

transport piece in the normal selective secretion of IgA. On the other hand, local synthesis and consequently increased concentration of IgA in the connective tissue ground substance adjacent to secretory epithelia may be decisive for the normal secretion of this immunoglobulin (6, 17). Synthesis of IgA normally occurs in the parotid gland as well as adjacent to many other secretory epithelia, as judged from the presence of IgA-containing plasma cells (1, 5, 6, 17). Therefore we studied the occurrence of immunoglobulins in the parotid gland of a patient deficient in IgA. In contrast with normal parotid glands, the plasma cells and the connective tissue ground substance adjacent to the acini were devoid of IgA. However, sections with IgM- and IgG-containing plasma cells in numbers as high as 45 and 35, respectively, were commonly encountered throughout this parotid specimen (Fig. 3); the corresponding values for normal specimens did not exceed 5. Immunoglobulin M and IgG were also readily detectable in the connective tissue ground substance of the IgA-deficient patient. His gastric mucosa likewise contained a higher number of IgM-cells than the other gastric specimens and did not contain detectable IgA (17).

Other investigators (1, 2, 18) have noted that IgG and, particularly, IgM may occur in the parotid secretions of patients lacking IgA. Furthermore, Crabbé and Heremans (19) found an unusual high number of IgM-containing plasma cells in the intestinal mucosa of two such patients. This supports the foregoing results. The selective secretion of IgM in IgA-deficient patients may be explained at least in part by enhanced local synthesis of IgM; but such local synthesis does not seem to occur adjacent to all secretory epithelia, in contrast with the normal local synthesis of IgA. There was no consistently increased number of IgM-containing plasma cells in the two nasal specimens from patients deficient in IgA. Hence, IgM may not be regarded as a general compensatory secretory immunoglobulin in IgA-deficiency states, although it may function as such in some secretions. Immunoglobulin G may occur in the secretions of IgA-deficient patients on account of transudation from serum, in addition to enhanced local synthesis. The factors stimulating local synthesis of IgM and IgG adjacent to some se-

cretory epithelia in the IgA-deficient patients remain unknown; the basis for the normal local synthesis of IgA also remains unknown.

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"Tactile" Stimulus Intensity: Information Transmission by Relay Neurons in Different Trigeminal Nuclei

Abstract. *Comparison of the information transmitted about the intensity of a steady "tactile" stimulus applied to facial skin by single trigemino-thalamic neurons in nucleus oralis and nucleus caudalis indicates that little information loss occurs at the medial lemniscal synaptic relay (nucleus oralis), but that it is gross within the nucleus caudalis.*

The parallel medial lemniscal and anterolateral components of the spinal somatic sensory pathways, although activated by "tactile" stimulation of the skin, do not contribute equally to sensory discriminative functions (1). This is true also for the homologues of these pathways in the brainstem trigeminal complex. Section of the spinal dorsal column, for example, produces among other things inability to locate or estimate the intensity of a "tactile" stimulus although its occurrence is appreciated. Conversely, spinal anterolateral tractotomy (or the analogous trigeminal tractotomy) increases slightly the threshold for detecting the stimulus, but does not significantly impair the subject's capacity to locate the stimulus and estimate its intensity.

Neural mechanisms which could account for these considerable functional differences between the medial lemniscal and anterolateral systems include (i) differing inputs from the cutaneous mechanoreceptors to the two systems, (ii) quantitative differences in synaptic linkage of primary neurons with second-

order relay neurons in the two systems, with more effective transfer of information in the medial lemniscal relay, and (iii) differences in synaptic organization in the diencephalon, or some combination of these. Structural and functional differences in the diencephalon are established for the two pathways (1), but analyses of the static functional properties of single second-order neurons in these pathways have not previously demonstrated differences sufficient to account for their different contributions to tactile sensibility (2).

We have used some statistical methods of information theory (3) to compare information transmission by single trigemino-thalamic neurons within the trigeminal nucleus oralis (lemniscal) and nucleus caudalis (anterolateral) (4) concerning the intensity of a steady mechanical indentation of the skin of the face.

Unanesthetized cats, immobilized with intravenously administered gallamine triethiodide, were used for all experiments. Primary neurons were studied in the decerebrate animal by

recording with tungsten microelectrodes from single cell bodies in the semilunar ganglion (5). For single-unit recording in the trigeminal complex, a two-stage operation was necessary to enable fixation of the head, appropriate exposure of the brainstem, and denervation of overlying tissues to be carried out under general anesthesia (halothane) some time before recording was begun in the unanesthetized animal. The procedures and criteria for identifying trigemino-thalamic neurons are described elsewhere (2).

