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PROPERTIES OF DIFFERENT FUNCTIONAL TYPES OF NEURONES IN THE CAT'S ROSTRAL TRIGEMINAL NUCLEI RESPONDING TO SINUS HAIR STIMULATION

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SUMMARY

1. Properties of neurones in the trigeminal nuclei principalis and oralis responding to movements of facial sinus hairs were studied in cats anaesthetized by I.V. infusion of pentobarbitone.

2. Using electrophysiological methods trigeminal neurones were classified into primary afferent fibres, trigeminothalamic relay neurones, interneurones and other unspecified higher order neurones.

3. When receptive fields of synaptically activated neurones were compared with those of primary afferent fibres, an often extensive convergence from first order on to higher order neurones was established. Out of 119 relay neurones six received input from one sinus hair only. Spontaneous activity was encountered about twice as often in synaptically activated neurones than in primary afferent fibres.

4. The responsiveness of single neurones was unstable over time in about one fifth of the population and then the total number of impulses discharged in successive responses could vary by as much as 500%. Unstable responsiveness occurred sometimes alone but was often accompanied by marked changes in the size or the configuration of the receptive field. Such instabilities were observed in all kinds of synaptically activated neurones but not in primary afferent fibres.

5. Afferent inhibition in relay neurones could be elicited from within the excitatory receptive field and appeared to be related to the activation of distinct receptor populations responding to specific stimulus parameters. Inhibition was also seen in interneurones following both mechanical stimulation of the skin and electrical stimulation of lemniscal fibre terminals in the contralateral ventromedial thalamus.

6. The results are discussed and compared with previous findings about sinus hair representation in the trigeminal nucleus and the ascending

lemniscal projection. The findings indicate that the concept of the 'static properties' of relay neurones is not adequate for all trigeminothalamic relay neurones and may require a critical reconsideration.

7. It is suggested that the afferent input from sinus hairs is effectively controlled at the level of the rostral trigeminal nuclei. This control may affect the spatial input to relay neurones, the temporal components of their responses and the intensity dimension of their transmission capacity. It is postulated that by these mechanisms tactile information from the sinus hair system is modulated according to the instantaneous sensory requirements of the behaving cat.

INTRODUCTION

In the trigeminal sensory system of the cat, afferent impulses originating from receptors in sinus hair follicles are quantitatively and qualitatively of great significance for tactile orientation. In several studies it has been reported that between one half and two thirds of mechanoreceptive units in the infraorbital nerve are associated with sinus hair receptors and that a single afferent nerve fibre innervates only one sinus hair follicle (Fitzgerald, 1940; Kerr & Lysak, 1964; Rowe & Sessle, 1972; Gottschaldt, Iggo & Young, 1973; Dykes, 1975). In the cat and other animals, slowly adapting units of two types make up the majority of these receptor afferents (Gottschaldt *et al.* 1973; Pubols, Donovik & Pubols, 1973 Kirkpatrick & Kruger, 1975) and, therefore, the trigeminal system appears to be particularly suited to study the central processing of discharges in slowly adapting primary afferent fibres.

A proposal was made by Schultz, Galbraith, Gottschaldt & Creutzfeldt (1976), in a study of the somatosensory cortex, that the complex information transmitted by the slowly adapting afferents concerning the velocity, amplitude, duration and direction of a sinus hair movement might be segregated by neuronal mechanisms into separate components. A possible location at which such mechanisms could operate is the trigeminal nucleus, within which modulation of the peripheral input by afferent inhibition and intranuclear, corticofugal and reticulofugal influences has been described by many authors (reviewed by Darian-Smith, 1973; Towe, 1973; Baldissera, Broggi & Mancia, 1967; Scibetta & King, 1969; Dubner & Sessle, 1971; Sessle & Dubner, 1971; Carmody and Rowe, 1974; Sessle & Greenwood, 1976; Greenwood & Sessle, 1976; Denny-Brown & Yanagisawa, 1973).

Earlier studies have provided some information about the representation of sinus hairs in different portions of the trigeminal nuclear complex (Gordon, Landgren & Seed, 1961; Kruger & Michel, 1962; Eisenman,

Landgren & Novin, 1964; Nord, 1968; Kerr, Kruger, Schwassmann & Stern, 1968; Rowe & Sessle, 1972; Mosso & Kruger, 1973). In the light of new knowledge about functional properties of different receptor types in sinus hair follicles, electrophysiological investigations have been directed to studying specifically the representation and response properties of neurones in the trigeminal nuclei receiving these afferents (Shipley, 1974; Kirkpatrick & Kruger, 1975; Young & Iggo, 1977). In the present study further observations on the functional properties of neurones in the rostral trigeminal nuclei and the trigeminal medial lemniscus with sinus hair afferents will be reported. In order to establish more clearly the changes in responses accompanying the transition from first order to higher order neurones special efforts were made to distinguish between the activity in primary afferent fibres, trigeminothalamic relay neurones and interneurones, using electrophysiological methods.

A short account of the results has been published (Young & Gottschaldt, 1975).

METHODS

Results were obtained from experiments on forty-four cats weighing $2{\cdot}7 \pm 0{\cdot}7$ kg. In the first six experiments anaesthesia was achieved by I.P. injection of pentobarbitone (40 mg/kg). In later experiments anaesthesia was induced with ethyl chloride and ether, a cannula was inserted into a saphenous vein and, following discontinuation of ether application, pentobarbitone was infused throughout the experiment. A rapidly administered dose of 10–12 mg/kg I.V. induced deep anaesthesia suitable for surgery. Subsequently, 3 mg/kg.hr of pentobarbitone were infused throughout the experiment, resulting in cumulative doses of between 45 and 55 mg/kg depending on the duration of an experiment which was limited to a maximum of 15 hr. Blood pressure was monitored via a cannula inserted into the femoral artery and was normally between 150 and 180 mmHg. In our experience the activity of second-order neurones deteriorated if the blood pressure was less than 120 mmHg and experiments were abandoned if the mean pressure dropped below this value for any length of time. End-tidal CO_2 concentration, varying with blood pressure, was measured and held between 3·0 and 4·5%, if necessary, by artificial respiration. In such cases, or when electrical stimulation was used, the animals were immobilized with gallamine triethiodide (Flaxedil). Immobilization was interrupted from time to time by injections of prostigmine, I.V., in order to monitor the level of anaesthesia. An electrically-heated blanket maintained body temperature at 36–38 °C. As surgical procedures a cannula was inserted into the trachea and craniotomies over the right cerebellum and the left parietal cortex were performed. After removal of the dura the exposed brain surfaces were covered with 2% agar solution to minimize pulsation. The cats were mounted in a stereotaxic frame, fixing the head using ear bars, and a clamp between the maxilla and orbit at the left side. In this way the right side of the head was accessible for stimulation.

In a first series of experiments the location and stereotaxic co-ordinates of the trigeminal nuclei oralis and principalis, the trigeminal medial lemniscus and the contralateral ventromedial thalamus were determined by mapping responses to facial sinus hair stimulation in successive transversal planes using fine, glass-insulated tungsten micro-electrodes of low impedance. A two-dimensional grid of 250 or

500 μm interpoint distance was thus obtained for several rostro-caudal levels in the Horsley-Clark system indicating the area and the topography of sinus hair representation in the rostral trigeminal nuclei and the contralateral thalamus as well as the course of the lemniscal projection system.

In the second series of experiments single unit activity was recorded using Insl-X insulated steel electrodes of 3·5–5 MΩ impedance. On the basis of the data from the first series of experiments these electrodes could be placed with high accuracy into the area of sinus hair representation in the trigeminal nuclei and the trigeminal medial lemniscus. Recording conditions with steel electrodes were usually very stable and single units could be investigated for periods of more than 6 hr.

