Features Peculiar to the Trigeminal Innervation

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SUMMARY: *The aspects of trigeminal sensory structure and function which are uniquely different from spinal systems are reviewed in this paper.*

In the periphery, several unique arrangements of sensory receptors are seen, and appear to have unique sensory functions. The receptors in the cornea, the nasal mucosa, and the tooth pulp are morphologically unspecialized and are associated with "protopathic" sensory experiences. The important sensory functions of the mammalian vibrissae are also discussed, as well as their relationship to the anatomically distinctive cortical "barrels".

Aspects of trigeminal proprioception are also of interest. The absence of spindles in some muscles and the unique central organization of trigeminal proprioceptive afferents in the jaw and extraocular muscles are of functional significance in the motor function of the jaw and the eye.

Trigeminal afferents are also involved in several complex autonomic reflexes. Characteristic changes in cardiovascular and respiratory function are elicited by various patterns of trigeminal sensory stimulation. These reflexes include the diving reflex, the oculo-cardiac reflex, naso-cardiorespiratory reflexes, and the trigeminal depressor response. The clinical significance of these reflexes is discussed.

Several coordinated behavioral responses including suckling are also elicited from trigeminal afferents. The evidence implicating trigeminal afferents in eating and drinking behavior is presented.

RÉSUMÉ: *Dans cette présentation, nous revoyons les aspects particuliers de la structure et de la fonction sensorielle du trijumeau qui diffèrent des systèmes spinaux.*

A la périphérie, nous voyons de nombreux arrangements uniques des récepteurs sensitifs qui également ont des fonctions sensorielles uniques. Les récepteurs de la cornée, de la muqueuse nasale et des dents sont non spécialisés morphologiquement et sont associés à des expériences sensitives "protopathiques". Les fonctions sensorielles importantes des "vibrisa" de mammifères sont également discutées, ainsi que leur relations avec les "barils" corticaux qui sont anatomiquement distincts.

Certains aspects de la proprioception trigéminale sont également d'intérêt. L'absence de "spindle" dans certains muscles et l'organisation centrale unique des afférences proprioceptives trigéminales de la mâchoire et des muscles extraoculaires sont d'importance fonctionnelle pour la fonction motrice de la mâchoire et de l'oeil.

Les afférences trigéminales sont également impliquées dans plusieurs réflexes autonomiques complexes. Différentes stimulations sensitive trigéminales produisent des changements caractéristiques dans les fonctions cardiovasculaires et respiratoires. Ces réflexes incluent le réflexe oculo-cardiaque, les réflexes naso-cardio-respiratoires et la réponse dépressive du trijumeau. Nous discutons de la signification clinique de ces réflexes.

Plusieurs réponses comportementales coordonnées tel le réflexe de suction, sont également provoquées par les afférentes trigéminales. Nous présentons en dernier lieu des arguments en faveur du rôle des afférences trigéminales dans le comportement accompagnant l'acte de boire ou de manger.

INTRODUCTION

The name "trigeminal" means, literally, three twins and refers to the fact that the sensory root of the fifth cranial nerve has three major subdivisions. These are the ophthalmic, the maxillary, and the mandibular branches which innervate, respectively, the upper, middle, and lower thirds of the skin of the face as well as the corneas, part of the oral and nasal mucosa, and the tooth pulps. Proprioceptive information from certain muscles related to the face and jaws is also transmitted by trigeminal afferents. The motor root innervates the muscles of mastication. The general properties of the trigeminal sensory system have been comprehensively reviewed (Darian-Smith, 1973). Many of these properties are similar to those of spinal nerves, although there are also some important differences. The aim of this review is to bring together those aspects of trigeminal sensory orgaization which differ significantly from the structural and functional organization of other cranial nerves, and of spinal nerves. The physiology of several reflexes elicited from trigeminal afferents is also discussed. Many of these peculiarities of trigeminal organization have some clinical significance, which is discussed in the context of the current understanding of trigeminal physiology.

PERIPHERAL RECEPTORS

The general somatic sensibility of the skin of the face is similar to that of skin elsewhere, although it is worth noting that the ability of trigeminally-innervated structures to detect and locate gentle mechanical stimuli is rivalled only by the skin of the fingertips and the mucosal surfaces of the external genitalia (Weinstein, 1968).