The stimulator used for activation of cutaneous mechanoreceptors was identical with one described previously (6), permitting precise, reproducible displacement of the skin with an error of less than $2\ \mu$; the tip of the indenting probe was 2 mm in diameter. The stimulus pattern used for all experiments was a rectangular indentation lasting 1000 msec, the range of indentation being $960\ \mu$. This amplitude range could

be fractionated into 16 equally spaced steps, which were the stimulus values routinely used for constructing the stimulus-response curves. Stimuli were presented once per 5 seconds, and ten responses were measured at each stimulus value. The number of spikes in each neural response was determined and displayed with standard counting procedures. Systemic blood pressure, expired P_{CO_2} and rectal temperature were monitored continuously.

Slowly adapting mechanoreceptors innervated by myelinated fibers were associated with the different types of hair follicles found on the face of the cat. These included the fine hair or pelage follicle and sensory hair follicles, both vibrissae and tylotrichs (7). Primary fibers never innervated more than one follicle type, and with sensory hairs usually a single follicle only; occasionally two or three tylotrichs were innervated by the one fiber. The largest receptive fields of fibers innervating

pelage follicles included upward of ten such hairs, and varied from 3 to 10 mm in diameter. The discharge patterns of these different receptor types in response to steady indentation were identical in all details we examined and for this reason require no separate consideration.

Fibers innervating each of the slowly adapting mechanoreceptor types projected to both nucleus oralis and nucleus caudalis. This was apparent from the not uncommon intranuclear recording of primary fiber responses. Not only may these same receptor types project to the two nuclei, but it is likely that individual fibers project to both nuclei (5).

The receptive fields of trigemino-thalamic neurons, both in nucleus oralis and in nucleus caudalis (in the region 1 to 3 mm posterior to the obex), were themselves indistinguishable, but they differed from those of slowly adapting primary fibers in several respects. These fields were always 3 to 30 times larger in area than those of primary fibers; they were continuous, and, further, all slowly adapting mechanoreceptor types within the receptive fields projected to the relay neuron.

A linear relation between the amplitude of the indentation of skin overlying a slowly adapting mechanoreceptor and its average discharge frequency has been demonstrated in the monkey's glabrous skin (6); in our experiments, a similar relation was observed for 23 of 29 such receptors in the hairy skin of the face of the cat. A similar relationship was observed for 15 of 19 slowly adapting trigemino-thalamic neurons within nucleus oralis (Fig. 1). Furthermore, the slopes of these curves for first- and second-order neurons did not differ significantly (expressed as sensitivity in Table 1) indicating that no significant transformation of the neural response had occurred with transmission across the first synapse within nucleus oralis.

Synaptic transmission within nucleus caudalis was less well organized. The discharge frequency of slowly adapting trigemino-thalamic neurons within this nucleus following stimulation usually varied greatly, and only a small component of this variability was accounted for by changes in the stimulus intensity. The "sensitivity" of these cells was much less than that of oralis units (Table 1).

An important question in considering this stimulus-response relationship is: How effectively does the mean firing