Isolated units were tested for tactile trigeminal inputs by manual stimulation of the facial skin and sinus hairs and their receptive field was determined. In order to establish the orthodromic latencies of responses by electrical stimulation, a bipolar steel electrode (tip distance 2 mm) was thrust into the skin at the centre of the receptive field. Using electrical stimulation of the terminals of lemniscal fibres it was determined whether a given trigeminal neurone could be activated antidromically or transsynaptically from the ascending lemniscal pathway. A bipolar glass-insulated steel electrode was placed into the caudal pole of the contralateral ventrobasal thalamus according to the stereotaxic coordinates of the thalamic sinus hair representation determined in the first series of experiments. Recording through the stimulating electrode, the optimal placement of the electrodes for stimulation of lemniscal fibre terminals was obtained at the position at which a maximal response, after movement of the contralateral facial sinus hairs, was encountered. The duration of electrical stimuli was 50 μsec.

Controlled quantitative mechanical stimuli were provided by an electromechanical stimulator which could be coupled with an 'angle stimulator' to move sinus hairs (Gottschaldt *et al.* 1973; Schultz *et al.* 1976).

Amplified recorded potentials were displayed on an oscilloscope, audiomonitored and stored on FM tape together with analogue signals of the movement of the electromechanical stimulator. Data were also transferred on-line to a PDP-12 computer which simultaneously generated a peri-stimulus-time-histogram of the neural response and an averaged signal describing the time course and amplitude of the monitored stimulator movements. Original recordings were displayed on a storage oscilloscope and photographed with a Polaroid camera. Impulses in given periods of time and their discharge frequency were measured with an electronic counter.

In some experiments the correct positioning of the stimulating and recording electrodes in the ventrobasal thalamus and the trigeminal nucleus, respectively, were verified by making lesion points and subsequent histological determination of their location.

RESULTS

Topographic representation of sinus hair afferents in the trigeminothalamic pathway

The fibres of the trigeminal nerve project on to the trigeminal nuclei in a topographic manner, showing a dorso-ventral and medio-lateral organization (McKinley & Magoun, 1942; Wall & Taub, 1962; Kruger & Michel, 1962; Darian-Smith & Mayday, 1960). Cells receiving inputs from facial sinus hairs, especially from the larger vibrissae, lie in the centre of the rostral trigeminal nuclei, between 5·2 and 6·5 mm lateral from the mid

line, occupying an area of 1–1·5 mm². The core of this area seemingly received input from vibrissae alone, whereas the surrounding parts could be activated from both sinus hairs and fur. Mapping the trigeminal projection on to the ventrobasal thalamus a similar observation was made: a central vibrissae area was surrounded by a shell of cells with inputs from sinus hairs and fur. This arrangement was also observed in the cortical projection of sinus hairs (Schultz *et al.* 1976) suggesting that the same principle of organization, laid down in the trigeminal nuclei, is preserved throughout the ascending lemniscal pathway.

The central area of the sinus hair projection in the medulla was surrounded medially and dorsally by cells receiving inputs from the foreface, nose, the upper and lower lip sinus hairs, the chin and the cheek. Neurones located ventrally to it received inputs from the skin surrounding the eye, ear and supraorbital region, while the lateral border was formed by the incoming primary afferent fibres. The most medio-dorsal margin of the nucleus contained cells with inputs from intraoral structures. In several animals this topographic representation of the face was found at five transverse planes mapped between 3 and 9 mm posterior to the zero level of the Horsley-Clark system. Single unit recordings were usually made in the region of sinus hair representation in the trigeminal nuclei.

Functional classification of trigeminal neurones

The activity of 404 single neurones responding to tactile stimulation of the face was studied. On the basis of their responses to electrical stimuli applied to the skin and the contralateral ventrobasal thalamus four populations of units could be distinguished. The horizontal histogram in the upper left part of Fig. 1 shows the distribution of latencies of responses in 234 trigeminal neurones to electrical stimulation in their facial receptive field. The vertical histogram in the lower right part of Fig. 1 shows the distribution of latencies of responses in 126 neurones following electrical stimulation of trigemino-lemniscal fibres terminating in the contralateral, caudal ventromedial thalamus. Neurones were considered to be primary afferent fibres if they responded with short latencies to cutaneous electrical stimuli (mean $1{\cdot}28 \pm 0{\cdot}3$ msec, $n = 101$), followed stimulus frequencies above 200 Hz faithfully and did not respond to thalamic stimulation.

Units were considered to be trigeminothalamic relay neurones if they were activated antidromically from the thalamus. The criterion for antidromic responses were all or nothing spikes occurring at stable latencies ($\pm 0{\cdot}2$ msec) ranging from 0·5 to 2·2 msec (mean: $1{\cdot}24 \pm 0{\cdot}3$ msec, $n = 68$). This mean latency is virtually identical to that recently reported by Sessle & Greenwood (1976). At latencies shorter than 1·5 msec the antidromic nature of the response was mostly unequivocal but at latencies

above 1·5 msec additional criteria were applied, such as the capacity to follow stimulus rates above 200 Hz with one to one responses or a positive collision test (Darian-Smith, Phillips & Ryan, 1963). A positive collision test is shown in the original records of Fig. 1, demonstrating the abolition of an antidromic response if the thalamic stimulus was given at the moment at which the orthodromic spike passed the recording electrode in the

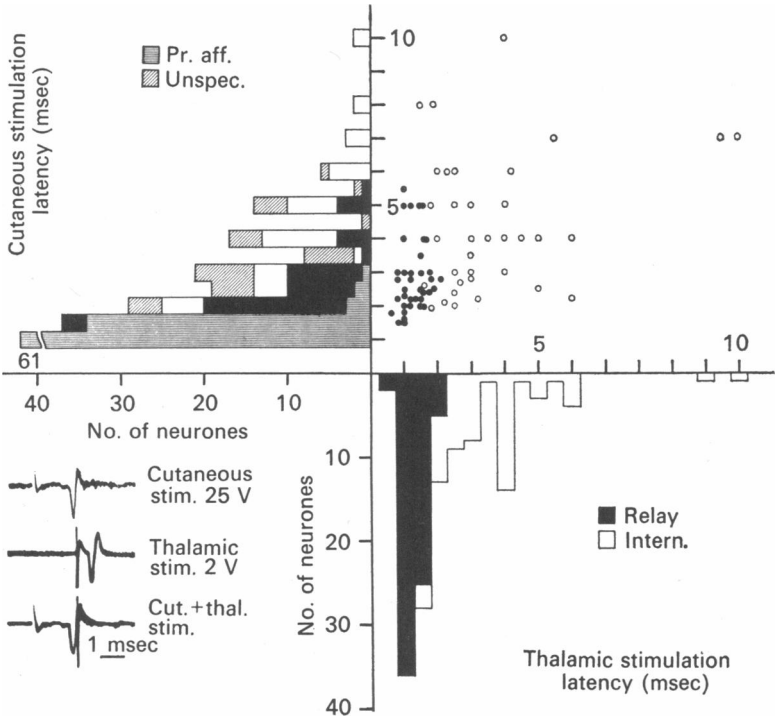

Fig. 1. Distribution of latencies of responses in different kinds of trigeminal neurones after electrical stimulation inside the cutaneous receptive field and in the contralateral ventromedial thalamus. The horizontal histogram in the upper left part shows the distribution of 234 latency measurements in trigeminal neurones following electrical stimulation of the skin. The vertical histogram in the lower right shows the distribution of 126 latency values after thalamic stimulation. Bin width 0·5 msec. The numbers for each type of unit at a given latency are plotted on top of each other. Primary afferent fibres, (Pr. aff.) relay neurones, interneurones and unspecified (Unspec.) higher order neurones were distinguished, according to criteria explained in the text, and considered separately. The filled circles in the upper right part of the Figure show the relationship between the latency of response in individual relay neurones after cutaneous (ordinate) and thalamic (abscissa) stimulation. The open circles show the analogous relationship for interneurones. The original records in the lower left part illustrate a positive collision test in a trigeminothalamic relay neurone.

trigeminal nucleus; thus causing collision of the orthodromic and antidromic impulse in the ascending lemniscal fibre.