The Cornea

The innervation of the cornea in species as diverse as dogfish, rabbits, and man is of interest in that the only nerve terminals found histologically in the corneas are fine, beaded filaments (Weddell and Zander, 1950). These terminations can be seen in the living human cornea with the aid of slit lamp microscopy, after staining with methylene blue. The absence of more specialized, encapsulated receptors has made the cornea an interesting model for several generations of psychophysical investigators. In particular, von Frey and his school claimed that pain was the only sensation perceived by humans when the cornea was stimulated by any means (von Frey, 1894). This association of pain sensibility and free nerve endings was advanced as *prima facie* evidence supporting the theory that morphologically distinctive receptors subserved specific qualities of sensation. That is, it was proposed that the sensation of pain was specifically due to the activation of free nerve endings, whereas warmth was subserved by Ruffini endings, cold by Krause's end bulbs, and touch largely by Meissner's corpuscles.

Other investigations, however, using diverse techniques to stimulate the cornea, found that their subjects could identify the sensations of touch, warmth and cold, in addition to pain (Stein, 1925).

The controversy apears to have been resolved by Lele and Weddell by a series of experiments at Oxford in 1956. These investigators showed their subjects could reliably distinguish touch, warmth, cold, and pain when a carefully controlled stimulus was applied to the cornea. Moreover, by reproducing the experiments of earlier workers, they were able to show that many of the results obtained thereby were unacceptable for technical reasons.

It is nevertheless interesting that Lele and Weddell's subjects perceived the sensations elicited from the cornea to be qualitatively different from that elicited by equivalent stimulation elsewhere on the skin. Some subjects were unable to adequately describe the sensation verbally, since words such as "touch", "tickle", and "itch" were not precisely appropriate to their experience. Psychological factors also were thought to be important, as many cooperative subjects felt threatened by even innocuous stimulation of the cornea, and were not able to allow a copper rod to come in contact with their cornea.

The Nasal Mucosa

The organization of receptors in the nasal respiratory mucosa is similar to that in the cornea in that only one morphological type of nerve terminal has been identified. These receptors are simple terminal arborizations, which conduct sensory information to non-myelinated axons in the trigeminal nerve (Cauna et al., 1969). These authors state that the nasal mucosa has a limited capability for the localization and discrimination of sensory modalities, although this does not seem to have been investigated in detail. Melzack and Eisenberg (1968) observed that gentle mechanical stimulation of the nasal mucosa evokes "a tingling sensation that may continue for many seconds or minutes, and stops only when the area is rubbed". This sensory "afterglow" can also be elicited, although less effectively, from trigeminal skin areas.

Tooth Receptors

Another unique receptor mechanism within the trigeminal innervation is the dental pulp receptor. It is widely stated that stimulation of dentine, or of the pulp itself, whether by chemical, electrical, thermal, osmotic or mechanical means, evokes only the sensation of pain in human subjects (for review, see Anderson et al., 1970). Mumford and Bowsher (1976), however, found that rather unpleasant sensations, not described as pain, may be experienced during pulpal stimulation at near threshold intensity. They suggest the re-introduction of the term "protopathic" to describe the ill-defined sensory experiences evoked by activity in unmyelinated or sparsely myelinated fibers, such as tooth pulp afferents in the absence of large fiber co-activation. Similar unpleasant, although not necessarily painful, sensations can be elicited from the cornea and possibly the nasal mucosa which, like the tooth pulp, are innervated by small diameter axones only.

The nature and location of the intradental receptors is not known with certainty. This is largely due to the technical difficulties associated with sectioning and staining the combination of calcified and soft tissues which constitute the tooth. Some nerve terminals appear to terminate in the inner layers of dentine, and other fibers certainly enter the dentinal tubules (Fearnhead, 1961; Anderson, 1975).

