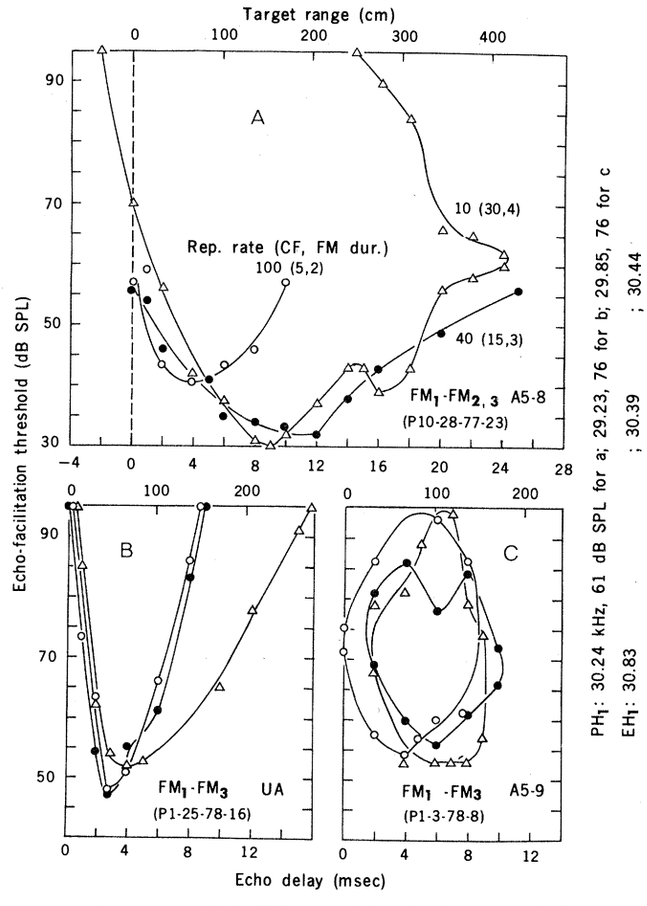

Fig. 2. Delay tuning curves for three neurons in the FM processing area. (A) A tracking neuron (FM_1-$FM_{2,3}$ facilitation) shows broad delay-tuning with thresholds near 30 dB SPL and a best delay of 8 to 12 msec (target range, 150 to 200 cm) for the (△) search (10 pairs per second) and (●) middle approach (40 pairs per second) phases. During the (○) terminal phase (100 pairs per second), the best delay shortens dramatically to 4.0 msec, the threshold increases to 41 dB SPL, and the delay-tuning curve becomes much narrower. (B) Range-tuned neuron (FM_1-FM_3 specialized). The delay-tuning curves are very sharp and nearly identical for the approach and terminal phases. The best delay is also the same, 2.7 msec. This neuron is tuned to a target 46 cm away—that is, during the late approach to terminal phase. (C) Another range-tuned neuron (FM_1-FM_3 specialized) demonstrating upper thresholds for facilitation. The curves are similar, and the neuron is tuned to a target that returns an echo of about 65 dB SPL from a distance of about 85 cm. The frequencies and amplitudes of the CF_1 components of the pulses (PH_1) and the frequencies of the CF_1 components of the echoes (EH_1) used for the measurements are shown at the right.

1B, the responses of this type of neuron to echo FM's become less prominent at 100 pairs per second than at lower repetition rates. As the echo FM's are increased in intensity, however, the responses become more prominent. In actual target-oriented flight, echo intensity gradually increases, so that responses to echoes would be still very prominent even in the terminal phase of echolocation.

For further quantitative studies of the response properties of tracking neurons, delay-tuning (or range-tuning) curves were measured by plotting the echo facilitation threshold as a function of the echo delay from the pulse (that is, as a function of the target range) at different repetition rates and signal durations mimicking the three phases of echolocation (Fig. 2A). The FM_1-$FM_{2,3}$ neuron represented in Fig. 2A, for instance, was broadly delay-tuned with a best delay of 9.0 msec when stimulated at ten pairs per second. The minimum echo facilitation threshold was 30 dB SPL (sound pressure level in decibels referred to 0.0002 dyne/cm^2 root-mean-square). At echo delays longer than 14 msec there was an upper threshold, above which the neuron did not show facilitation. The delay-tuning curve for 40 pairs per second is similar to that for ten pairs per second, but without an upper threshold. At 100 pairs per second, there is a marked shortening of the best delay to 4.0 msec, and the curve is sharp. (At this rate, the next pulse-echo stimulus pair occurs at a delay of 10 msec.) The minimum threshold is 41 dB SPL. The neuron is apparently tuned to respond best to an echo from a target 69 cm away in this stimulus condition. It should be noted that the threshold is as low as 43 dB SPL for a 2-msec echo delay, that is, for a 34-cm target range. This neuron thus demonstrates the response properties of a tracking neuron.

