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Pontine Reticular Formation Neurons: Relationship of Discharge to Motor Activity

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Source: *Science*, New Series, Vol. 196, No. 4290 (May 6, 1977), pp. 678-680

Published by: American Association for the Advancement of Science

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Accessed: 13-03-2022 23:34 UTC

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9. Bats change pulse designs throughout the various phases of echolocation (1-3). For bats whose orientation cries are composed primarily or exclusively of an FM component, the following changes have been observed in both laboratory and field studies. During the search phase, as the bat cruises with no apparent target holding its attention, pulses are relatively long (3 to 12 msec) and are emitted at a rate of about 10 per second. In the approach phase of goal-directed flight, the location, distance, size, and other target attributes are presumably evaluated. During this period the tempo of pulse emission increases and pulse durations are shortened, which precludes any overlap of the outgoing pulse and returning echo. In the terminal phase, the repetition rate can be as high as 200 pulses per second with pulse durations continuing to shorten as the bat holds its course for final interception. During this last 100 msec or so of goal-directed flight, pulse durations can be as short as 0.5 msec.
10. O. W. Henson, Jr., and G. Pollak, *Physiol. Behav.* **8**, 1185 (1972).
11. The inferior colliculus is greatly hypertrophied in *Tadarida* and can be seen through the thin skull as two white masses protruding between the cerebral cortex and the cerebellum.
12. In the Plexiglas restraining chamber, signs of an awake condition include (i) frequent spontaneous movements of the shoulders, wings, feet, and mouth, which differ from extreme struggling indicative of pain; in such cases, refreshing the cotton wisps with additional procaine results in a cessation of struggling movements; (ii) reflex withdrawal upon gently poking the wing or shoulder; and (iii) overt, coordinated drinking when water is applied to the lips with a dropper.
13. Designed as described by W. C. Kuhl, G. R. Schodder, F. K. Schroder, *Acoustica* **4**, 519 (1954).
14. In five units only one or two durations were tested. In three other units 0.86-msec pulses were used in addition to the longer durations.
15. O. W. Henson, Jr., *J. Physiol. (London)* **180**, 871 (1965); N. Suga and P. H.-S. Jen, *J. Exp. Biol.* **62**, 277 (1975).
16. All stimuli were designed to mimic the natural biosonar cries of the bat. *Tadarida* emit pulses with durations ranging from about 9 to 0.5 msec. The first harmonic of the FM cries typically sweep from about 50 to 24 kHz over the duration of the pulse. Constant frequency components of 26 kHz having durations of several milliseconds are often present during the search phase of echolocation. The biosonar signals of *Tadarida* (family Molossidae) are similar to those of the big brown bat, *Eptesicus fuscus* (family Vespertilionidae) (J. A. Simmons, personal communication).
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19. Supported by NSF grant P4B1855-000.

24 May 1976; revised 26 November 1976

## Pontine Reticular Formation Neurons: Relationship of Discharge to Motor Activity

**Abstract.** *The discharge correlates of pontine reticular formation units were investigated in unrestrained cats. In agreement with previous investigations using immobilized preparations, we found that these cells had high rates of activity in rapid eye movement sleep, and responded in waking to somatic, auditory, and vestibular stimuli at short latencies, many having polysensory responses and exhibiting rapid "habituation." However, despite the sensory responses of these cells, most unit activity could not be explained by the presence of sensory stimuli. Intense firing occurred in association with specific movements. Units deprived of their adequate somatic, vestibular, and auditory stimuli showed undiminished discharge rates during motor activity. Discrete sensory stimuli evoked sustained unit firing only when they also evoked a motor response. We conclude that activity in pontine reticular formation neurons is more closely related to motor output than to sensory input.*

Studies of pontine reticular formation (PRF) units, usually performed in anesthetized, decerebrated, or immobilized preparations, have emphasized the sensory responses of these cells (1, 2). It has been repeatedly demonstrated, in experiments using both natural and electrical stimulation of sensory systems, that many of these neurons are polysensory and show response attenuation with stimulus repetition (2). The present investigation studied the discharge correlates of medial PRF units in unrestrained, behaving cats. We find that most unit discharge does not result from sensory stimuli impinging upon the animal, but rather relates closely to the cat's motor activities.