In a recent autoradiographic study, Pimenidis and Hinds (1977) showed that labelled proteins were transported axoplasmically from the trigeminal ganglion to be widely dispersed in the dentine of the rat molar teeth. This was taken as evidence that sensory nerves ran in dentine as far as the enamel-dentine junction. However, positive identification of the labelled structures as nerves is not possible with this technique. It is possible, for example, that the proteins may have been transported from the sensory terminals to enter the odontoblasts or the dentinal tubules.

The available evidence suggests that the dentinal innervation is unlikely to account for pain due to dentinal stimulation, since the application of protein denaturants (Anderson and Matthews, 1966) or local anaesthetics (Anderson et al., 1958) onto cut dentine does not abolish pain. Furthermore, the sensation of pain is not elicited by the topical administration onto dentine of acetylcholine, bradykinin, or 5-hydroxytryptamine which evoke severe pain when applied to bare nerves in the skin (Anderson and Naylor, 1962; Dellow and Roberts, 1966).

Another theory proposes that the odontoblast, which has a process that may extend through the thickness of the dentine, transduces the stimulus in some unknown manner, and passes a signal on to the subodontoblastic plexus of nerves by some coupling process. This theory is based upon ultrastructural reports showing that the terminal part of the intratubular nerve is closely apposed to the odontoblastic process (Frank, 1966; Arwill, Edwall, Lilja, Olgart and Svensson, 1973). The intratubular

nerve terminal is expanded and packed with microvesicles. However, the lack of vesicles in the cytoplasm of the odontoblastic process makes it unlikely that this is a "synaptic" connection transferring receptor signals from the odontoblast to the nerve. An alternate possibility for this arrangement is that the terminations are autonomic efferents, which influence the dentine-depositing activity of the odontoblasts (Avery, 1974).

A more widely accepted theory of pain transduction in the tooth pulp was proposed by Brännström (1963), and seems to accommodate much of the experimental evidence. This hypothesis suggests that the pain receptors are located in the pulp, and that they are sensitive to a mechanical disturbance resulting from displacement of the fluid in the dentinal tubules. This could account for the observation that painful stimuli to the teeth may cause fluid movement across dentine (Anderson et al., 1967; Brännström et al., 1968) and displacement of odontoblast cell bodies (Brännström, 1960a, b, c). The presumptive receptors in this theory are the fine, unmyelinated terminals lying within the soft tissue of the pulp (Harris and Griffin, 1968). At least some of these terminals are thought to be sensory, since they disappear after deafferentation of the teeth (Arwill et al., 1973).

A recent observation of unknown significance is that the intradental sensory terminals appear to be coupled. This was deduced from the demonstration that the propagation of an action potential antidromically along a single pulpal fiber will in some instances lead to the propogation of a second action potential away from the tooth in another fiber (Matthews and Holland, 1975). Coupling of this nature between sensory terminals has not been identified in any other mammalian receptor system.

The Vibrissae

The vibrissae are specialised tactile hairs which are found chiefly in the perioral region of most mammals, including some primates (Ling, 1966; van Horn, 1970). These hairs have been shown to have an important exploratory role in rats. If the vibrissae of a rat are shaved off or denervated, the ability of the rat to find its way through a maze is significantly impaired. The deficit in exploratory behavior is less if the vibrissae are removed from only one side of the face, but the rat tends to keep his intact side close to the walls (Vincent, 1912). The sightless mole, which depends entirely upon touch for its awareness of obstacles in its environment, has an unusually large number of vibrissae on its snout. Electrophysiological studies have indicated that vibrissal afferents can signal the direction, amplitude and rate of displacement of individual vibrissae, which is consistent with their possible exploratory function (Kerr and Lysack, 1964; Zucker and Welker, 1969; Dykes, 1975). More recently, it has been suggested that the vibrissae in some marine mammals may be able to detect airborne or waterborne vibrations from a remote source (Poulter, 1972; Stephens, Beebe and Poulter, 1973). This is thought to play a role in echo location in species which localize objects in their environment by sonar. On the basis of a detailed study of the information transmitted in afferents from the vibrissae of seals and cats, Dykes (1975) postulated that these hairs may provide fine textural information about surfaces in their environment.

A variety of receptor types is associated with the vibrissal follicle, including a morphologically unique lanceolate ending of unknown function (Patrizi and Munger, 1966; Andres and von Düring, 1973). The afferent innervation of the follicles is unusually rich. It has been estimated that as many as 150 axons enter a single large vibrissal follicle in rats (Vincent, 1913), while up to 65% of the myelinated, trigeminal cutaneous afferents carry vibrissal information in the cat (Dykes, 1975).

There do not appear to be any quantitative data comparing the receptor properties of perioral hair in humans with other hairs. In monkeys, however, the functional properties of mechanoreceptors innervating this area are qualitatively similar to those of other hairy skin areas (Kerr and Lysack, 1964).

TRIGEMINAL MUSCLE RECEPTORS AND MUSCLE AFFERENTS

Proprioceptive information from some jaw and extraocular muscles is transmitted along trigeminal afferents. The subject of muscle spindles in the jaw muscles is of interest not because of morphological differences in the spindles, but because of the controversy relating to the apparent absence of spindles in some muscles, and the unique arrangement of the pathway and mode of termination of trigeminal muscle afferents.

The presence of spindles in all of the jaw elevating muscles in humans, *viz*, masseter, temporalis and medial pterygoid, is now well established (Freimann, 1954). Whether or not spindles are to be found in the jaw opening muscles has been the subject of considerable debate; however, the anterior belly of the digastric of macaques is said to have no muscle spindles (Dmytruk, 1974): data from human muscles do not appear to be available.

Histological studies of the lateral pterygoid muscle in various primates have produced a variety of results. Muscle spindles have not been found in this muscle in rhesus or squirrel monkeys (Smith and Marcarian, 1967), although their presence in two species of macaques has been observed (Karlsen, 1969; Dmytruk, 1974). Spindles have also been observed in human lateral pterygoids (Gill, 1971). Dmytruk (1974) has suggested that differences in the biomechanical function of the lateral pterygoid in different primate species may explain these results. His hypothesis is that the proprioceptive function normally served by lateral pterygoid muscle spindles is taken over by spindles in the horizontal part of the temporalis muscle in those species whose lateral pterygoids have no spindles.

The functional organization of the stretch reflexes in the jaw closing muscles in man have not been widely studied. Desmedt and Godaux (1975) devised a technique for electrically stimulating the masseteric nerve. The recruitment pattern for the M- and H-responses in the masseter was similar to the classical triceps surae pattern. However, the H-response could be elicited only during active closure of

the jaw. These authors also observed that vibration of the masseter produced an enhanced stretch reflex in that muscle. In limb muscles, vibration reduces the stretch reflex. Godaux and Desmedt suggest that this difference in the response of the masseter is due to the presumed absence of spindle input from the jaw opening muscles. That is, vibration of the masseter activates only the muscle spindles in jaw closing muscles. However, in the limb, the vibration of agonists also spreads to antagonistic and other muscles which do contain spindles, whose inputs lead to the characteristic depression of the stretch reflex.

The extraocular muscles of lambs, pigs, calves, some monkeys and man contain muscle spindles, while cats have a more simple form of stretch receptor (Cooper et al., 1955; Bach-y-Rita, 1972). Receptors resembling the feline receptor have also been observed in the distal part of the extraocular muscles in man (Cooper, et al., 1955). The presence of spindles in the extraocular muscles is intriguing since their functional significance in the control of eye movements is obscure. The spindle afferents, for example, do not exert strong reflex effects on the motor neurones of the extrafusal fiber of the extraocular muscles. However, reflex inhibition or, occasionally, excitation of lateral rectus motor neurones has been elicited during active contraction of that muscle in cats (Bach-y-Rita, 1972). It is not surprising to observe that the mechanisms and reflexes for the control of eye movements differ from those which control limb movements. Since the movements made by the eye muscles occur against a relatively constant load (Collins et al., 1975), a load servo function of the type exerted by spindles in other muscles is probably not necessary (Stein, 1974), nor does a length servo seem appropriate to muscles which are not subject to unexpected perturbations. Henn and Cohen (1976), in a series of elegant experiments, have shown that all parameters of any eye movement are coded in pre-oculomotor neurones before the movement begins. Feedback from length or load sensitive spindles is not necessary for a saccade, and would in any case occur too slowly.