The latencies of responses to cutaneous electrical stimuli in relay neurones ranged from 1·5 to 5·5 msec (mean $2{\cdot}77 \pm 1{\cdot}0$ msec, $n = 48$), being on average twice as long as in primary afferent fibres. If in individual relay neurones response latencies to antidromic and cutaneous stimuli were compared (filled circles in the upper right part of Fig. 1) it was evident not only that the majority of relay neurones was monosynaptically activated from the periphery but also that relay neurones with a presumably polysynaptic input were not uncommon. It can also be seen that fast conducting lemniscal fibres did not necessarily originate from cells receiving a monosynaptic peripheral input. In order to expand the sample of relay neurones, micro-electrode recordings were also made directly from lemniscal fibres at the meso-diencephalic junction. Sixty-six single units were encountered and fifty-one of them with responses to contralateral sinus hair movements were considered to be ascending fibres of trigeminothalamic relay neurones. The mean latency of responses to cutaneous stimulation in forty-one of these neurones was $4{\cdot}45 \pm 1{\cdot}85$ msec, thus corresponding approximately to the value which would have been expected from adding the response latencies after cutaneous and thalamic stimuli obtained from relay neurones in the rostral trigeminal nuclei. The discharge properties and receptive field characteristics of the lemniscal fibres were comparable to those of relay neurones identified in the trigeminal nuclei and therefore both groups will be considered together, amounting to a total number of 119.

A third population of fifty-eight trigeminal neurones was considered to constitute interneurones. They responded trans-synaptically to thalamic stimuli at latencies of between 1·6 and 11 msec (mean $3{\cdot}6 \pm 1{\cdot}8$ msec, $n = 58$) and had response latencies to cutaneous stimulation of between 2·0 and 10·0 (mean $4{\cdot}85 \pm 2{\cdot}6$ msec, $n = 52$). The responses to both cutaneous and thalamic electrical stimuli in interneurones were usually repetitive, increasing in stability and number of impulses with the stimulus strength while the latencies decreased. A plot of latencies to thalamic stimuli against those to cutaneous stimuli measured in individual interneurones (open circles in Fig. 1) indicated that most interneurones were polysynaptically activated from the skin but that some were also monosynaptically excited. Possibly, recurrent collaterals from ascending axons of relay neurones constitute a part of the pathway over which interneurones were excited by both the cutaneous and the thalamic stimuli.

Ninety-three units were considered to be second or higher order neurones but could not be specified as either relay or interneurones. This group consisted of neurones which could not be activated from the contralateral

thalamus or which could not be adequately investigated. The latency distribution of responses to cutaneous stimuli ranged from 2 to 6 msec (mean $3{\cdot}47 \pm 1{\cdot}0$ msec, $n = 33$). In this respect and also in their receptive field characteristics and response properties neurones of this group seemed to include interneurones and relay neurones which failed to respond to thalamic stimulation. One possible reason for such failure is illustrated in Fig. 2 for a relay neurone with a polysynaptic afferent input. In this case

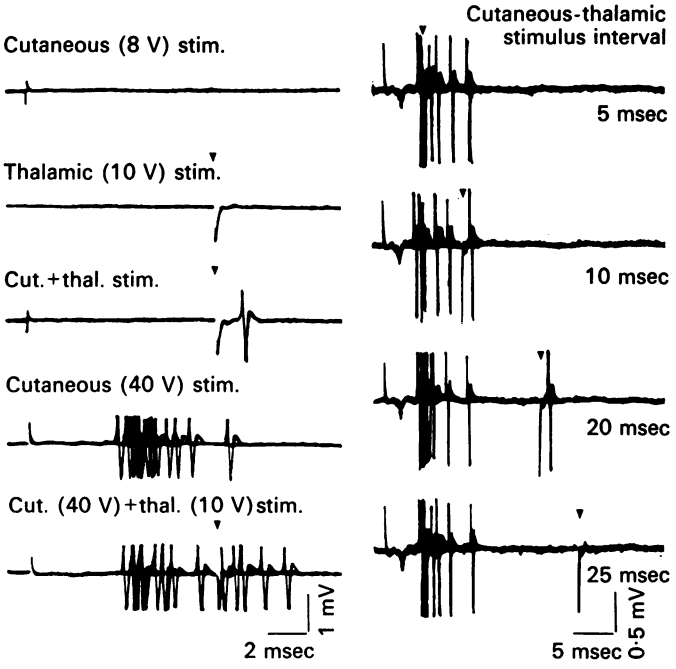

Fig. 2. Facilitation of antidromic responses in relay neurones. Each record in the left column consists of ten superimposed traces and demonstrates, in the upper three records, facilitation of an antidromic response in a relay neurone by a preceding subthreshold cutaneous stimulus. The lower two records show a long latency (4·5 msec) response to suprathreshold cutaneous stimulation and its further enhancement by additional thalamic stimulation. The right column illustrates for the same neurone in single sweep recordings the time course of the facilitatory effect of cutaneous stimulation on to the antidromic response. Note different amplitude calibrations.

the antidromic response was obtained only if the thalamic stimulus was preceded by a cutaneous mechanical or electrical stimulus and even a subthreshold cutaneous stimulus facilitated the antidromic invasion of the cell. With stronger cutaneous stimuli a repetitive irregular response was obtained which was enhanced and prolonged by additional thalamic

stimulation. The time course of the facilitation of the antidromic response illustrated in the right column of Fig. 2 lasted for up to 20 msec following a single cutaneous stimulus.

These observations suggest that subthreshold depolarizations of the cell membrane may have been generated both orthodromically and antidromically, resulting in mutual facilitation. The phenomenon of facilitation of the antidromic invasion of relay neurones by a cutaneous stimulus was observed several times and makes it possible that some of the unspecified second order neurones may have been relay neurones in which the antidromic impulse failed to invade the cell body.

Properties of primary afferent fibres

Of 338 units recorded in the rostral trigeminal nuclei and responding to light tactile stimuli 40 % were classified as primary afferent fibres ($n = 134$). Usually, but not always, they discharged with initially positive spikes, often of large amplitude.

In some cases the same afferent fibre could be recorded while advancing the micro-electrode for up to 300 μm. Ninety-two fibres innervated sinus hair follicles and always responded to movement of only one sinus hair, regardless of its size or its position in the face. Of all fibres, 63 % were activated from slowly adapting receptors. The population of sinus hair afferents comprised all kinds of units previously described in the cat (Gottschaldt *et al.* 1973): rapidly adapting high velocity threshold units, 30 %, rapidly adapting low velocity threshold units, 1 %, slowly adapting St I units, 32 %, and slowly adapting St II units, 37 %, including 4 % St IIb units.

Convergence of afferent inputs and excitability characteristics in synaptically activated neurones

In contrast to the findings in primary afferent fibres, neurones synaptically activated from the skin responded only rarely to movements of just one single sinus hair. 66 % of 258 higher order neurones received input from sinus hairs and in only ten of them (4 %) was the receptive field confined to a single sinus hair. In all three groups of second or higher order neurones, simultaneous input from sinus hairs and surrounding or interspersed fur occurred more frequently than input from sinus hairs alone (Table 1). In those neurones in which the receptive field included both sinus hairs and fur, it was particularly evident that convergence of different kinds of receptors occurred, such as slowly adapting units from the sinus hair follicles and rapidly adapting units from the fur.