Units were studied with previously described recording and sensory stimulation techniques (3). All cells considered in this study were localized to the pontine gigantocellular tegmental field ("FTG")

(4), one of the most commonly explored areas in unit studies of the PRF (1-3, 5). A total of 70 units were recorded in nine cats.

In the waking cat, most PRF units were found to have a low level of background activity intermixed with phasic bursts of discharge that occurred in conjunction with spontaneous movements (Fig. 1A).

Table 1. Unit activity rates (discharges per second) before, during, and after a 3-minute period of stimulus reduction. The units' discharge rates were not reduced by the procedure. The standard deviation is that of the arithmetic mean.

Parameter	Before	During	After
Geometric mean	1.00	8.32	8.33
Arithmetic mean	4.94	11.94	12.59
Standard deviation	7.82	8.65	8.57

A subset of these units ( $N = 21$ ) belongs to the previously described neuronal group which shows no background activity in waking or sleep (3). The remaining cells were active in sleep, particularly during phasic discharge bursts occurring in rapid eye movement (REM) sleep.

Unlike studies in acute preparations, which have reported a high proportion of unresponsive units (1, 2), we found that all PRF cells showed phasic discharge bursts during active waking. Sensory responses were examined in detail. Seventy-one percent of the PRF cells responded to somatic stimuli, 57 percent to vestibular stimuli, 40 percent to auditory stimuli, none responded to stroboscopic visual stimuli, and 57 percent were polysensory (6).

Discrete 0.5-msec shock stimuli were applied to the receptive fields of units responding to natural somatic stimuli. No response occurred in 4 of the 12 cells tested, the remaining units responding at a latency between 14 and 40 msec, in agreement with previous studies (1, 2). However, only one or two unit firings could be elicited by this stimulus, even at an intensity which produced a clear muscle twitch. Similarly, discrete auditory stimuli evoked responses between 15 and 33 msec, but never elicited more than two spike discharges. When the intensity of the somatic shock was raised to a level at which a behavioral response was evoked, a more sustained discharge occurred, but this was time-locked to the motor activity, rather than to the stimulus (Fig. 1B).

While natural stimuli could repeatedly elicit unit activity, the duration and intensity of unit discharge was not closely related to the eliciting stimulus. For example, stimulation applied by placing a cotton swab in the concha of the ear produced intense discharge in three PRF cells. However, the discharge normally continued with undiminished rate for 1 to 10 seconds after the swab was removed from the ear, ending abruptly with a change in ear position. Rhythmic movement of the stimulus did not produce rhythmic discharge in the unit. Furthermore, in most PRF units we observed discharges at rates equal to or exceeding those induced by our most effective stimuli during small, spontaneous movements. These observations suggested the hypothesis that unit discharge was related to motor activities. Therefore, we observed 35 units for periods of at least 2 hours, during active waking. We were able to identify consistent, individually distinctive motor correlates of discharge in 32 of the cells. These included head and neck ( $N = 21$ ), ear ( $N = 3$ ), forepaw ( $N = 1$ ), scapula ( $N = 2$ ), tongue ( $N$

= 2), and facial ( $N = 3$ ) movements.