The afferent fiber from the jaw muscle spindles and extraocular proprioceptors join trigeminal sensory branches and pass with them to the trigeminal sensory ganglion in the middle cranial fossa. The pseudo-unipolar cell bodies of some, if not all, eye muscle proprioceptive afferents are located in this ganglion, and their axons proceed along the sensory root to the pons (Manni et al., 1968; Alvarado-Mallart et al., 1975).

The jaw muscle afferents, however, enter the central nervous system with the trigeminal motor root, and their cell bodies are located in the mesencephalic nucleus (Ramon y Cajal, 1909; Szentagothai, 1948; Alvarado-Mallart et al., 1975). The consequence of this is that stretch reflexes in the masticatory muscles are not abolished by section of the trigeminal sensory root (McIntyre, 1951).

TRIGEMINAL SENSORY NUCLEI

Trigeminal afferents terminate in a complex of nuclei in a manner which differs from that of other cranial and spinal nerves. Proprioceptive information is transmitted to the trigeminal mesencephalic nucleus (vide infra).

Most somatosensory information, however, is relayed in the *main sensory nucleus* and/or the *nucleus of the spinal tract*. The latter has several morphologically distinctive subdivisions in mammals (Meessen and Olzewski, 1949). The structural and functional characteristics of these components in the trigeminal nuclear complex have been reviewed (Darian-Smith, 1973).

One aspect of trigeminal nuclear organization which has attracted the interest of clinicians and neurophysiologists is the apparent partial localization of sensory modalities in different parts of these nuclei. Sectioning of the trigeminal tract at the level of the obex in man results in a diminished sensitivity to noxious stimuli applied to the face without total abolition of the sense of touch. This operation has been used to alleviate facial pain in conditions such as inoperable malignacies and trigeminal neuralgia (Sjögvist, 1939).

Denny-Brown and Yanagisawa (1973) examined residual sensory function in monkeys with chronic lesions of central trigeminal structures and differential section of cranial sensory nerves. They concluded that the descending trigeminal tract is the site of convergence of afferents of the fifth, seventh, and tenth cranial nerves, and the second and third cervical sensory nerve roots, which innervate overlapping areas of skin. Defects in sensation such as the raised threshold to noxious stimulation which resulted from trigeminal tractotomy were attributed to diminished central spatial summation. This central summation of inputs via the various cranial sensory nerves is thought to be normally more important for the reception of pain than temperature, and more important for the reception of temperature than touch.

The mesencephalic nucleus of the trigeminal nerve is unique for a variety of reasons. Firstly, it is the only group of primary afferent cell bodies that is located within the mammalian central nervous system. The cell bodies of spinal afferents, by comparison, are located in dorsal root ganglia. The histological features of the nucleus were described by Ramon y Cajal (1909), who called it the Accessory Trigeminal Motor Nucleus. Its functional significance remained controversial until 1942, when Corbin and Harrison demonstrated that passive stretch of the jaw closing muscles caused increased neuronal activity in this nucleus. It is now known that the peripheral processes of cells in the mesencephalic nucleus innervate the muscle spindles in the jaw closing mucles: additionally, a group of cells in the caudal part of the nucleus innervate periodontal mechanoreceptors (Cody et al., 1974).

Fillenz (1955) found single units in the mesencephalic nucleus of cats that responded to passive stretch of various extraocular muscles. However, she presented no evidence to establish that these responses were in primary afferent neurones. There is some anatomical evidence supporting the concept that the cell bodies of extraocular muscle proprioceptors are

located in the mesencephalic nucleus (Alvarado-Mallart et al., 1975), although the physiological evidence for this concept is lacking (Cody et al., 1972). At least some of the extraocular proprioceptor cell bodies are located in the trigeminal ganglion (Manni et al., 1968; Lennerstrand and Bach-y Rita, 1974).

The activity of jaw muscle spindle afferents in the mesencephalic nucleus has been recorded during normal chewing in unanaesthetized monkeys and cats (Matsunami and Kobota, 1972; Taylor and Cody, 1974).