If a given second order neurone could be activated from more than one sinus hair it was certain that at least as many afferent fibres converged on

TABLE 1. Data obtained from 404 single units with facial receptive fields are included in the Table: 338 neurones were recorded in the rostral trigeminal nuclei and sixty-six from the terminals of lemniscal fibres in the contralateral caudal ventromedial thalamus. Figures marked by a star indicate that data about the respective parameter of the response were not collected from all neurones in this group. The percentage values therefore refer to the number of neurones from which data in each section were obtained (indicated as total sum)

	Prim. affer. fibres		Relay neurones		Interneurones		Unspecified higher order neurones		Higher order neurones total	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Total number of neurones studied	134		119		58		93		270	
Receptive field										
One sinus hair	92	69	6	5	3	5	1	1	10	4
Only sinus hairs	—	—	23	19	5	9	21	26	49	19
Including sinus hairs	—	—	55	47	26	45	31	38	112	43
No sinus hairs	42	31	35	29	24	41	28	35	87	34
Total sum	134	100	119	100	58	100	81*	100	258*	100
Receptive field unstable	—	—	20	17	6	10	8	10	34	13
Sensitivity unstable	—	—	25	21	12	21	17	21	54	21
Out of total	134 =	100	119 =	100	58 =	100	81* =	100	258* =	100
Spontaneous activity										
Yes	25	19	58	49	22	42	28	37	108	44
No	109	81	61	51	31	58	47	63	139	56
Total sum	134	100	119	100	53*	100	75*	100	247*	100
Slowly adapting (tonic) responses	84	63	65	70	24	44	41	55	130	59
Rapidly adapting (phasic) responses	50	37	27	30	30	56	33	45	90	41
Total sum	134	100	92*	100	54*	100	74*	100	220*	100

to this neurone as there were sinus hairs included in the receptive field. In 84 of the 171 second order neurones with sinus hair input it was determined exactly from how many sinus hairs a response could be elicited. Fig. 3 represents the result of this analysis detailed for the three groups of second order neurones. As can be seen, neurones of all three groups received inputs from variable numbers of sinus hairs and no major difference between the three groups was evident. The ten neurones with input from only one sinus hair are included in the histogram of Fig. 3 but overrepresent this group since none of the other eighty-seven neurones with sinus hair input which were not included in this analysis could be driven from only a single sinus hair. In any case, the results shown in Fig. 3 and Table 1 clearly demonstrate that the great majority of synaptically activated neurones received a spatially convergent input.

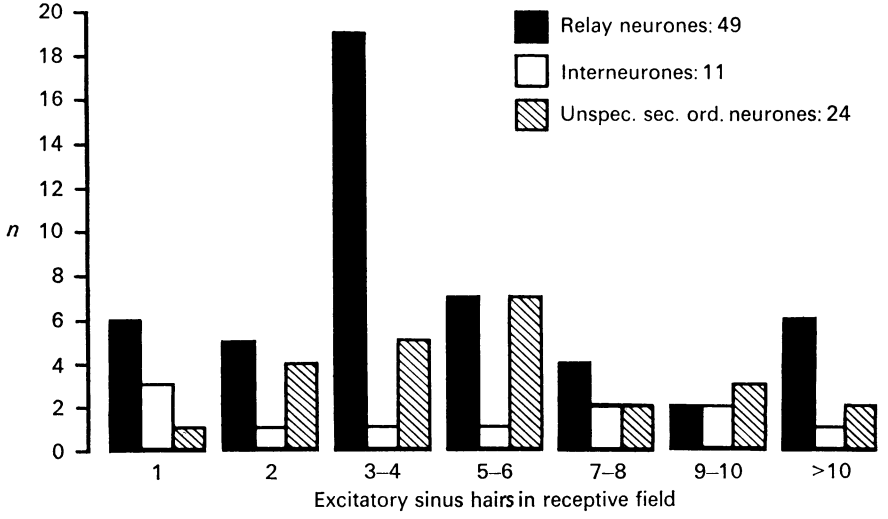

Fig. 3. A histogram showing the number of sinus hairs from which excitatory responses in individual relay neurones, interneurones and unspecified second-order neurones could be obtained.

A higher order neurone was classified as responding tonically even if the occurrence of a tonic discharge required a simultaneous input from many rapidly and slowly adapting primary afferent fibres converging on to this neurone. With this taken into account, tonic responses to a steady stimulus were obtained in 70% of relay neurones, 44% of interneurones and in 55% of the unspecified higher order neurones (Table 1). The six relay neurones with single sinus hair input all responded with a phasic-tonic discharge to a hair displacement of longer duration. In three of these six relay neurones the response was directionally sensitive suggesting

activation from St I primary afferent fibres. In the other relay neurones with input from more than one sinus hair directional sensitivity occurred but was often difficult to determine, especially if a neurone responded to movement of neighbouring sinus hairs in opposite directions.

Spontaneous activity (Table 1), observed in 19, 1 % of primary afferent fibres, was more common in all groups of synaptically activated neurones. Forty-nine per cent of relay neurones, 42 % of interneurones and 36 % of the unspecified higher order neurones showed spontaneous activity. Afferent high velocity threshold units and most of the slowly adapting primary afferent fibres could be entrained by a vibratory stimulus of 440 Hz. No synaptically activated neurone was able to follow this stimulus but one relay neurone with single sinus hair input could be entrained with a discharge of 220 impulses/sec for a few seconds.

Changes in responsiveness and receptive field size in synaptically activated neurones

In 21 % of all kinds of synaptically activated neurones a spontaneously occurring variability over time was observed in the responses to repeated, identical mechanical stimuli. The variability of responses was accompanied by an additional instability of the receptive field size in 17 % of relay neurones and likewise in 10 % of interneurones and unspecified higher order neurones. This instability normally was characterized by a more or less concentric increase and decrease of the receptive field area. As more subtle changes the boundary of the receptive field remained constant but inside of it the most sensitive area shifted from one part of the receptive field to another. For instance, it was observed in a relay neurone with a large receptive field that the stimulation of one particular sinus hair initially gave the most intense response but over several minutes movement of this sinus hair became gradually ineffective while the response elicited from another, not neighbouring sinus hair continuously increased until eventually this sinus hair formed the most sensitive part of the receptive field. Changes in responsiveness and the receptive field configuration usually occurred together but in some cases only the responsiveness or the receptive field size varied. A premise to detect such changes was to observe a unit for a sufficient period of time and the percentage of neurones showing this phenomenon might have been higher if all units could have been studied longer.

The demonstration of the mutability of a receptive field by accurate mapping in brief time intervals was difficult but it was possible to measure the accompanying changes of responsiveness over time. For this purpose a constant stimulus was given at a rate of 1/sec and the number of impulses elicited by thirty stimuli was counted in constant intervals and for fixed

periods of time over up to 45 min. Fig. 4 shows the result of this analysis for two relay neurones with large receptive fields as indicated in the face figurines. The responses of the relay neurone illustrated in Fig. 4*A* varied over time but the size of the receptive field remained unchanged. Two

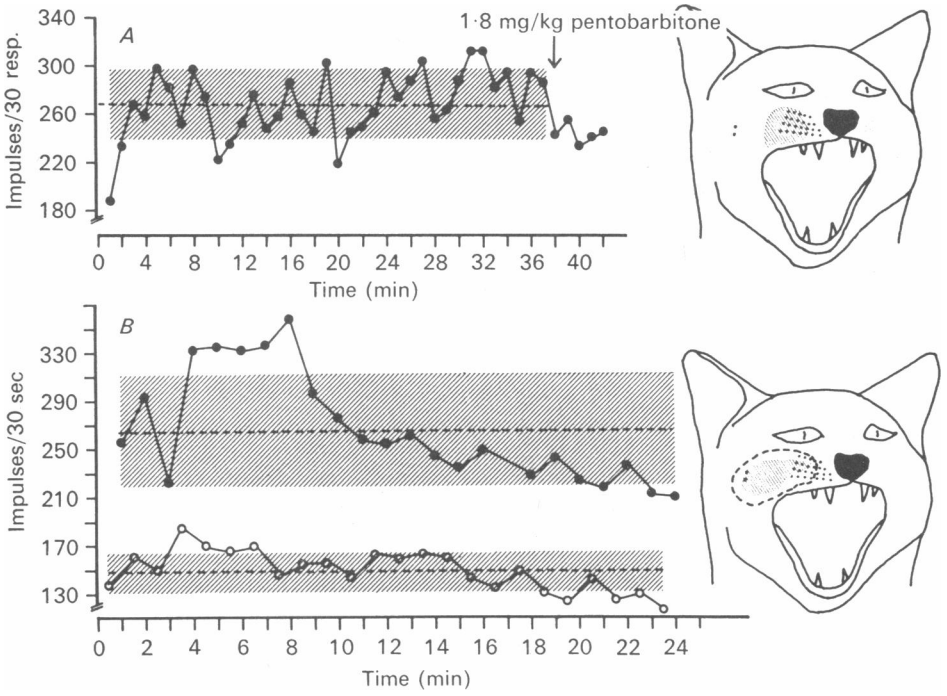

Fig. 4. Changes in responsiveness in two trigeminothalamic relay neurones.