Obviously, spontaneous behaviors result in a variety of vestibular, proprioceptive, somatic, and auditory stimuli. In order to determine whether or not stimuli generated by motor activity were responsible for the unit responses, randomly selected cells responding to vestibular, auditory, or localized somatic stimuli were subjected to a procedure designed to eliminate or reduce all identified sensory inputs. Vestibular stimuli were eliminated by an atraumatic head restraint system (7). The receptive fields of somatic cells were locally anesthetized with injections of lidocaine supplemented by topical application of lidocaine jelly. Auditory input was attenuated in responsive cells by blocking the ear canals with wax. Unit rates were not reduced by these procedures (Table 1) (8). Phasic unit discharge continued to be correlated with motor activity (Fig. 1C). However, steady hand pressure applied to the face and neck areas, which tends to relax the muscles to which pressure is applied, can produce a dramatic reduction in discharge, even though it is a less effective restraint. Similarly, if cats are adapted to the atraumatic restraint system by being placed in it for periods of several hours, both phasic electromyographic (EMG) and unit activity will decrease.

We saw rapid response decrement with stimulus repetition in many of these cells, similar to that reported in paralyzed or anesthetized preparations, and often described as "habituation" (1, 2). However, we observed that unit response cessation was correlated with loss of the behavioral response to the stimulus. For example, two PRF cells responded when any object was rapidly brought toward the cat's eyes. This stimulus elicited a behavioral flinch response. The intensities of the behavioral and unit responses were tightly correlated, and the responses disappeared simultaneously after three to four repetitions of the stimulus. Three of the 19 FTG cells tested showed no response decrement with stimulus repetition. Two of these fired during tongue extensions which could be induced by pushing the tongue to the rear of the oral cavity. Another unit fired during head shaking which could be triggered by placing a foreign object in either ear. In these three cases the behavioral response to the stimuli also showed no decrement with stimulus repetition. All units which exhibited response decrement with repeated sensory stimulation failed to show rate decrement during repetitive motor activities such as grooming. Unit discharges, phase locked to rhythmic movements, continued without attenuation for the du-

ration of the motor activity (Fig. 1D). Rhythmic, movement-related discharge lasting as long as 30 minutes was observed in cells which showed response attenuation after just three or four applications of somatic, auditory, or vestibular stimuli.

The high rates of discharge during spontaneous behaviors demonstrate that noxious stimuli are not required to activate these cells (5). The rhythmicity of firing, time-locked to movements, and of-

ten reciprocal in simultaneously recorded units, also argues against any simple relationship between activity in these cells and nonspecific "arousal."

Our findings indicate that the sensory responsiveness of PRF neurons in unrestrained cats is similar to that previously found in anesthetized, decerebrated, or paralyzed cats, in terms of the stimulus modalities to which these neurons respond, the latencies of response, the sizes of receptive fields, and the presence of