The second distinction of the mesencephalic trigeminal nucleus is that it is the first structure in the mammalian nervous system in which the electrical, or electrotonic, coupling of neurones was convincingly demonstrated (Baker and Llinás, 1971). Since that time, electrical coupling between neurones has also been shown in the inferior olive (Llinás et al., 1973), the lateral vestibular nucleus (Korn et al., 1973), and the abducens nucleus (Gogan et al., 1974).

A consequence of electrical coupling between neurones is the synchronization of firing of the coupled cells. This has been most convincingly demonstrated in the inferior olive (de Montigny and Lamarre, 1973). The functional significance of the synchronization of firing in proprioceptive afferents from the jaw muscles and/or mechanoreceptive afferents from periodontal receptors is not clear.

The anatomical basis for the physiologically demonstrated coupling is thought to be the zones of adhesion between the somata and between the somata and initial segments of the mesencephalic cells which have been observed in animal material (Hinrichsen and Larramendi, 1968) and in tissue culture (Hild, 1957).

The third unique feature of the mesencephalic nucleus is the presence of synapses on the cell bodies of the primary afferents (Ramon y Cajal, 1952; Hinrichsen and Larramendi, 1968, 1969). The site of origin of these presynaptic inputs, and whether the synapses are inhibitory or excitatory is not known. The presence of synapses on the cell bodies of primary afferents

suggests that the inflow of sensory information from jaw muscle proprioceptors and periodontal mechanoreceptors may be subject to presynaptic control. The sensitivity of some other sensory systems is known to be subject to centrifugal control. The best documented examples are the muscle spindle (Matthews, 1964), the organ of Corti, and the vestibular organ (Klinke and Galley, 1974), although the efferent control in these instances is exerted at the level of the receptor. This raises the interesting possibility that jaw muscle proprioceptors are subject to control both at the receptor (by means of the fusimotor fibers) and at the sensory nucleus.

A second possible function for the presynaptic endings on mesencephalic endings is that they may regulate the strength of the coupling between electronically coupled neurones. Indeed, synapses of this general type have been found on all electrotonically coupled neurones, which suggest that synaptic influences may be an intrinsic feature of this form of cellular communication (Bennett, 1972).

CORTICAL "BARRELS"

Another anatomical feature which is peculiar to the trigeminal system is the presence of so-called "barrels" in the trigeminal projection area of the sensorimotor cortex of some species. These barrels are cytoarchitectonically identifiable groups of cells related to the vibrissae of the contralateral face. These structures were first identified in the Sm1 cortex of the mouse (Woolsey and Van der Loos, 1970). Subsequent studies showed a one-to-one relationship between individual barrels and individual vibrissae. In a remarkable demonstration of the dependence of central neuronal organization upon functional peripheral structures, Van der Loos and Woolsey (1973) showed that deafferentation of a single vibrissa in a young rat led to histological alterations in the structure of the corresponding cortical barrel.

In a comparative anatomical survey of 27 mammalian species, cortical barrels were found in representatives of three of the seven mammalian orders examined (Woolsey et al., 1975). The major points emerging from this study were the following:

(a) barrels were in general found in rodents and some marsupials, but not in carnivores or primates;

(b) the number of barrels and organization of their fields correspond closely to the arrangement of the vibrissae in the contralateral sensory field;

(c) the barrels are confined to layer IV of the Sm1 face area (or, at least, what is thought to be the Sm1 face area in those species in which cortical mapping studies have not been made);

(d) the presence or absence of barrels is not reliably correlated with vibrissae-related exploratory behaviour.

The functional or evolutionary significance of the barrels is unknown They appear to represent a morphologically specialized form of the columnar organization of the somatosensory projection areas in the mammalian cortex.

THE DIVING REFLEX

A characteristic pattern of physiological adjustments to diving has been described for many species of reptiles, birds, and mammals, including man (see Andersen, 1966, for review). The particular pattern of responses differs from one species to another, but usually includes bradycardia, redistribution of blood flow to various organs, and apnea. Such responses are appropriate in animals during diving, since the redistribution of blood flow favors the central nervous system and the heart at the expense of other tissues which are les vulnerable to periods of transient, but often severe, hypoxia.