A: unstable responsiveness in a relay neurone with stable cutaneous receptive field (shaded area in the face figurine). The ordinate gives for each point of the curve the total number of impulses counted in thirty responses to successive identical mechanical stimuli applied within the receptive field during the first half of every minute and at a stimulus rate of 1/sec. No stimuli were given during the second half of every minute and there was no spontaneous discharge. Cutaneous latency: 2·8 msec, antidromic latency: 0·8 msec. The arrow indicates intravenous injection of pentobarbitone 1·8 mg/kg.

B: the upper curve was obtained as in *A* and shows the number of impulses discharged in response to thirty mechanical stimuli. The lower curve represents the number of impulses discharged spontaneously during the 30 sec which preceded the 30 sec of stimulation. The shaded area in the face figurine indicates the extension of the receptive field during low, the dashed line during high responsiveness. Cutaneous latency: 5 msec, antidromic latency 1 msec. In *A* and *B* the mean discharge during the entire observation period and the standard deviation from the mean are indicated in each curve by the horizontal dashed line and the hatched band, respectively.

sinus hairs were stimulated together and the number of impulses elicited by thirty stimuli varied between 186 and 310. Abrupt and slow changes of responsiveness occurred. After thirty-seven min observation time 1·8 mg/kg pentobarbitone were injected I.V. and both the number of impulses and the variability in the responses subsequently appeared to be slightly reduced.

The relay neurone illustrated in Fig. 4*B* varied in both its responsiveness and the size of its receptive field. The shaded area in the face figurine depicts the receptive field size at low responsiveness, the dashed line at high responsiveness. This neurone had a sizeable spontaneous activity and therefore the number of impulses during 30 sec of spontaneous activity and during 30 sec of stimulation (1/sec) were alternately counted. During the observation period the evoked response increased suddenly, remained at a high level for about 5 min and then declined steadily during the following 15 min. The spontaneous activity also varied and appeared to follow roughly the changes in the size of the evoked responses. In other neurones it also was observed that changes in responsiveness and spontaneous activity occurred simultaneously, the latter being high at increased and low at reduced responsiveness.

The relay neurones shown in Fig. 5 had a receptive field restricted to two supraorbital sinus hairs and responded at times to movement of only one of them and at other times to movement of both sinus hairs. In this case identical stimuli were continuously applied for 10 min at a rate of 1/sec and the number of discharged impulses was counted during every 15 sec. The curve in Fig. 5*A* illustrates that the number of impulses per fifteen responses varied irregularly over time by as much as 500%. This is particularly evident if individual responses to the 570 consecutive stimuli are compared (Fig. 5*B*). The response to stimulus no. 318, for example, showed a distinct tonic discharge during the steady part of the sinus hair displacement but only 8 sec later no response at all occurred during the same stimulus phase. The variable responsiveness of this relay neurone is also documented by the three post-stimulus time histograms in Fig. 5*C* which were assembled from forty-five consecutive responses at time I, II and III, as indicated in Fig. 5*A*.

The stability of responses over time was also tested in the same manner in several slowly adapting primary afferent fibres. Individual responses to identical stimuli varied for not more than one or two impulses and in no case changes were observed comparable to those illustrated for the relay neurones in Figs. 4 and 5.

Inhibition in trigeminothalamic relay neurones

The peri-stimulus time histograms in Fig. 5*C* document another feature in the response of this relay neurone which demonstrates an example for processing of slowly adapting afferent responses at the first synaptic level.

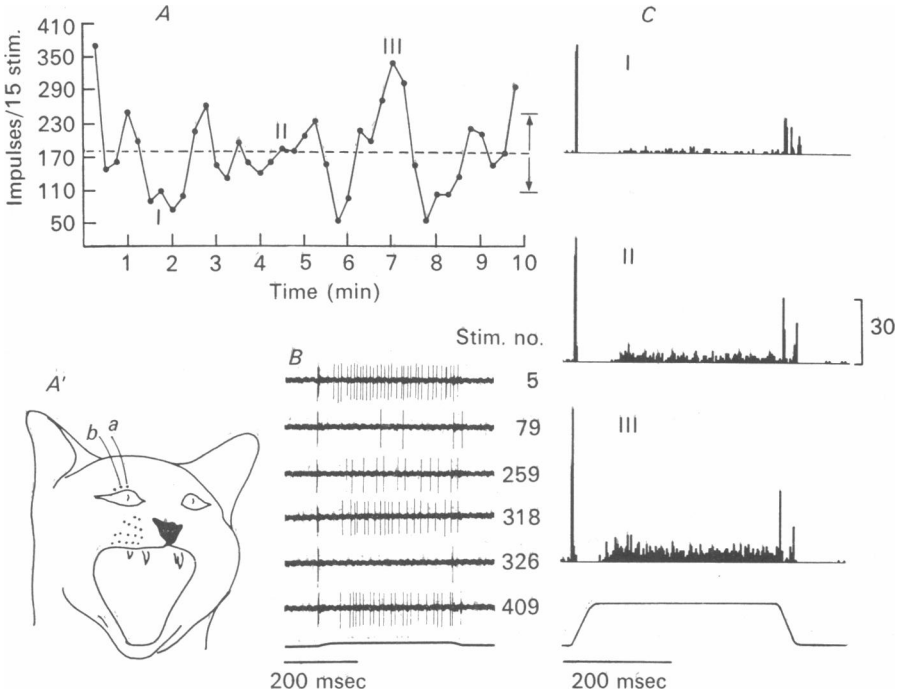

Fig. 5. Changes in responsiveness in a trigeminothalamic relay neurone. Each point in *A* represents the number of impulses in fifteen successive responses during 10 min of continuous stimulation at a rate of 1/sec. The dashed line indicates the mean response during the ten minutes, the arrows the standard deviation from the mean. The receptive field was confined to two supraorbital sinus hairs (*A'*). Specimen records of individual responses are shown in *B* with the number of the respective stimulus given to the right. The three peri-stimulus time histograms in *C* I, *C* II and *C* III were assembled from forty-five responses taken during low (I), medium (II) and high (III) responsiveness at times indicated in *A*. Bin width: 2 msec. Note the absence of the dynamic response in all histograms. Cutaneous latency 2·8 msec, antidromic latency 1·2 msec.

In the original records (Fig. 5*B*) a second unit can be discerned that discharged with a smaller action potential only at the onset of the stimulus. The activity of this unit was incorporated into the three histograms and accounts primarily for the peak at the stimulus onset. However, the

dynamic response to the initial movement component of the stimulus, always prominent in slowly adapting primary afferent fibres, was almost completely suppressed in the discharge of the relay neurone while the tonic response, if at all present, was almost constant during the steady component of the stimulus, irrespective of the level of responsiveness at