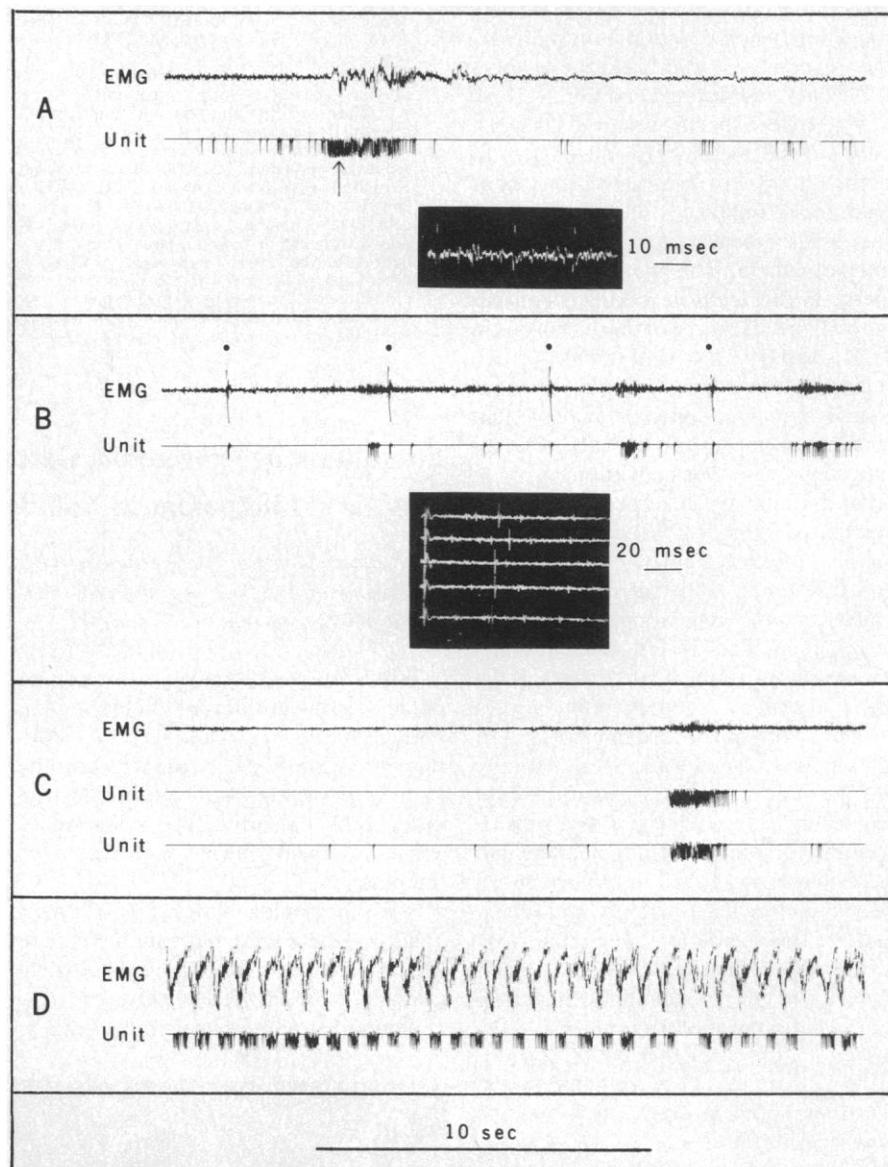


Fig. 1. Relationship of PRF unit discharge to motor activity. (A) Polygraphic display of unit firing in unrestrained cat. Unit discharge is accompanied by phasic EMG activity. (Inset) High speed oscilloscopic tracing from same record (arrow) demonstrating the absence of artifact in the microwire recording. This unit had an average signal-to-noise ratio. (B) Unit responses to strong shock stimuli were brief, most discharge being time-locked to movements (augmented EMG) occurring during stimulation rather than to the shock stimulus itself. Dots indicate time of delivery of 1-msec shock stimulus to receptive field. (Inset) Brief response time-locked to shock in microwire recording of same unit. (C) Two units with different spontaneous activity levels simultaneously recorded during head restraint. Augmented unit discharge was correlated with muscle contraction. (D) During grooming, unit discharged rhythmically, with bursts time-locked to movements. Head motion created the slow rhythmic artifact in this broad-spectrum EMG recording. Grooming had been in progress for 20 minutes and continued for an additional 5 minutes. Abbreviations: EMG, electromyogram of dorsal neck muscles; Unit, the pulse output of a window discriminator. (A) and (D) are from the same cell. The 10-second marker applies to all four panels, exclusive of the two insets.

response attenuation with stimulus repetition (1, 2). However, while sensory stimulation can trigger brief responses in these units, PRF neurons exhibited sustained bursts of unit discharge only in conjunction with specific motor activities. Indeed, discharge rates in PRF neurons were undiminished after the elimination of identified sensory inputs.

These findings suggest a parsimonious explanation of many conditioning, sensory, and sleep cycle studies of PRF neurons. The apparent selectivity of PRF discharge for "noxious" stimuli (5), the very long latency and duration of certain sensory responses (1, 2, 5), and the changes in PRF activity during conditioning (2, 9) may all reflect specific motor discharges. Only careful monitoring and control of motor activity can determine if sensory or conditioned influences on unit firing are separable from the motor changes that accompany them. The motor-related discharge in PRF cells in waking is consistent with the discharge of these neurons in REM sleep (10), a time of intense activation of motor systems (11). Our observations in the unrestrained cat indicate that discharge is not selective for REM sleep, but rather for motor activation.

