Olds (*2*). However, with continued testing, the animals eventually settle down to low, stable thresholds with lever-pressing rates of several thousand responses per hour.

Also worth mentioning is how an animal behaves when the current reaches the level that stops it from feeding. The animal stops feeding abruptly and then exhibits searching behavior around the box, sniffing and rearing on its hind legs. The behavior is not that of an animal satiated for food (which normally goes to sleep) but of an animal actively searching for something. The stimulation appears to distract the animal from feeding rather than reducing its hunger.

At the end of testing, the animals were perfused and their brains were sectioned in order to determine the location of the electrode tips. All electrodes were medial to the fornix with the majority located in the ventromedial nucleus. Some were located in the dorsomedial nucleus of the hypothalamus and others fell in between these locations. Three animals had electrodes in the arcuate nucleus. An analysis of threshold levels with respect to location failed to reveal any relation between these specific nuclear groups and the effectiveness of stimulation.

The most significant aspect of these data is that the self-stimulation thresholds in the ventromedial area are positively correlated with both the escape and the stopping of feeding thresholds. This has three important implications.

1) This positive correlation shows that the self-stimulation behavior observed is not a result of the current spreading (presumably laterally) to other areas in the brain which are known to produce self-stimulation. It indicates that the electrode site which stops feeding behavior when stimulated also has rewarding properties, and that continued stimulation eventually becomes aversive.

2) The data question the concept of a major punishment system coursing through this area. Stimulation certainly produces escape behavior that is in keeping with the ambivalent results found in the earlier studies. However, stimulation is at least as rewarding as stimulation of the medial forebrain bundle, as far as threshold measures are concerned. This is incompatible with the idea that the ventromedial area is primarily part of a punishment system.

3) The data warrant the suggestion that the ventromedial system stops feeding, not because it activates some satiety mechanism, but because the stimulation in this area elicits searching behavior which is incompatible with feeding. It appears that the ventromedial area of the hypothalamus may be organized similarly to, and parallel with, the lateral hypothalamus and medial forebrain bundle. Both areas are rewarding and drive producing, although the exact nature of the drives elicited in the ventromedial nucleus are as yet undetermined.

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8. Supported by NIH grants MH 13189 and GM 01789.

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Taste Stimuli: Time Course of Peripheral Nerve Response and Theoretical Models

Abstract. *The responses of a taste nerve in rats to sodium chloride were integrated over successive 10-millisecond intervals and averaged. The time course of the mean responses consisted of a 30-millisecond latency, a rapid rise to a maximum, and a slower decline to a sustained level. The chemoreceptor theories of Beidler and Paton failed to predict the relation between phasic response and time or concentration.*

The neural response of sensory systems often consists of initial, rapidly changing (phasic) components, which are followed by prolonged, relatively stable (tonic) activity (*1*). The biophysical bases for these components as well as their information content have received a variety of interpretations. In systems such as vision, audition, and somesthesis, the phasic activity is believed to be an important, if not predominant, representation of environmental events. Such designations of the primary importance of phasic response components are often based on observations of rapid behavioral re-

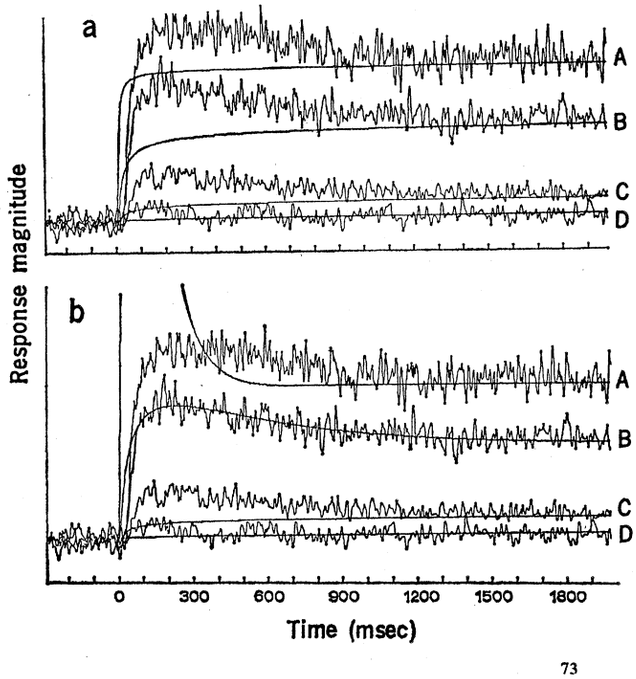

Fig. 1. Comparisons of observed responses (uneven lines) and responses predicted by theoretical models (smooth lines) for four concentrations of NaCl: (*A*) 1.0*M*, (*B*) 0.1*M*, (*C*) 0.01*M*, and (*D*) 0.001*M*. Zero time is the time of stimulus arrival at the tongue. (a) Predictions based on Beidler's theory (*4*). (b) Predictions based on Paton's theory (*6*).

sponses to the rapidly changing patterns of stimulation to these systems. For these systems, explicit models have been developed which attempt to account for both phasic and tonic components of the neural responses (*2*). In other systems, notably gustation, the phasic components are generally believed to be merely onset transients, containing little or no environmental information. Consequently, the tonic component of gustatory responses has received intensive study on the assumption that it provides most of the behaviorally relevant afferent input (*3*). Even the biophysical models of gustatory transduction processes are usually only applied to tonic response data (*4*).