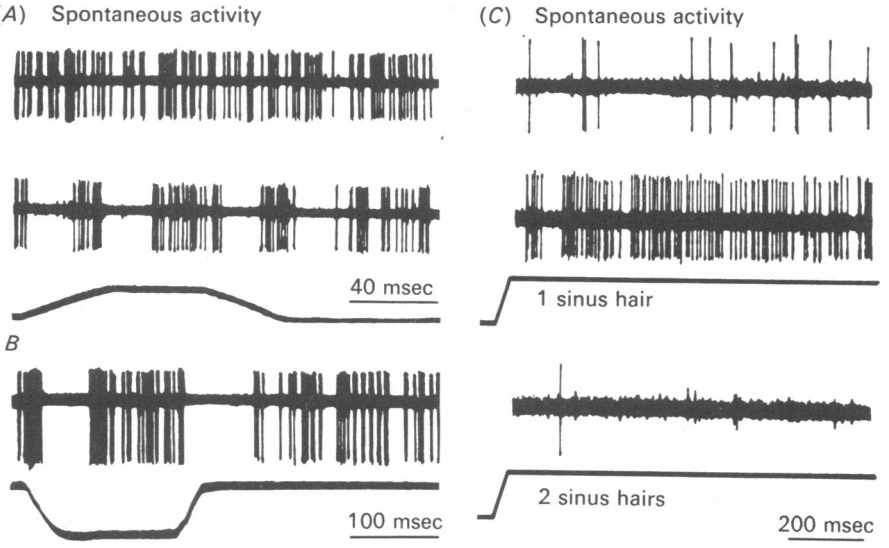

Fig. 6. Afferent inhibition in three trigeminothalamic relay neurones. Ten superimposed traces are shown in each record in *A* and *B*, single sweeps in all records in *C*. The upper record in *A* represents spontaneous activity, the lower record the time course of the monitored mechanical stimulus. The middle record shows inhibition of spontaneous activity following each change in movement velocity of the stimulus. Antidromic latency 1·5 msec. The receptive field included all vibrissae and interspersed fur. In *B* the stimulus (lower trace) evoked excitatory responses and inhibitory periods following movement of the sinus hair in both directions. Antidromic latency 1 msec. The receptive field included sinus hairs and fur. The upper trace in *C* shows spontaneous activity of a relay neurone that responded with a strong tonic discharge to a manual steady deflexion of one sinus hair (middle trace in *C*). Inhibition of the tonic response occurred at simultaneous deflexion of another neighbouring sinus hair (lowest record in *C*). The time course of the sinus hair deflexion is indicated below the spike records. Antidromic latency 1·2 msec. The excitatory receptive field was confined to only two sinus hairs.

a given time. Seemingly, inhibitory mechanisms eliminated the velocity dependent component of the response resulting in a discharge related only to the amount and the duration of the sinus hair displacement.

The records in Fig. 6 suggest that inhibition acting on relay neurones with input from sinus hairs may depend on the activation of receptors

responding specifically to different stimulus parameters, such as the acceleration or deceleration, the velocity or the amplitude of a displacement. All three relay neurones illustrated in Fig. 6 included sinus hairs in their receptive fields and all were spontaneously active. The upper trace in Fig. 6*A* shows ten superimposed sweeps of spontaneous activity and the middle trace ten superimposed sweeps of discharges recorded when a controlled mechanical stimulus was applied inside the receptive field. Each time the velocity of the stimulus changed there followed an inhibitory period lasting up to 30 msec. With the given stimulus constellation no clear excitatory response was evident suggesting that relay neurones may receive afferent inputs with both excitatory and inhibitory components and that in this stimulus situation the inhibitory components were more effective. In the unit shown in Fig. 6*B* the stimulus onset first caused an increased discharge with a subsequent inhibitory period followed again by a short phase of excitation. The return movement of the stimulus also was followed by an inhibitory period suggesting that in this relay neurone inhibition was caused only by the movement component of the stimulus which possibly arose from the activation of velocity sensitive mechanoreceptors. The relay neurone in Fig. 6*C* received excitatory input from two sinus hairs and inhibitory input from a third sinus hair. A strong tonic discharge was caused by a steady deflexion of one sinus hair. If the bending of this sinus hair also involved a deflexion of the neighbouring inhibitory sinus hair the tonic response was almost completely abolished, and it can be assumed that the tonic inhibitory effect was associated with the activation of slowly adapting receptors in the follicle of the inhibitory sinus hair.

Quantitative aspects and the time course of inhibition in relay neurones were studied using the conditioning-test stimulus paradigm. Time courses of inhibition lasting 100 msec and more with maxima between 10 and 20 msec were found. However, for these investigations only the combination of an electrical conditioning and a mechanical test stimulus were available and the results therefore are only of restricted value in the clarification of the effects of interacting mechanical stimuli on to responses in relay neurones. This problem will be reinvestigated in a future study.

Properties of interneurones

The receptive fields of interneurones were on average larger than in relay neurones and often extended over two or three dermatomal divisions of the trigeminal nerve. The higher degree of convergence on to interneurones was also reflected in the smaller proportion of interneurones with inputs only from sinus hairs (Table 1). In thirty-four interneurones with inputs from sinus hairs this proportion was 1 to 3·25 (8 to 26) while it was 1 to 1·9 (29 to 55) in eighty-four relay neurones. It was expected that the

higher convergence on to interneurones would facilitate spatial summation and thus result in a higher proportion of tonic responses in interneurones than in relay neurones. On the contrary, 56% of the interneurones responded with a phasic discharge to a sustained mechanical stimulus.

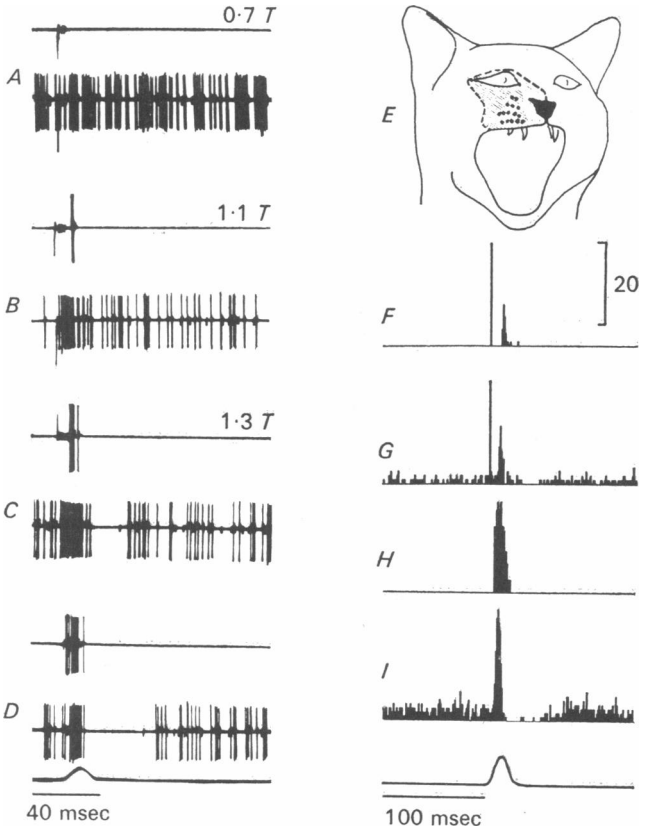

Fig. 7. Inhibition of the responses in an interneurone following both thalamic and cutaneous stimulation. Upper records in *A* to *C* show transsynaptic responses to thalamic stimuli at three different strengths, lower records show the effect of the thalamic stimuli on to activity evoked by continuous manual stimulation in the receptive field (*E*). Upper record in D shows the response to a mechanical stimulus and the lower record the inhibitory period in the evoked activity following the mechanical stimulus. Each record in *A–D* consists of ten superimposed sweeps. *F*: peri-stimulus time histogram of twenty-five responses to thalamic stimuli at 1·1 threshold, *G*: thalamic stimuli given during continuous manual tactile stimulation, *H*: peri-stimulus time histogram of twenty-five responses to controlled mechanical stimuli, *I*: controlled mechanical stimuli superimposed on continuous tactile stimulation in the receptive field. Latency to thalamic electrical stimulation: 10 msec.

A smaller proportion of interneurones than relay neurones showed spontaneous activity and this may indicate that interneurones were under effective inhibitory control.

As the interneurones responded transsynaptically to cutaneous as well as to thalamic stimuli, inhibition could be elicited from both stimulation sites. This is qualitatively demonstrated for an interneurone without spontaneous activity in Fig. 7, in which the upper traces show ten superimposed responses to thalamic stimuli of three different strengths (*A* to *C*) and to brief mechanical stimuli applied to the skin (*D*). If these stimuli were used as conditioning stimuli the lower traces show their effects on discharges evoked by continuous manual stimulation inside the receptive field. At sufficient intensities of the conditioning thalamic stimuli (Fig. 7*B*, *C*) an early facilitation became apparent in the peripherally evoked discharge followed by an inhibitory period (Fig. 7*C*, *G*). In this interneurone inhibition was also elicited by applying a natural conditioning stimulus inside the receptive field from which the test response was simultaneously evoked by continuous manual stimulation (Fig. 7*D*, *H*, *I*). A comparison of the effects of conditioning stimuli given either to the thalamus or the skin suggest that each excitation of the interneurone elicited a subsequent inhibitory period, presumably mediated by a neuronal negative feed-back loop.

In some interneurones conditioning thalamic stimuli inhibited cutaneous test responses about as effectively as did cutaneous conditioning stimuli thalamic test responses. In most cases conditioning stimuli inhibited the test response more effectively from either the thalamic or the cutaneous stimulation site and then the test response could be suppressed completely for periods of 10–100 msec following a conditioning stimulus at the more effective site. Time courses of this mutual inhibition are shown for three interneurones in Fig. 8. In all cases a mechanical stimulus was applied to the skin and an electrical stimulus to the thalamus. In the curves shown in *A* and *B* the duration of the inhibition following central or peripheral conditioning stimuli were about equal in each individual neurone regardless of which stimulus evoked the larger inhibitory effect or where the conditioning stimulus was applied. The onset and the peak of the reduction of the test response was different, however, in different neurones and dependent also on the site at which the conditioning stimulus was applied. The reduction of the test response could be preceded by a short phase of occlusion or facilitation and at long intervals of the conditioning-test stimuli it could be followed by a weak increase of the test response (Fig. 8*B*, *C*). Qualitative observations, such as those illustrated in Fig. 7, suggest that the strength of the conditioning stimulus determined the strength of inhibition, but no systematic studies on the changes in its time

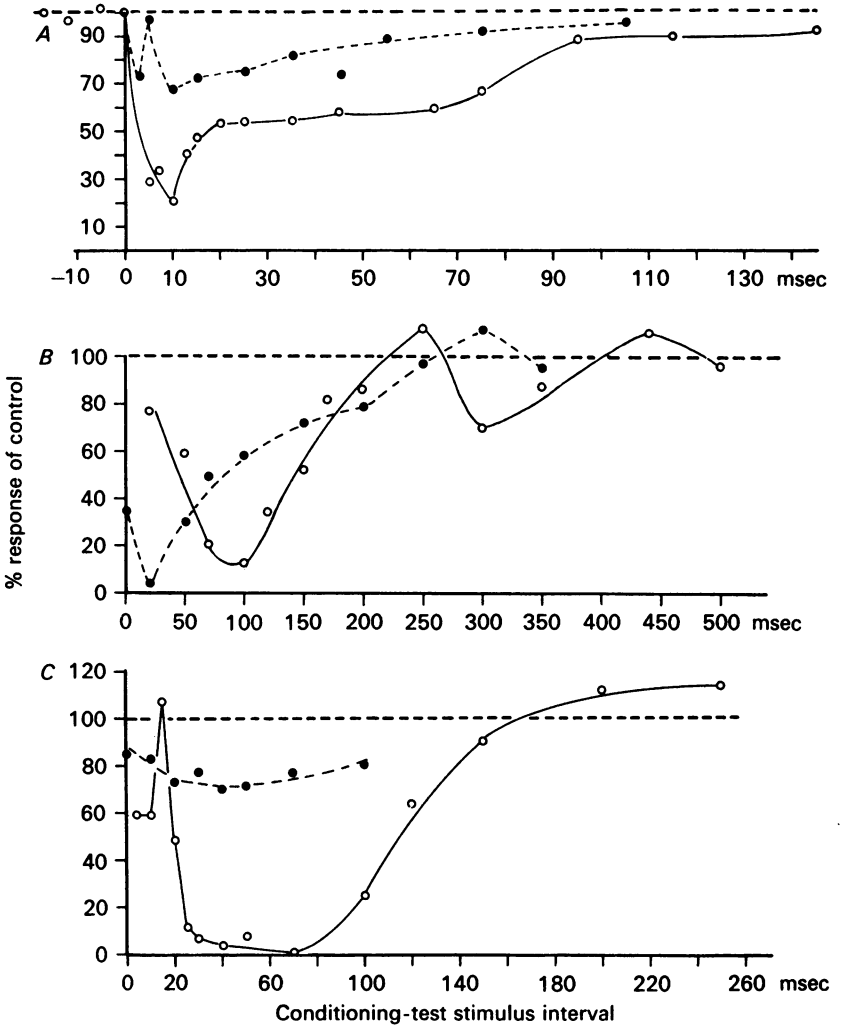

Fig. 8. Time course of inhibition of test responses to thalamic and cutaneous stimulation following conditioning stimuli in the skin and in the contralateral thalamus, respectively. In the three interneurones of which the curves in *A*, *B*, and *C* were obtained, thalamic stimuli were electrical and cutaneous stimuli mechanical. *Filled circles*: thalamic stimulus preceded cutaneous test stimulus; *open circles*: cutaneous mechanical stimulus preceded thalamic test stimulus. Each point in *A* is the mean value obtained in ten test responses at the given conditioning-test intervals; in *B* and *C* each point is the mean value from twenty-five measurements. The data were obtained by peri-stimulus time histogram analysis and thus no standard deviation from the mean can be given. The duration of the mechanical stimulus was in *A*: 190 msec (rise time 10 msec), in *B*: 310 msec (rise time 10 msec) and in *C*: 21 msec (rise time 10 msec).

course have been made. Our results indicate, however, that responses in interneurones with inputs from sinus hairs are subject to strong inhibitory influences and by the time courses of this inhibition it is presumed that presynaptic mechanisms participate in these effects.

DISCUSSION

Previous studies (Eisenmann *et al.* 1964; Rowe & Sessle, 1972; Darian-Smith *et al.* 1963; Walker, 1939; Carpenter & Hanna, 1961) have shown that the major proportion of the lemniscal trigemino-thalamo-cortical projection is relayed through the main sensory and oral trigeminal nucleus and that most neurones in these nuclei, having an ascending projection, send their axon towards the contralateral ventromedial thalamus via the medial lemniscus. In order to study these trigeminothalamic relay neurones it was necessary not only to differentiate between the activity in primary afferent fibres and synaptically activated neurones but also to identify positively relay neurones and interneurones in contrast to other unspecified higher order neurones. The criterion to identify relay neurones by their antidromic response to stimulation of the terminals of their projecting fibres and by the collision method is generally accepted. Our criterion to identify interneurones was more conservative than in a previous investigation of the cuneate nucleus (Andersen, Eccles, Schmidt & Yokota, 1964) in which all neurones not or only transsynaptically responding to thalamic stimulation were classified as interneurones. Although in this way we may have categorized some interneurones as unspecified higher order neurones, we avoided relay neurones being erroneously classified as interneurones which could not, for any reason, be activated antidromically from the thalamus. The unspecified higher order neurones could also have included trigeminal neurones with projections to the cerebellum (Darian-Smith & Phillips, 1964) or to the thalamus outside the lemniscal pathway.

In the present study a surprisingly large number of 134 primary afferent fibres was recorded in the trigeminal nucleus. Of these ninety-two fibres innervated sinus hair follicles and 69 % were slowly adapting, a proportion in agreement with our previous results obtained by recording single fibres of the infraorbital nerve (Gottschaldt *et al.* 1973) and the findings of other workers (Fitzgerald, 1940; Kerr & Lysak, 1964; Zucker & Welker, 1969; Nilsson, 1969; Rowe & Sessle, 1972; Pubols *et al.* 1973). Only Dykes (1975) described a much smaller percentage (20·8 %) of sinus hair afferents to be slowly adapting. All studies agree, however, that a single primary afferent fibre always innervates only one sinus hair follicle. For the measurement of the extent of spatial convergence on to synaptically activated neurones

in the trigeminal nucleus it is therefore essential to distinguish these neurones clearly from primary afferent fibres which has not always been done convincingly in previous investigations (Nord, 1968; Shipley, 1974; Kirkpatrick & Kruger, 1975).

Evidence for spatial convergence of sinus hair afferents on to single second order neurones has not yet been presented in a systematic manner, although drawings of receptive fields in several reports indicate that convergence is the rule rather than the exception in the trigeminal nucleus (Darian-Smith, Proctor & Ryan, 1963; Darian-Smith *et al.* 1963; Kruger & Michel, 1962; Rowe & Sessle, 1972). In the caudal trigeminal nucleus Gordon *et al.* (1961) found convergence of several vibrissae in most second order neurones but the proportion of tonic responses was markedly reduced compared with the proportion among primary afferent fibres. Convergence was also conspicuous in the results of Eisenman *et al.* (1963), obtained from the rostral trigeminal nuclei, and the majority of neurones responded with tonic discharges. Our present findings support the results of the latter study and show in greater detail that in all types of synaptically activated trigeminal neurones a substantial proportion of tonic responses may be obtained, while convergence from primary afferent fibres subserving sinus hair follicles occurs in the imposing majority of post-synaptic neurones.