Pontine animals have been shown to be capable of exhibiting a wide variety of complex motor behaviors (12), and must therefore retain sufficient neuronal substrate for the regulation of complex movements. The PRF's medial zone, whose unit activity is reported here, is the principal source of pontine reticular projections to the spinal cord; more than half of its neurons send their axons directly into the ventral, motor areas of the cord (13). Many of these neurons also receive monosynaptic input from the cerebellum and other areas related to motor control (14). Therefore, the anatomy and physiology of this region are compatible with the behavioral data reported here, which suggest a major role for PRF neurons in the regulation of motor output.

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6. We tested 31 cells for somatic, 44 for vestibular, 25 for auditory, 32 for visual, and 25 for polysensory responses.
7. Socket nuts were imbedded in the head-plug acrylic cement. During restraint, socket wrenches were fitted into the nuts and fixed in a stereotaxic head holder.
8. A total of 12 units were subjected to the stimulus reduction procedure. With the cat unrestrained, 10 of the 12 gave maximal responses to vestibular stimuli, and 2 to somatic stimuli. In the somatic cells, the 3-minute postrestraint period was drawn from the first waking period occurring 4 hours after the restraint had ended, to allow for dissipation of the local anesthetic agents. The procedure reduced discharge in only one unit (by 30 percent) relative to the rate before restraint. Six of the units had higher rates during the stimu-

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12 October 1976

## Sesquiterpene Progenitor, Germacrene A:

### An Alarm Pheromone in Aphids

**Abstract.** *Germacrene A*, the elusive biogenetic "parent" of many sesquiterpenes, has been isolated from the spotted alfalfa aphid and identified as a new intrageneric aphid alarm pheromone.

When attacked by a predator, certain aphids secrete droplets of fluid from their cornicles (Fig. 1). This secretion contains an alarm pheromone, which in the manner of a dying gasp, signals danger to other aphids nearby. The response of aphids is to walk, fall, or leap away from the plant.

Since the phylogenetic relationships of aphids at the subfamily level have been difficult to determine on morphological grounds, we have tried to utilize the aphid alarm pheromones as unique chemical

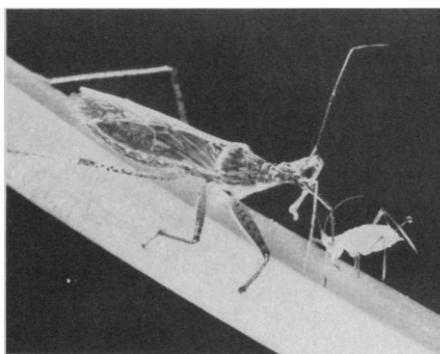


Fig. 1. After attack by a nabid predator, the aphid secretes a droplet of fluid from the cornicles which contain the alarm pheromone.

taxonomic characters. The discovery of (*E*)- $\beta$ -farnesene as a broadly interspecific alarm pheromone in the subfamilies Aphidinae and Chaitophorinae (1) demonstrated their apparent close relationship, whereas their relationship to the subfamily Drepanosiphinae remains unclear and has not been resolved on morphological grounds (2). We were therefore anxious to investigate the alarm pheromone chemistry of representative species in the Drepanosiphinae. Our cross-reaction tests revealed that the sweetclover aphid, *Therioaphis riehmii* (Börner), and the spotted alfalfa aphid, *Therioaphis maculata* Buckton, both drepanosiphins, did not respond to (*E*)- $\beta$ -farnesene but demonstrated strong alarm responses to injured siblings, an indication of the presence of a new alarm pheromone.

From approximately 2 liters of the closely related spotted alfalfa aphid, *Therioaphis maculata* Buckton, we isolated, by column chromatography over Florisil and silica gel, 9 mg of a biologically active, but highly unstable hydrocarbon. This compound was active against both sweetclover and spotted alfalfa aphids (3). Mass spectral analysis (4) of this