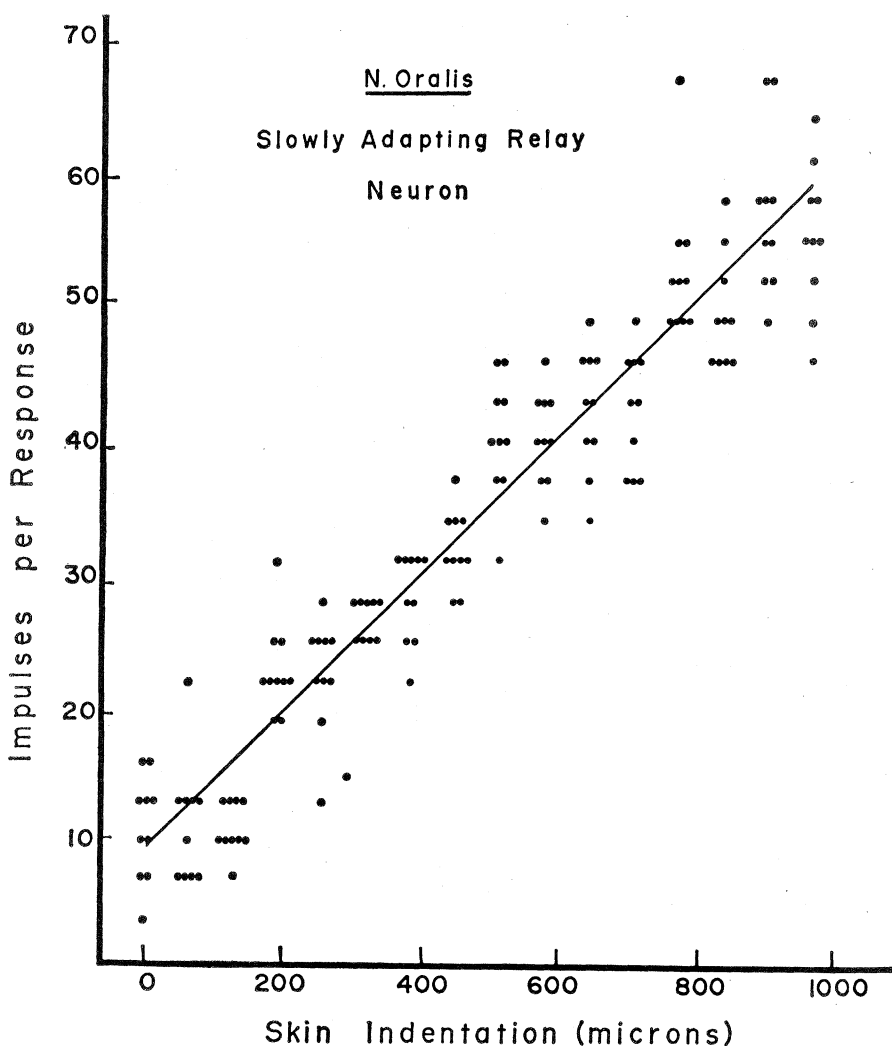


Fig. 1. Stimulus-response curve for a trigemino-thalamic neuron in nucleus oralis. Receptive field 11 by 9 mm, lateral to outer angle of eye. Stimulus duration was 1000 msec. The best fitting straight line is indicated. The tip diameter of the stimulus probe was 2 mm.

rate of a single response of a particular neuron unequivocally define the amplitude of the cutaneous indentation? Statistical procedures relevant to information theory (3) permit such analysis. These procedures, related to the analysis of variance, permit a partitioning of the output variability into a component which covaries with the input (and provides a measure of the "amount of information" transmitted by the system) and a second component which is independent of the input—the "noise" of the system. Characteristic of most communication systems is that there is an upper limit to the amount of information which may be transmitted, defined as the channel capacity of the system. The channel capacity may be experimentally determined by progressively increasing the input information (in our experiments by increasing the number of possible values of the stimulus intensity over the fixed range of 960μ) until an asymptomatic value of the transmitted information is attained.

Figure 2A illustrates the experimental estimation of the channel capacity for information transmitted about stimulus intensity by a slowly adapting cutaneous mechanoreceptor. The channel capacity was 2.5 bits of information per response, approximating the mean value for the channel capacity of 19 such units (Table 1), and indicates that about five different categories ($2^{2.5}$) of stimulus intensity could be differentiated without error from the average discharge frequency of a single response of the receptor. Discrimination along the intensive continuum from the responses of relay neurons in nucleus

Table 1. Stimulus-response relations. The channel capacities of relay and nonrelay neurons within each nucleus did not differ significantly and have been pooled in this table. Data are given as the mean value of channel capacity and the standard error of the mean; numbers in parentheses are the numbers of observations.

Neuron type	Sensitivity (impulses/100 μ)	Channel capacity (bits)
Receptor afferents	6.5 ± 1.2 (23)	2.40 ± 0.06 (19)
Nucleus oralis	7.3 ± 1.6 (17*)	$2.09 \pm .07$ (18*)
Nucleus caudalis	2.7 ± 0.6 (20†)	$1.07 \pm .07$ (22†)

* Fifteen neurons are trigemino-thalamic cells.

† Twelve neurons are trigemino-thalamic cells.

oralis did not differ significantly from that observed at the receptor (Fig. 2B; Table 1); again, four or five stimulus categories could be unequivocally identified by the mean discharge frequency of a single response. No significant loss of information resulted from transmission across synapses in nucleus oralis. However, a considerable amount of information about stimulus intensity was lost after synaptic transmission within nucleus caudalis (Fig. 2C) (channel capacity = 1 bit; see Table 1); the transmitted information allowed detection of the stimulus with an amplitude of 960μ , but permitted no definition of its intensity.