Receptive field sizes of neurones in the ventromedial thalamus suggesting extensive convergence in the ascending trigeminal pathway have been reported by some authors (Darian-Smith, 1964; Rowe & Sessle, 1968; Emmers, 1965; Hayward, 1975) but others have described most, if not all, thalamic neurones as responding to movement of one vibrissa only (Waite, 1973; Suosa, Oswaldo-Cruz & Gattass, 1971). Quite similar conflicting results have been obtained at the cortical level where, in some studies, convergence from many sinus hairs or equivalent face areas on to cortical neurones has been reported but not in others (Armstrong-James, 1975; Pubols, Pubols, DiPette & Scheely, 1976; Darian-Smith, Isbister, Mok & Yokota, 1966; Schultz *et al.* 1976; Welker, 1971, 1976).

Recently Hellweg, Schultz & Creutzfeldt (1977) compared whisker responses in thalamocortical fibres and cortical cells and reported significant tonic activity to be absent in all cortical cells, although 54% of eighteen identified thalamocortical fibres responded with strong phasic-tonic discharges all of which could be elicited by stimulation of only one or at the most two sinus hairs. These findings, suggesting that the activity in a substantial proportion of slowly adapting primary afferent fibres is relayed to the precortical level without convergence or major changes in the discharge pattern, are not quite in agreement with our results. It is conceivable, however, as Brown, Gordon & Kay (1974) and Schultz *et al.*

(1976) proposed, that 'pure lines' carrying information from only one peripheral nerve fibre exist in the medial lemniscus and its cortical projection. In our study only six relay neurones (5%) with latencies shorter than the mean exhibited such properties and it remains to be clarified whether a higher percentage of 'pure line' neurones is present in the thalamo-cortical than in the trigemino-thalamic projection of the sinus hair system. The different findings may also be explained by the short latencies (mainly between 2·5 and 3·5 msec) which Hellweg *et al.* (1977) reported for responses following electrical stimulation of the infraorbital nerve. This seems to indicate that the encountered thalamo-cortical fibres represented predominantly the faster components in the ascending projection to the cortex. The reasons for the often striking differences among all studies of the central sinus hair representation regarding the degree of convergence or the proportion of tonic responses may also lie in different experimental procedures and, in particular, the type and level of anaesthesia employed.

A blindfolded cat uses the sinus hairs primarily for spatial orientation in prey-catching behaviour which may be completed within one tenth of a second following physical contact between its sinus hairs and the prey. The complexity of this behaviour and the speed with which it is accomplished indicate a dynamic interaction of sensory input and motor output at subcortical or subthalamic level. By contrast, the sleeping cat is not wakened by stroking the sinus hairs, despite the enormous amount of afferent impulses elicited by such manipulations. These observations suggest that during natural behaviour the cat has active control over the input from the peripheral sinus hair system. This conclusion finds support in our frequent observation of instable receptive fields and responsiveness in single synaptically activated trigeminal neurones. Similar findings were previously reported by Gordon *et al.* (1961) in the caudal trigeminal nucleus but it was thought that they represented activity in neurones belonging to the reticular formation. Reticular neurones, however, lie outside the trigeminal nucleus, have cutaneous receptive fields usually extending over the whole face and sometimes beyond the dermatomal limits of the trigeminal nerve (Darian-Smith *et al.* 1963; Sessle & Greenwood, 1976). None of our relay neurones had these properties. On the other hand, in previous studies it has been shown that the transmission of impulses in the rostral trigeminal nuclei can be modulated by a variety of control mechanisms operating via the nucleus caudalis, through corticofugal pathways and via the reticular formation (Scibetta & King, 1969; Young & King, 1972; Wiesendanger, 1969; Dubner, 1967; Dubner & Sessle, 1971; Sessle & Dubner, 1971; Hernandez-Peón & Hagbarth, 1955; Baldissera *et al.* 1967; Hernandez-Peón, O'Flaherty & Mazzuchelli-O'Flaherty, 1965).

In our experiments the origins of the variability of the response properties observed in all kinds of synaptically activated neurones were not investigated. However, Greenwood & Sessle (1976) recently demonstrated that the transmission capacity of relay neurones in the rostral trigeminal nuclei is continually enhanced by tonic facilitation relayed or originating in the caudal trigeminal nucleus. When synaptic transmission in nucleus caudalis was blocked by cooling, this facilitation was no longer effective resulting in a marked reduction of the receptive field size and the responsiveness of single trigeminothalamic relay neurones. Spontaneous and random fluctuations in the activity of this control system alone would already account for our observations but we suggest that other facilitating and inhibitory influences of as yet undisclosed provenance participate in the modulation of response properties in trigeminal neurones. The findings illustrated in Figs. 4, 5 and 6 indicate that the control of the input-output relationship in relay neurones may affect a spatial component, manifested by a variation in the extent of, and the sensitivity within the receptive field, as well as a temporal component evidenced by the fluctuations in responsiveness of single relay neurones and by the time courses of inhibition obtained with the conditioning-test stimulus paradigm. Furthermore, Carmody & Rowe (1974) demonstrated that the transmission capacity of single relay neurones i.e. the intensity dimension of a response, may be altered by preceding conditioning stimuli. Our records of Figs. 6 and 7 show clearly and in agreement with Jänig, Schoultz & Spencer (1977) that inhibition can be generated not only in form of the surround type but also by a combination of natural stimuli within a continuous excitatory receptive field. Therefore, each stimulus applied inside the receptive field of a trigeminal neurone may generate a complex pattern of afferent excitation and inhibition which is modulated further by influences exerted from other control stations. At present it is still unknown to what extent the spatial, temporal and intensity component of the input–output relationship in relay neurones are controlled by pre- or post-synaptic mechanisms and how and to what degree they can be modulated independently from each other.

On the basis of the physiological evidence now available it must be doubted that the concept of the so-called 'static properties' of neurones projecting through the lemniscal pathway (Darian-Smith, 1973) is applicable for all trigeminothalamic relay neurones. This concept implies small and constant receptive fields and stable transmission properties of relay neurones but our results as well as those by Greenwood & Sessle (1976) and Carmody & Rowe (1974) suggest extensive afferent convergence, mutability of receptive fields and unstable transmission properties in many relay neurones. Perhaps not in all but in many trigeminal neurones the functional receptive field which can be measured in a given experimental

situation appears to be smaller than the largest possible receptive field which would be determined by the existing synaptic connexions with afferent fibres. This view is fully corroborating the recent results of Denny-Brown & Yanagisawa (1973). These authors concluded that, generally, individual neurones in the trigeminal nuclei must receive inputs from many afferent fibres, partly via monosynaptic connexions and partly via polysynaptic pathways involving the intrinsic fibre system extending throughout the trigeminal brainstem nuclear complex. They also demonstrated that the size of a dermatome, and this we understand to reflect the integral of single receptive field sizes in a population of relay neurones, is functionally variable and is determined by the balance between the activity in inhibitory and facilitatory systems controlling the degree of afferent convergence on to higher order neurones.

Similarly, this and the subsequent paper (Gottschaldt & Young, 1977) provide evidence that the functional response to a given stimulus is usually different from the responses which would be expected if primary afferent discharges were simply passed on to higher order neurones. One consequence of the activity of the control mechanisms seemingly operating in the trigeminal nucleus can also be the separation of different response parameters contained in the slowly adapting primary afferent discharges, as originally suggested by Schultz *et al.* (1976).

Taking the physiological findings and the behavioural observations together it seems possible that the way in which single neurones of the trigeminal system respond to tactile stimuli varies according to the instantaneous sensory requirements of the animal in a given behavioural situation.

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