The stimulus which elicits the diving reflex is contact of the face with water (Andersen, 1963a). If the trigeminal nerve is sectioned, the normal cardiovascular and respiratory changes do not occur during diving. Intact conscious animals are normally quiet and relaxed during immersion. However, after the trigeminal nerve is sectioned, immersion provokes violent struggling and the outward signs of alarm. In ducks, the ophthalmic branch of the trigeminal nerve is the most important afferent pathway for the diving reflex (Andersen, 1963a), although in dogs the maxillary nerve

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may be more important (Angell-James and Daly, 1972). The details of the central pathways involved in this reflex are not known. The participation of higher centers does not appear to be necessary, as the reflex persists essentially without change after decerebration (Andersen, 1963b). The cardiovascular changes are abolished by vagotomy or atropine, which suggests that the bradycardia is mediated primarily by the vagus nerve.

The effect of immersion of the face in water is less dramatic in man than in diving species. The heart rate of ducks, for example, may decrease by 80% from the resting rate; a reduction of 15-30% is common in human subjects. Water temperature is thought to be a factor in this response in human subjects, with cold water provoking a greater bradycardia than water at body temperature (Moore et al., 1972). However, the basic nature of the diving reflex, even in man, is shown by the fact that it can over-ride the tachycardia which accompanies moderate exercise. Bergmann, Campbell and Wildenthal (1972) showed that an exercise tachycardia of 140 beats min-1 was abruptly abolished when the face was immersed, despite continuation of the exercise.

In addition to its general physiological interest, the diving reflex in man may be of some clinical consequence. For example, the increased vagal tone occurring during the diving reflex has been successfully used for acute relief of the symptoms of paroxysmal atrial tachycardia (Wildenthal et al., 1975). In each of seven subjects tested, immersion of the face in cold water was successful in converting the disturbed rhythm to a normal sinus rhythm.

In another recent report (Nemiroff, 1977), it was pointed out that the onset of hypoxic brain damage as a result of drowning in cold water may occur later than was previously thought. Successful resuscitation of drowning victims who had been submerged for as long as 38 minutes has been achieved in several instances. This is attributed to the reflex maintenance of cerebral perfusion during diving, in comparison to asphyxiation by other means.

The suggestion has also been made that the diving reflex may be involved in eliciting the onset of active ventilation at birth. Respiratory movements in newborn lambs and rabbits are inhibited when their heads are bathed in water, independent of the water temperature (Tchoubroutsky, et al., 1969). The inference is that, immediately after birth, inhibition of fetal ventilation is removed, and breathing begins. One difficulty with this hypothesis is that, although water and, to a lesser extent, saline inhibit respiration, tracheal and amniotic fluid do not have this effect (Johnson et al., 1973).

OCULO-CARDIAC REFLEX

Another trigeminally-elicited reflex which results in bradycardia was described by Aschner (1908) who showed that gentle mechanical pressure applied to the eyball leads to a decrease in heart rate. This reflex has recently been investigated in detail by Gandevia et al. (1977). They showed that the reflex bradycardia is mediated by increased vagal efferent activity and decreased sympathetic tone to the heart. Eyeball pressure is most effective in eliciting bradycardia during apnea.

The physiological significance of this reflex is not known. However, the oculo-cardiac reflex has been advocated by clinicians for the acute treatment of paroxysmal atrial tachycardia (Levine, 1951). Katz and Bigger (1970) noted that the severe bradycardia or even cardiac arrest which may be reflexly elicited by ophthalmic surgery can be attributed to the oculocardiac reflex. Gandevia et al. (1977) suggest that the cardiac side effects of surgery of the eye may be reduced by increasing the frequency of pulmonary ventilation.