Rats can make rapid taste decisions on the basis of the gustatory stimulation provided by licking. A discrimination between NaCl and distilled water required less than 250 msec (*5*). Thus, sufficient information for quality discrimination must be available in the portion of the neural response which immediately follows stimulus onset. Knowledge of the time course of these neural responses is certainly relevant to understanding the rat's behavior as well as to theories of chemoreception.

Two major approaches have been taken by Beidler (*4*) and Paton (*6*) in the development of theories of chemoreception. Both assume that a reversible interaction between the stimulus, S, and the receptor sites, X, is the initial step in the process leading to a response:

$$S + X \underset{k_2}{\overset{k_1}{\rightleftharpoons}} SX \qquad (1)$$

where k_1 and k_2 are, respectively, the association and dissociation rate constants of the reaction, and S specifies the concentration of the stimulus. Beidler (*4*) also discards phasic responses and assumes that the response magnitude is directly proportional to the fraction of receptor sites which are occupied and that the response is in equilibrium at all times, whereas Paton (*6*) assumes that the response magnitude is proportional to the rate of stimulus-receptor interaction and that the response goes to equilibrium as a function of k_1 and k_2. Therefore, the two theories make different predictions for the time course of the response, and these predictions may be compared to the observed relationship between response magnitude and time.

There is a lack of information on the temporal characteristics of gustatory neural responses. In earlier studies of single fibers in the chorda tympani nerve, nerve impulses were counted for intervals of 100, 200, or 1000 msec (*7, 8*). Such studies typically indicated maximum activity in the first interval of analysis, but often failed to indicate how the stimulus onset was determined. Thus, much of the phasic portion of gustatory responses is unknown, since the first poststimulus data point was also the maximum response. The actual response latency and the time of occurrence of the maximum response magnitude was unclear, because stimulus onset at the tongue was rarely determined. Studies of the response of the whole chorda tympani were subject to similar difficulties because of the time distortion of resistor-capacitor summators or the 100-msec intervals of frequency processors, as well as the lack of indication of stimulus onset (*9*). In addition, the use of single concentrations of stimulus compounds left the relation of stimulus concentration to the few observed temporal characteristics unresolved.

Table 1. Correlations between observed and predicted responses.

NaCl concentration (M)	Correlation coefficient	
	Beidler's theory (*4*)	Paton's theory (*6*)
0.001	− 0.358	− 0.354
0.01	− 0.016	0.074
0.1	0.446	0.863
1.0	0.610	− 0.198

To obtain gustatory data suitable for biophysical modeling of both phasic and tonic portions of the response, we presented a wide concentration range of controlled stimuli, with known stimulus onset, and obtained integrated responses during successive 10-msec intervals (*10*). A comparison of both Beidler's and Paton's theories with these data demonstrated that neither could account for the phasic portion of the responses.

The data were recorded from five male albino rats weighing 370 to 466 g. They were anesthetized, and the chorda tympani nerve was conventionally exposed for whole nerve recording (*11*). The tongue was placed in a Plexiglas chamber with inflow and outflow tubes. The arrival of a stimulus solution in the tongue chamber produced a reflectance change, which was detected by a phototransistor (*12*). The amplified neural activity was integrated by a digitally controlled summator (*10*). The summator output and the phototransistor signal were recorded on magnetic tape. The stimulus solutions were prepared with distilled water (specific conductance less than 5×10^{-6} mho/cm^3) and reagent grade NaCl. The stimulus presentation sequence was randomized, and every stimulus except distilled water was followed by three rinses of distilled water. The recorded data were converted from analog to digital form, averaged, and plotted on a PDP-15 computer (Digital Equipment Corporation) (*13*). Following stimulus onset there is a latency of about 30 msec, a rapid rise to a maximum around 200 msec, and a decline over the next second toward a sustained response level (Fig. 1). These latency data agree closely with the response latencies obtained in another study (*14*). Response latencies of 27, 33, and 27 msec were observed to 0.1, 0.5, and 1.0M NaCl, respectively.

Both Beidler's (*4*) and Paton's (*6*) theories make the same prediction for the equilibrium magnitude, R:

$$R = AS/[(k_2/k_1) + S] \qquad (2)$$

where A is a constant (the maximum response magnitude in Beidler's theory and k_2 in Paton's theory), and S, k_1, and k_2 are as defined for Eq. 1 (*15*). Estimates of the equilibrium response magnitudes were the mean magnitudes over the last 600 msec of the averaged responses to 0.01, 0.03, 0.10, 0.30, 1.0, and 2.0M NaCl. A statistically significant ($P < .001$) fit of Eq. 2 to these data was obtained by the method of least squares. Thus, both theories predict the observed relation between the concentration of the stimulus and the magnitude of the tonic response. The significant fit of the chemoreceptor theories to the equilibrium response data agrees with the similar finding of Beidler (*4*), although the data in each case were processed in a very different manner (*13*).

The two theories make different predictions for the phasic portion of the response. From Beidler's sole dependence on a mass-action model, it follows that the reaction was in equilibrium at all times (*4*). Thus, his theory predicts that the response magnitude will vary with time as described by Eq. 2, as the stimulus concentration varies in time (*16, 17*) as a function of diffusion. On the other hand, Paton's theory

predicts that the response magnitude will vary as a function of time according to:

$$R = \frac{S}{S + k_2/k_1}\left(k_2 + k_1 S e^{-(k_1 S + k_2)t}\right) \quad (3)$$

where t is the time, and S, k_1, and k_2 are as defined in Eq. 1. Predictions for Beidler's theory were computed from Eq. 2. A nonlinear regression program fit Paton's theory to the averaged response to 0.1*M* NaCl, and predictions for other concentrations were then computed from Eq. 3 (*13*). Product moment correlation coefficients between observed and predicted responses for both theories for the concentrations shown in Fig. 1 are given in Table 1. Neither theory adequately describes the relation between the observed response and time. Paton's theory does predict phasic responses, but encounters great difficulty with the range of stimulus concentrations employed.

The phasic response, which is so poorly predicted by Beidler's and Paton's theories, has been observed in many investigations (*9, 11*). It has sometimes been argued that the phasic portion of the response is due to a property of the nerve since recordings from taste bud receptor cells do not show a phasic response. However, the receptor cell responses are all much slower than the "subsequent" neural responses (*17, 18*), and consequently such slow potentials cannot be the actual receptor potentials.

The significance of the phasic portion of the neural response is emphasized by the results of the behavioral decision experiment (*5*). Taking both the response latency and the time required for central processing into account, we suggest that the rising portion of the responses, which is nearly linear with respect to time, may convey the information required for rapid taste quality discrimination (*19*). Thus, the phasic portion of gustatory neural responses deserves further study in theoretical terms also.

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6-Hydroxydopa Depletion of Brain Norepinephrine and the Facilitation of Aggressive Behavior

Abstract. *A significant increase in shock-induced aggression occurs in the rat 4 days after an intraventricular injection of 90 micrograms of 6-hydroxydopa. Both fluorescent histology and biochemical assay demonstrate that brain norepinephrine is reduced by 90 micrograms of 6-hydroxydopa, while brain dopamine remains unaltered. This suggests that one form of aggressive behavior (shock-induced aggression) is modulated through a central noradrenergic system.*

Central administration of 6-hydroxydopamine has been shown to produce a long-lasting depletion of brain catecholamines (*1*) as well as a central degeneration of catecholamine terminals (*2*). Intracisternal injection of this drug into rats produces a progressive increase in shock-induced aggression that persists for as long as 6 months after a single 200-μg dose (*3*). Prior administration of desmethylimipramine, a drug that blocks uptake of amines into catecholamine terminals alters both the catecholamine-depleting and the behavioral effects of 6-hydroxydopamine (*4*). Since both brain norepinephrine (NE) and dopamine (DA) are affected by 6-hydroxydopamine, it is unclear as to which neurotransmitter is responsible for the facilitation in aggressive behavior that is observed. The introduction of 6-hydroxydopa pro-

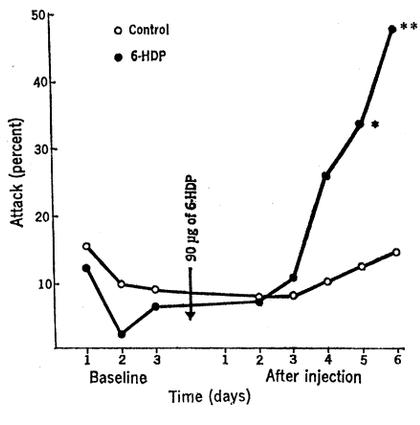

Fig. 1. Time course of the development of facilitated shock-induced aggression after 6-hydroxydopa (*6-HDP*). Symbols: * $P < .05$, ** $P < .01$; two-tailed *t*-test, control versus treated animals.