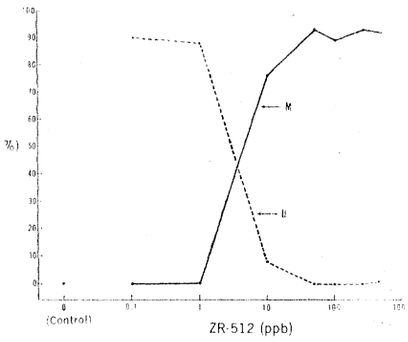

Fig. 1. Percentage of metamorphosed (*M*) and unmetamorphosed (*U*) cyprids at each concentration of ZR-512, showing a threshold value between 1 and 10 ppb. The average mortality for each concentration was 11 percent.

days, the cyprids in the experimental vessels ceased their searching behavior within several hours and lay on their sides with their attachment appendages free of the bottom. This was taken as an indication of the onset of metamorphosis. Complete adults with beating cirri appeared as early as 24 hours after the initial exposure. Some cyprids initiated metamorphosis but failed to attain the normal adult form.

After an average duration of 6 days, the numbers of metamorphosed, unmetamorphosed, and dead cyprids were recorded (Table 1). These results are expressed graphically in Fig. 1, which indicates a threshold concentration between 1 and 10 ppb.

Time effect tests on a small sample ($N = 100$) indicated that 3 hours of exposure to 100 ppb of ZR-512 was sufficient to produce a total effect. One hour of exposure to the same concentration caused only 50 percent of the cyprids to metamorphose.

Experiments with ZR-515 showed that it did not cause premature metamorphosis, nor did this hormone mimic prevent settling and metamorphosis of cyprids that were provided with the proper substrate.

The preceding results are confined to the effects of two synthetic hormone mimics on a single crustacean species. We cannot come to the conclusion that these potential insecticides will disrupt the marine crustacean life cycles without first testing their action on other important groups, such as decapods, copepods, and amphipods.

It appears that the compound ZR-512 may be a useful tool in studies of barnacle development (*8*). There is a further possibility that a synthetic juvenile hormone mimic might be developed as an antifouling agent, since there can be no doubt that an unattached barnacle is a dead barnacle.

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13 October 1972

Evoked Potential Correlates of Expected Stimulus Intensity

Abstract. *The electrophysiological responses to a flash of medium intensity have different wave shapes in trials in which the occurrence of bright stimuli or dim stimuli is expected. When a bright or dim stimulus is signaled, the potentials evoked by the medium stimulus resemble the responses evoked by a real bright or dim flash.*

The wave shape of a visual evoked potential (VEP) is primarily determined by two factors: (i) the physical parameters of the stimulus that can be changed by the experimenter, and (ii) the significance or meaning of the stimulus that is dependent on subjective experience. With regard to the first factor, it has been demonstrated that stimulus intensity (*1*), spectral composition (*2*), and frequency and duration (*3*) influence the VEP. Modification of the VEP by the second factor has been reported with regard to uncertainty about the nature of the forthcoming stimulus (*4*). It has been shown that affective meaning can significantly alter the response evoked by a visual stimulus (*5*). We have reported on changes in the VEP by classical conditioning. We found that during acquisition, changes in the significance of the stimulus were accompanied by modifications of the later activity of the evoked potentials (*6*).

In the experiment reported here, different wave shapes were obtained for potentials evoked by visual stimuli of constant intensity, whose perceived intensities were modified by psychological set. All data were derived from monopolar scalp recordings of 20 college students. One active electrode was located on the midline, 2.5 cm above the inion (Oz); the other was at the vertex (Cz). The electrode at the left earlobe was used as reference, and that at the right earlobe as ground. Evoked potentials were recorded by means of a Grass model 78 wide-band a-c electroencephalograph amplifier, whose low-frequency cutoff filter was set at 0.3 hertz. The high-frequency cutoff filter of the driver amplifier was set at 100 hertz, and the gain at 5 μv/mm. The evoked potentials were summed by a Mnemotron computer (CAT 1000) and written out on a Moseley XY plotter.

The subject was seated in an acoustically shielded enclosure, so that he was looking directly into a viewing hood which was flush against the one-way mirror of the enclosure. On the other side of the glass window a Grass PS-2 photostimulator was mounted and set at No. 2 intensity. The stimuli were presented in front of the photostimulator located 50 cm from the subject's eyes and subtended the central 20° of the visual field.

The visual stimuli were flashes transmitted through three different neutral density filters, which were used to reduce the light intensity of the photostimulator by a definite ratio. The dim stimulus corresponded to 20 percent transmittance and the bright stimulus to 80 percent transmittance. For the stimulus of medium intensity, we used a filter that allowed 50 percent transmittance. All stimuli were 2-inch ($\sim$ 5-cm) squares which were placed in a random access projector.

Before the first group of trials (R_1), the subjects were told that they would be presented with a bright flash and a dim flash. They were instructed to press one of two microswitches after each stimulus to indicate whether they had seen a bright or dim flash. The subjects were also told that a specific tone would precede the occurrence of a bright flash, and that a different tone would precede the dim flash. For half of the subjects a 1500-hertz tone preceded the bright flash and a 2500-hertz preceded the dim flash; for the other subjects, this order was reversed. The tones were discriminable by all subjects and preceded the flashes by a random interval of 2 to 4 seconds. In R_1, the bright and dim flashes were presented 25 times each, in random order.

Before the second group of trials (R_2), the subjects were informed that four different flashes would be presented: two bright flashes and two dim flashes. They were told that both bright flashes would be preceded by the same tone that had previously preceded the bright flash, while both dim flashes would be preceded by the same tone that had previously indicated the occurrence of the dim flash. In actuality, we presented three different light intensities—bright, dim, and medium—in random order. The bright flash and dim flash were presented 75 times each, while the medium flash was presented 50 times. For 25 trails the medium flash was preceded by the tone that previously indicated a bright flash. For the other 25 trials, the medium flash was preceded by the tone that previously preceded the dim flash. All flashes were presented with an interstimulus interval of 3 to 6 seconds. The third group of trials (R_3) was an exact duplication of the second, to examine the possible effects of habituation.

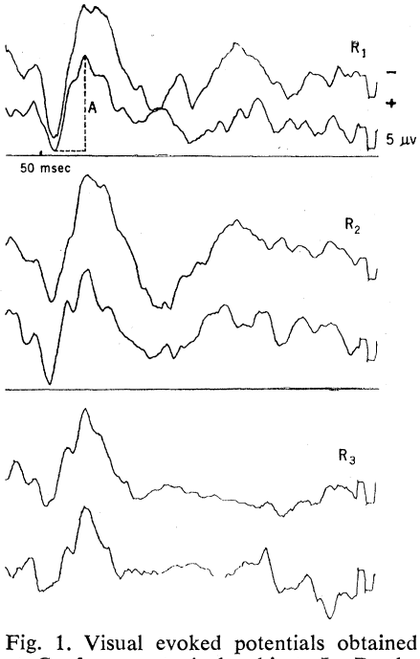

Fig. 1. Visual evoked potentials obtained at Cz for one typical subject. In R_1 the top potential was evoked by a bright flash and the bottom one by a dim flash. In R_2 and R_3 all the potentials were evoked by a stimulus of medium intensity. The top traces were obtained with a medium stimulus preceded by a signal indicating the onset of a bright stimulus. The bottom traces represent the potentials evoked by the same medium stimulus, but preceded by a tone signaling the onset of a dim stimulus. Negative deflections are up; the time base is 500 msec. The calibration pulse at the end of each wave form is equal to 5 μv; A, amplitude.

Changes in the evoked potentials obtained at Oz were assessed by measurements of the peak-to-peak amplitude of the late component (negative peak at 145 to 165 msec). At Cz, peak-to-peak measurements were determined for amplitude, as shown in Fig. 1. Statistical comparisons of the data obtained during the three groups of trials were made by an analysis of variance (*7*).

Figure 1 shows the evoked potentials of a typical subject through the three blocks of trials. The amplitude differences in the evoked potentials obtained to the bright and dim stimuli are large for R_1. The averaged evoked responses during R_2 and R_3 were obtained to the medium stimulus, and also show amplitude differences.

The presentation of a bright flash and a dim flash during R_1 results in amplitude differences at Oz and Cz (Fig. 2). For R_2 and R_3, differences in amplitude appear only at Cz. An analysis of variance for the data obtained at Oz did not yield a significant main effect. However, the interaction between intensity and trial group was significant at $P < .05$ ($F = 3.13$). The analysis of variance for the data obtained at Cz yielded a significant main effect at $P < .05$ ($F = 4.80$). