

the capillaries before being touched, and when deliberately contacted showed intensive and characteristic (11) cleansing. Pure regurgitated fluid, by contrast, is innocuous, and appears to function strictly as diluent. Droplets of this fluid placed on the floor of the glass arena were quickly encircled by ants and eaten. No tests were made with other predators. However, as judged from the demonstrated repellent action of quinones to other insects, spiders, and some vertebrates (12), there can be no doubt that *Vonones* must also be able to effect its defense in other contexts.

Two subtle additional features of this chemical weapon bear mentioning. Quinones are unstable in water, and the fact that *Vonones* makes up its solution just prior to use may reflect a functional need to do so. Moreover, the two quinones, individually, are crystalline at ambient temperatures, which would make awkward the glandular storage of either alone. In mixture, the melting point is depressed (13), providing the animal with a fluid, and hence appropriately dispensable, glandular content.

*Vonones sayi* belongs to the order Laniatores, together with over 2000 other species (14). Some of these were observed by one of us (T.E.) in Panama and Uruguay, and they apparently also discharge quinones, as judged by the characteristic color and odor of their effluent. In one species, quinones had been identified previously (15), although their defensive use against predators had not been recognized.

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4. *Vonones*, like other arachnids, are fluid feeders. In the laboratory they drank freely from open water sources and sucked the juices from pieces of freshly killed insects.
5. Verified by autopsy, which showed the glands to contain no visible trace of brown secretion.
6. The pellets collect uncontaminated by gut fluids, since freezing does not induce regurgitation.
7. Volume calculated from microscopic measurement (with ocular micrometer) of pellet diameter.

8. This regurgitative output corresponds to about one-half the estimated capacity of the highly branched "stomach" (anterior plus posterior midgut), from which the effluent presumably stems.
9. The animals were weighed at intervals of 1 to 3 hours after milking. They regained weight at the same rate, whether offered both food (pieces of freshly killed cockroaches) and water (wet paper toweling), or water alone.
10. Filter paper impregnated with acidic solution of potassium iodide and starch.
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13. The relative proportion of the two quinones in the secretion, determined by gas chromatographic comparison with mixtures of known concentrations of the authentic quinones, ranged from 1:1 to 1:3 in favor of the dimethyl quinone (based on four samples). Mutual depression of melting point (to below laboratory temperature:  $\approx 20^\circ$ ) at this

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## Neuron Activity Related to Short-Term Memory

**Abstract.** *Nerve cells in the monkey's prefrontal cortex and nucleus medialis dorsalis of the thalamus show changes of firing frequency associated with the performance of a delayed response test. Most cells increase firing during the cue presentation period or at the beginning of the ensuing delay; spike discharge higher than that in intertrial periods is present in some cells throughout the delay. These changes are interpreted as suggestive evidence of a role of fronto-thalamic circuits in the attentive process involved in short-term memory.*

For more than a generation behavioral scientists have been investigating the deleterious effect of injury to the granular frontal cortex on short-term memory. This effect is best demonstrated in primates by the deficit resulting from ablation or functional depression of the so-called prefrontal cortex in performance of a delayed response test (1), whether it be the test originally devised by Hunter (2) or a variant thereof. A role of this part of the cerebral cortex in transient mem-

ory function has thus been operationally established, although it is not yet clear what precisely this role is.

We have explored in the monkey the electrical activity of nerve cells of the prefrontal cortex and of its thalamic projection nucleus, the nucleus medialis dorsalis, in the course of performance of a delayed response task. The basic hypothesis behind this work was that, if these structures are involved in some aspect of transient memory function, their neurons should manifest distinct temporal variations of spike discharge related to the events taking place in delayed response trials. Moreover, we anticipated that such variations, if present, might provide some insight into the specific role of these neurons in memory function.

Five adult rhesus monkeys were trained in the performance of a delayed response task with the use of a modified version of the Wisconsin General Test Apparatus. The experimental animal, partially restrained by a special rigid collar (3), sits in front of a transparent plastic window that gives him view of a well-illuminated compartment containing the test objects. Two white wooden blocks of identical form and proportions are placed on a black surface, one on the right and the other on the left, in the animal's field of vision. Directly in front of the objects, under the window, are two small doors covered with spring-loaded lids.

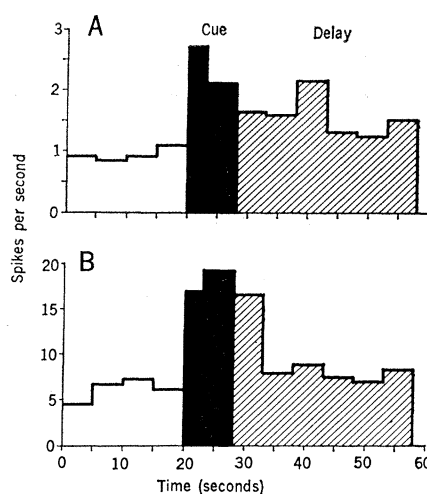
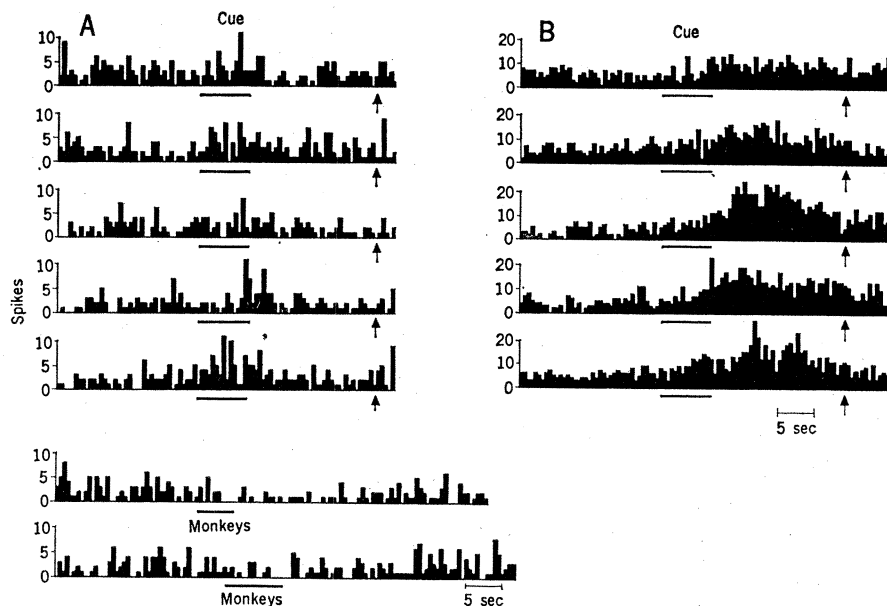


Fig. 1. Average firing of two units during five delayed response trials with 30-second delays, 20 seconds of spontaneous activity record preceding each trial. (A) Unit in prefrontal cortex; (B) unit in nucleus medialis dorsalis (MD).

Fig. 2. Frequency histograms (0.5-sec bins) of two units (A and B) in prefrontal cortex during five trials with 18-second delays. Cue presentation periods marked by horizontal lines. Arrows mark the lifting of the blind and unlocking of doors which terminate the delay and immediately precede the animal's response. The two lower excerpts from the unit at left (A) represent tests of stereo tape-recorded cries of monkeys at the time of their daily feeding, played back to the experimental animal by means of overhead loudspeakers.



Each door allows the animal to reach one of the objects by using the corresponding hand. Between test trials the doors remain locked and a sliding blind blocks the view of the objects. A trial is initiated by the lifting of the blind, after which a piece of apple is placed in a small well under one of the objects in full view of the animal. The blind is lowered immediately thereafter, thus terminating the "cue" period.

A period of delay ensues, at the end of which the doors are unlocked and the blind lifted. The animal is thus permitted the choice of one object. If the correct ("baited") object is chosen, the animal retrieves the reward. If the other is chosen, the trial is terminated by relocking the doors, showing the reward to the animal, and lowering the blind. The position of the reward is changed in random order from trial to trial. Throughout the procedure the monkey can be observed by the experimenter through a one-way vision screen.

After having been trained to correct performance on delays of at least 15 seconds in duration, the animals were surgically prepared for chronic single-unit recording of action potentials by means of roving metal microelectrodes. This was accomplished by use of a method previously described (4), somewhat modified for application

to the monkey. Unit discharges were extracellularly recorded in the prefrontal cortex (area FD of von Bonin and Bailey) (5), including the banks of the sulcus principalis, and in the nucleus medialis dorsalis of the thalamus (MD), mainly in its parvocellular region. Unit records were taken during intertrial periods of at least 45 seconds in order to establish baseline levels of spontaneous firing and during test trials with delays of durations between 15 and 60 seconds. The performance of all the animals was nearly 100 percent correct, particularly at delays in the 15- to 30-second range, which were the ones most often used. Electrolytic tissue marks, made by small currents at various points along the microelectrode tracts, permitted histological determination of unit locations.

Almost all the units investigated (57 in MD, 110 in prefrontal cortex) showed rather irregular patterns of spontaneous firing while the animal was at rest during intertrial periods. The MD units generally displayed higher

frequencies of firing than the cortical units did and, similar to units in other thalamic nuclei, a tendency to discharge in periodic groups or bursts of action potentials (6).

In the course of delayed response trials the majority of units (58 percent of those in MD, 65 percent in prefrontal cortex) increased their spike activity to levels higher than those prevalent in intertrial periods. Some units exhibited a higher discharge rate during cue presentation, others during the delay, and still others during both cue and delay periods (Figs. 1 and 2). The magnitude of the activation varied widely between different units, some reaching discharge levels more than tenfold higher than the spontaneous discharge level. Increased firing was in some units preceded by an inhibitory phase covering the beginning or the entirety of the cue presentation period. This inhibition was most conspicuous in units showing maximum discharge during the delay (Fig. 3). In some delay-activated units the increased firing

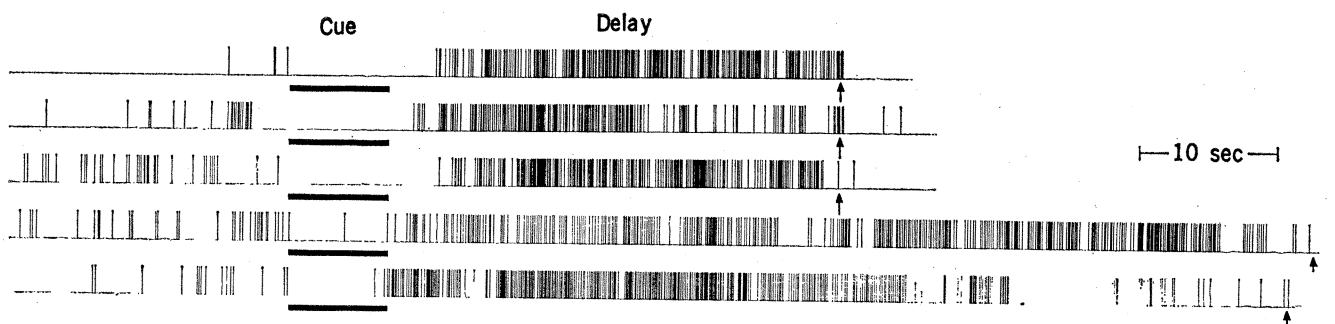


Fig. 3. Firing of a prefrontal cortex unit in five consecutive trials with delays of 32, 32, 32, 67, and 65 seconds, respectively, from top to bottom. Spikes are represented by standard vertical lines in a graphic display obtained by a computer method. Event indicators as in Fig. 2.

persisted throughout the delay period, slowly and irregularly declining toward baseline in the course of it. Figure 3 shows a unit activated for almost the entire duration of delays longer than 1 minute (7).

A minority of units (14 percent in MD, 17 percent in prefrontal cortex) was characterized by an inhibition beginning with cue presentation and followed, during the delay, by gradual return to the intertrial firing level. The remainder of the units (28 percent in MD, 18 percent in prefrontal cortex) were apparently unaffected by the events of delayed response trials.

Records of eye movements, obtained concomitantly with unit records, show no evident correlation between such movements and unit activity in the areas explored (8).

Natural stimuli, presumably significant to the animal, were tested on a few units. Such stimuli failed to produce excitatory changes comparable to those observed in most units during delayed response trials. The frontal unit illustrated in Fig. 2A is especially interesting in this regard for, while it was slightly activated on every trial at cue presentation and beginning of delay, it was no less consistently inhibited by the tape-recorded cries of other monkeys at feeding time.

Although cerebral regions outside the prefrontal cortex and MD were not systematically explored, records were obtained from 48 cells or fibers in posterior cingulate cortex, corpus callosum, posterior commissure, caudate nucleus, and thalamic nuclei other than MD. In this assorted sample, 27 units did not change firing frequency in delayed response trials, while 9 and 12 were respectively excited and inhibited during either cue or delay. The majority of those activated were found in intralaminar thalamic nuclei (centrum medianum, parafascicularis). Caudate units showed a tendency to inhibition by cue presentation.

The temporal patterns of firing frequency observed in prefrontal and thalamic units during cue and delay periods suggest the participation of these units in the acquisition and temporary storage of sensory information which are implicated in delay response performance. Their function, however, does not seem to be the neural coding of information contained in the test cues, at least according to a frequency code, for we have not found any unit showing differential reactions to the two positions of the reward.

It is during the transition from cue to delay that apparently the greatest number of prefrontal units discharge at firing levels higher than the intertrial baseline. This may be the basis of the d-c negative potential shift that has been reported to occur at that time in the surface of the prefrontal cortex; it also may help to explain the observation that electrical stimuli are maximally disruptive to performance when applied to that cortical area at the end of the cue period and beginning of the delay (9).

We believe that the excitatory reactions of neurons in MD and granular frontal cortex during delayed response trials are specifically related to the focusing of attention by the animal on information that is being or has been placed in temporary memory storage for prospective utilization. These reactions are probably an integral component of a basic function of the prefrontal-MD neuronal circuits in active attention. This view is in agreement with evidence obtained by behavioral experiments (10) and by studies of the prefrontal syndrome in man (11), which indicates a fundamental disturbance of attentive mechanisms in frontal lobe injury. However, the question of how the frontothalamic system may be functionally articulated with other cerebral structures to play the postulated role in attention requires further investigation.

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## Ultraviolet Absorption in Lenses

Zigman (1) used data on the photo-oxidation of aromatic amino acids to suggest "a possible chemical basis for lens coloration." His findings may be of some interest with respect to the problem of cataract formation, but his speculations on the significance of such pigments in relation to the function of the lens ignore most of the available literature on the subject.

That melanin-like compounds are formed in the lenses of primates has been known for decades (2); Wald measured the absorption of primate lenses in the near-ultraviolet region and assessed their role in reducing chromatic aberration (3). From the

lenses of a variety of lower vertebrates we extracted a dialyzable, heat-stable substance that accounted for their very considerable absorption in the near-ultraviolet region (4). On the basis of chromatographic behavior and fluorescence, we tentatively characterized these lens pigments as pteridines. More recently, Cooper and Robson (5) have re-examined squirrel and human lenses; they report the extraction, in large amounts, of a compound that appears identical to ours in all important respects.

The matter can thus be summarized in terms that are now quite general. The lenses of nearly all diurnal verte-