Unlike tracking neurons, range-tuned neurons have relatively constant delay-tuning curves regardless of the repetition rate of paired stimuli. The delay-tuning curves of one FM_1-FM_3 neuron are shown in Fig. 2B. This neuron did not respond at all to the echo and only very poorly to the pulse when delivered at a low repetition rate. In a situation mimicking the middle approach and terminal phases, however, it responded vigorously to a pulse-echo pair with a best delay of 2.8 msec, which corresponds to an echo from a target at 48 cm. The minimum facilitation threshold was 47 dB SPL. The delay-tuning curves were very sharp and nearly identical for these two phases of echolocation. During the simulated search phase, the delay-tuning curve was also sharply tuned. The threshold for facilitation rapidly increased with echo delay beyond the best delay of 4.0 msec. This neuron is thus specialized to respond only during the late approach and early terminal phases, when the target would be at a range near 48 cm. We also found range-tuned neurons that were excited by echoes only during the search phase. In such neurons, the delay-tuning curves were broad and the best delays were between 12 and 18 msec (target range, 200 to 300 cm). Neurons tuned to a target closer than 200 cm were also found. Our data suggest that the FM processing area contains a population of neurons tuned to targets at different distances. We do not yet know whether this population is systematically organized—for instance, along an axis for target range.

At their best delay, the response magnitudes of some range-tuned neurons were nearly the same to echoes over a broad amplitude range of more than 5 to 10 dB above facilitation threshold, while those of other neurons were nonmonotonically related to the echo amplitude. When the response was extremely nonmonotonic, the neurons did not respond at all to an intense echo, so that their delay-tuning curves were "closed." The range-tuned neuron represented in Fig. 2C, for instance, responded best to an echo of about 65 dB SPL with a delay of 4 to 6 msec. Another range-tuned neuron was also found that had a closed delay-tuning curve and responded best to an echo of about 40 dB SPL with a delay of 12 to 15 msec. Therefore their primary function may be the detection of certain FM components only from targets of an appropriate size at a particular distance.

Like peripheral neurons, neurons in the midbrain auditory nuclei, which respond to both the pulse and the echo in the same way regardless of echo delay, are essential for range coding (*2, 7, 8, 10*), but are probably at the lowest level in processing range information. These neurons are inadequate to produce directly the response properties of higher-order neurons such as the range-tuned neurons represented in Fig. 2. What is required is a population of neurons with various recovery cycles, including facilitation of the response to the second sound in a pair (*2, 7, 8*). As theorized by Suga and Schlegel (*7*) and demonstrated in our data, the bat's auditory system contains more sophisticated ranging neurons, which probably integrate the activity at lower levels for processing range information. To understand the neural mechanism for ranging, neural network models should incorporate the response properties of primary or primary-like auditory neurons, neurons with a broad spectrum of recovery cycles, and neurons specialized for responding selectively to an echo with a specific delay from an emitted pulse.

Behavioral experiments on range discrimination clearly indicate that "CF-FM" bats such as *Pteronotus* use the FM component for ranging just as "FM" bats do (*6*). The essential components in the pulse and echo for the excitation of range-tuned neurons are particular combinations of FM components, so that the mechanism for processing range information in the mustache bat is likely to be a conservative feature of the nervous system common to both CF-FM and FM bats (*22*). Ablation studies with a typical FM bat (*Myotis lucifugus*) suggest that the auditory cortex is not essential for performing simple obstacle avoidance tasks (*23*), but this area may be necessary for higher-level perception of range information in more complex echolocation tasks such as prey capture.

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19. When the bats were anesthetized for surgery, recording of single-unit activity was made 3 to 15 hours after the initial injection of 30 mg of sodium pentobarbital per kilogram of body weight. If an electrode was placed at nearly the same place in the auditory cortex of the same animal a few days or a few weeks later, using no general anesthesia, the data obtained were nearly the same as those obtained from the lightly anesthetized bat. We thus believe that our data are not significantly affected by light anesthetization. According to J. A. Simmons, Feng *et al.* (*12*) recorded delay-tuned neurons from lightly anesthetized bats.
20. Facilitation threshold is defined as the smallest amplitude of the echo that evokes just noticeable facilitation.
21. The dash and slash mean, respectively, successive and simultaneous deliveries of two sounds for maximum excitation of combination-sensitive neurons. For instance, H_1-FM_2 means that FM_2 should be delivered after H_1 for best facilitation, and CF_1/CF_2 means that CF_1 and CF_2 should be delivered simultaneously. A multiple suffix—for instance, $FM_{2,3}$ in H_1-$FM_{2,3}$—means that either FM_2 or FM_3 delivered after H_1 effects the same or similar facilitation. The H_1-FM facilitation neurons are those whose response to FM is facilitated by H_1 or its components CF_1 and FM_1, so that this category includes all H_1-FM_2, H_1-FM_3, H_1-FM_4, H_1-$FM_{2,3}$, H_1-$FM_{2,4}$, H_1-$FM_{3,4}$, and H_1-FM_{2-4} facilitation units. The FM_1-FM-facilitation neurons are those whose response to FM is facilitated by the FM_1 component of H_1, but not by CF_1, so that this category includes FM_1-FM_2, FM_1-FM_3, and FM_1-$FM_{2,3}$. The CF_1/CF facilitation neurons are those whose response to CF is facilitated by CF_1, so that this category includes CF_1/CF_2, CF_1/CF_3, $CF_1/CF_{2,3}$, and $CF_1/CF_{3,4}$. A detailed investigation of the response properties of CF_1/CF facilitation neurons will be reported separately (N. Suga, W. E. O'Neill, T. Manabe, *Science*, in press).
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Reducing Epileptic Seizures Through Operant Conditioning of Central Nervous System Activity: Procedural Variables

Abstract. *Operant conditioning of the sensorimotor rhythm of the human electroencephalogram with time-outs contingent on epileptiform activity reduces epileptic seizure rates in patients whose seizures are not well controlled by medication. A comparison of this procedure with time-out training alone demonstrates that operant conditioning of the sensorimotor rhythm is neither necessary nor sufficient for seizure reduction.*

Operant conditioning, or biofeedback, of particular electroencephalographic (EEG) rhythms has been applied successfully as a treatment for epilepsy in humans who have not responded well to medication (*1-6*). With few exceptions (*3, 6, 7*), the method has involved operant conditioning of the sensorimotor rhythm (SMR). This rhythm is a 12- to 14-Hz sinusoidal waveform recorded from the scalp over the sensorimotor cortex. Operant conditioning of the SMR has been correlated with a reduction in the frequency of epileptic seizures (*4, 5*). Further, an increase in SMR activity has been assumed to reduce the seizure rate through a decrease in cortical excitability (*8*). There is reason, however, to question such a relationship between SMR conditioning and reduced seizure rate.

In every experiment in which reductions in seizure frequency were reported to follow SMR training, the conditioning procedure included a clearly signaled "time-out" contingent on EEG slow waves, spike activity, or high-voltage scalp electromyographic (EMG) activity. A time-out is a period during which reinforcement is not available. That is, SMR was not reinforced during epileptiform activity or gross body movements, and the unavailability of reinforcement was indicated to the subject by a signal.

The omission of reinforcement could act as an aversive stimulus. It has been established that time-outs punish skeletal behaviors (*9*). With respect to the SMR plus time-out (SMR + TO) procedure, the time-out may suppress EEG slow-wave and spike activity. The time-out might also lead to the development of either avoidance or escape responses, that is, the acquisition of some response that prevents or terminates activity associated with the time-out. A decrease in the probability of epileptiform activity might account for a decrease in the frequency of seizures preceded by such activity (*10*). Consequently, the procedural variable that leads to reduced seizure activity in SMR training procedures might be the signaled removal of reinforcement rather than the SMR training itself (*11-13*). We have now demonstrated that the SMR + TO procedure is no more effective than a time-out alone (TO) procedure.

Seven epileptic outpatients with long histories of responding poorly to medication were obtained from the epilepsy clinic at McMaster University Medical Centre. Each patient chosen to be a subject met the following criteria: no major metabolic disorders; no sensory precipitation of seizures; seizures not primarily nocturnal; some motor involvement in clinical seizures; clear interictal epileptiform activity, which reliably triggered the time-out circuit; and seizures described clinically as being poorly controlled by medication.

Medical files and interviews were used to determine the mean seizure rate, clinical history, seizure manifestation, medication schedule, and interictal EEG pattern. One or two 40-minute recording sessions were also used to determine whether interictal epileptiform activity reliably triggered the time-out circuit. Serum concentrations of prescribed medication were held constant throughout the experiment (*14*). Four subjects received TO training and three received SMR + TO training. Descriptions of each subject are presented in Table 1.

There were two 40-minute sessions per week over a period of 210 days. During a 30-day period before training began (eight sessions), seizure and EEG data were collected, but no feedback was delivered. The remaining 180 days were devoted to training sessions. Previous SMR investigations indicate that subjects who improve do so within 6 months of training. Subjects and their families were provided with small notebooks for detailed monitoring of auras and seizures. No records were kept by the one mentally retarded subject in each group; their data were obtained from family, friends, teachers, and counselors.

The training procedure was modeled after that of Lubar and Bahler (*4*). Each session consisted of 5 minutes of baseline recording without feedback, 15 minutes of feedback contingent on activity recorded alternately on each succeeding sessions from C_3-T_3 or C_4-T_4 (*15*), 15 minutes of feedback from the contralateral electrodes, and a final 5-minute baseline. Stimulus presentation and online data analysis were carried out by a computer (PDP Lab-8/E).

The EEG was monitored through silver-silver chloride scalp electrodes (Grass) connected to two matched EEG

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