These experiments demonstrate that single second-order neurons of the medial lemniscal system (nucleus oralis) can transmit information to the thalamus with an accuracy comparable to that of subjective estimates of the magnitude of most unidimensional stimuli by the human observer (3). Normally, however, the tactile stimulus will be multidimensional; stimulus site, contact area, and its shape may each change simultaneously with the intensity, and each of these factors will influence the frequency of discharge of the unit. The

ambiguity of this interaction is presumably resolved at successive relay nuclei by the profile of response in the total neuron population engaged by the tactile stimulus.

The pattern of information transmission within nucleus oralis and nucleus caudalis was unchanged if the first 100 msec, or 500 msec only, was analyzed. Usually, the channel capacity for a unit was increased slightly as the response period analyzed was increased, but the differential between the information transmitted in the two nuclei was unchanged.

The differential transmission of information within the trigeminal homologues of the medial lemniscal and anterolateral systems provides a neural basis for some aspects of their very different contributions to tactile discrimination. This differential transmission of information could be experimentally modified by increasing the area of contact of the stimulus probe. Increasing the probe tip diameter from 2 to 8 mm had little effect on information transmission in nucleus oralis. However, this increase in contact area facilitated definition of stimulus intensity by relay cells in nucleus caudalis,

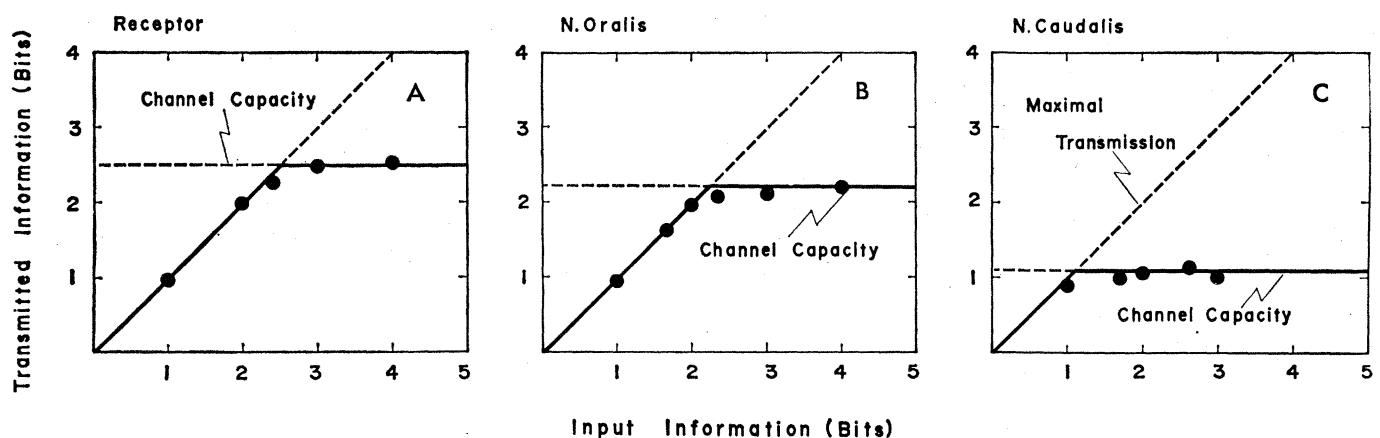


Fig. 2. Estimation of channel capacity for different trigeminal neurons. (A) Slowly adapting receptor innervating a single vibrissa. Range of stimulus intensity is 960μ . As the input information was increased by successively subdividing this range into 2, 4, 5, 8, and 16 categories, the transmitted information increased to a limiting value of 2.5 bits of information per response (the channel capacity), indicating that $2^{2.5}$ (about five) stimulus categories could be differentiated from the response with certainty. (B) Slowly adapting relay neuron in nucleus oralis. Channel capacity equals 2.2 bits (that is, $2^{2.2} = 4$ to 5 categories that could be differentiated from a single response). (C) Slowly adapting relay neuron in nucleus caudalis. Channel capacity is 1.1 bits, that is, a binary decision only, whether or not the stimulus had occurred, was possible. The stimulus probe tip was 2 mm in diameter for all observations.

in a few neurons increasing the information transmitted by a single response to 2 bits (that is, allowing discrimination of four categories). This suggests that each primary fiber had less effective excitatory action on second-order neurons in nucleus caudalis than in nucleus oralis; definition of stimulus intensity by a caudalis neuron without loss of information might then occur only when the stimulus parameters ensure engagement of a maximum number of convergent excitatory fibers.

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Cues: Their Relative Effectiveness as a Function of the Reinforcer

Abstract. *Two cues, either size or flavor of food pellet, were conditionally paired with either malaise induced by x-ray or pain induced by shock in four groups of rats. The combination of flavor and illness produced as conditioned decrement in consumption, but that of size and illness did not. Conversely, the combination of size and pain produced an inhibition of eating, but flavor and pain did not. Apparently, effective associative learning depends on central neural convergence of the paired afferent input.*

Pavlov (1) proposed that "any natural phenomena chosen at will may be converted into conditioned stimuli." For example, any discriminable cue, such as an audible tone or a visible light, which precedes a food reinforcer on several occasions can elicit responses associated with feeding in the absence of the reinforcer as confirmed by much experimental evidence.

However, consideration of the adaptive responses of rodents to poisoned foods may require qualification of Pavlov's notion. Animals that survive a poisoning attempt subsequently avoid the poisonous food but not the place where the food was consumed (2). In this situation, the visual, tactual, and other stimuli defining the place of the poison do not become conditional stimuli, perhaps because they are not as intimately associated with eating as the gustatory and olfactory stimuli are.

In our experiments, we attempted to discover whether nongustatory attributes of food (for example, size of pellet) could serve as conditional stimuli (CS) with illness as the unconditioned stimulus (US). We compared the relative effectiveness of both gustatory and nongustatory stimuli as cues when the consequence of eating was

either a general internal malaise or a specific peripheral pain.

Four groups of eight young adult male rats (300 g, Sprague-Dawley) were trained with one form of food that was conditionally paired with the noxious stimulus and another form of the food that was not so paired (Table 1). Two size groups received food pellets of similar flavors but different sizes. The large size was a whole Purina Chow pellet (approximately 2.5 by 1.5 cm); this was cut into four equal parts for the small size. Two groups received pellets of the same size, but differing in flavor of the coating. Quartered pellets were rolled in flour or in powdered sugar so that their flavor differed but their appearance was similar. Some animals had small pellets associated with the noxious stimuli; others had the large pellets so associated. Flour and sugar were balanced in the same way.

Table 1. Stimulus combination used in conditioning four groups of animals.

Groups	Cue (CS)	Reinforcer (US)
1	Size of pellet	X-ray (illness)
2	Flavor of pellet	X-ray (illness)
3	Size of pellet	Shock (pain)
4	Flavor of pellet	Shock (pain)

The animals were habituated to eating the nonconditional form of the food for 1 hour each day. After a week, conditioning began. During each conditioning day the conditional form of the food was provided during the 1-hour feeding period, and the noxious stimulation was applied. Five conditioning days were carried out every 2 to 4 days. On the intervening days, the animals ate the nonconditional form of the food without the noxious stimulation. Two days after the final conditioning session the animals were tested with the conditional form of the food without noxious stimulation. The latency to begin eating and the total amount consumed in 1 hour were observed. Similar observations were recorded for consumption of the nonconditional food the day before and the day after the test.

One flavor group and one size group were conditioned with electric shock delivered to the paws by an electric shock generator with constant current through a grid floor of the eating compartment. Shocks (0.2-second pulses) were delivered immediately after the rat put the conditional form of the food pellet into its mouth. The intensity caused the rat to drop the pellet (approximately 2.0 ma). The animal received a shock when it placed a pellet in its mouth during the 60-minute conditioning session.

The other flavor group and the other size group were conditioned with x-ray. [Previous studies demonstrated that ionizing rays produce behavioral effects similar to those of toxins but without the peripheral pain of an injection (3).] An exposure to 50 r of 280 filtered x-ray (half-value layer, 1.4 mm of Cu) was delivered in 4.5 minutes immediately after each 60-minute conditioning session.

The flavor of the pellet was an adequate CS when combined with x-rays. Every animal in the flavor-x-ray group ate more of the nonconditional flavored food than of the conditional flavored food. The animals showed little hesitation in picking up either form of food and sampling it; thus the amount eaten was a more effective measure than latency to begin eating. However, the size of the pellet did not acquire this same conditional power although it was associated with identical x-ray treatment. By comparison, the size of the pellet was an excellent conditional stimulus when paired with shock to the