NASO-CARDIORESPIRATORY REFLEXES

The presence of foreign bodies or liquids, or irritant gases in the nose (or pharynx) provokes a series of reflex cardiovascular and respiratory responses which are qualitatively similar to those elicited by diving, e.g. bradycardia, apnea, and redistribution of flow to favor the central nervous system (Angell-James and

Daly, 1972; White and McRitchie, 1973). Other responses to stimulation of the nasal mucosa include closure of the glottis, which presumably accompanies the apnea (Yokota, 1972); or, under appropriate conditions of stimulation, sneezing may occur (Tomori and Widdicombe, 1969; Batsel and Lines, 1975). The apnea, glottic closure and sneezing clearly function to prevent the entry of foreign particles, irritant gases and liquids into the airways. The value of the cardiovascular responses to stimulation of the nasal mucosa is less obvious.

The receptors for these reflexes are the mechanoreceptors of the nasal mucosa, whose afferents are located in the trigeminal nerve. The integration of the trigeminal input with the cardiovascular and respiratory systems is said to occur mainly at trigemino-bulbar sites (White and McRitchie, 1973).

TRIGEMINAL DEPRESSOR RESPONSE

Yet another trigeminally-evoked reflex involving cardiovascular changes has been proposed. Kumada et al. (1977) found that low intensity electrical stimulation of the spinal trigeminal nucleus in the cat evoked a sustained depression of mean arterial blood pressure which is accompanied by a transient bradycardia. Similar reflex changes could also be elicited by stimulation of the principal sensory nucleus and peripheral trigeminal afferents, but not the mesencephalic or motor nuclei of the trigeminal nerve. This pattern of responses is said to be qualitatively different from those of the diving, oculo-cardiac and naso-cardiorespiratory reflexes, in which the blood pressure is usually slightly elevated and the bradycardia is sustained.

The possibility should be considered that these differences are due to the use of electrical stimulation of trigeminal structures rather than physiological stimulation.

BEHAVIORAL REFLEXES

In addition to serving as the afferent limb of several autonomic reflexes, trigeminal afferents are also involved in co-ordinated behavioral responses.

The best known of these are probably the responses of infants to tactile stimulation of the face and mouth. In the "rooting" reflex, touching the face of an infant will cause it to re-orient its head so that the object can be taken into its mouth. In the suckling reflex, a tactile stimulus on the lips or oral mucosa elicits reflex suckling. A detailed description of these reflex behavioral responses has been given by Peiper (1961).

There is also some evidence implicating trigeminal sensory pathways in aspects of eating and drinking behaviour. Zeigler and Karten (1973, 1974) reported that bilateral lesions in central trigeminal structures, notably the trigeminal lemniscus, lead to characteristic changes in the behavior of rats and pigeons. Food and water intake was reduced, the spillage of food during eating increased, and a sustained loss of weight occurred after the trigeminal lesions were made. These authors noted that changes of this type occur in animals when electrolytic lesions are placed in the lateral hypothalamus, i.e. the so-called "lateral hypothalamic syndrome" (Anand and Brobeck, 1951). On the basis of their observations, Zeigler and Karten contend that during the placement of electrolytic lesions in the lateral hypothalamus, the trigeminal lemniscus is frequently damaged, and that it is this trigeminal lesion, rather than the lesion in the lateral hypothalamus itself, which produces the aphagia and adipsia of the lateral hypothalamic syndrome (If this is the case, then presumably the increase in food and water intake elicited by electrical stimulation of the lateral hypothalamus can also be attributed to excitation of the nearby trigeminal structures.)

These authors noted that, although their trigeminal-lesioned animals elected to eat less than control animals, they would nevertheless readily swallow appetizing liquid foods which were placed in their mouths with an eye dropper.

One possibility suggested by these authors to explain their findings is that trigeminally innervated structures may normally function to meter oral food and water intake (Adolph, 1950) and that this metering function is disrupted by the central trigeminal lesion. Certainly, the observation of increased food spillage during eating suggests a disturbance of oral sensory function.

CONCLUSIONS

The unique features of the physiology and morphology of the trigeminal sensory system have been reviewed. Many aspects of trigeminal physiology have been less intensively studied than their counterparts in spinal systems. However, the existing body of knowledge makes it clear that trigeminal mechanisms are very often significantly different. Consequently, extrapolation from anatomical or functional studies on spinal mechanisms to the trigeminal system or vice versa must be made with caution.

ACKNOWLEDGEMENTS

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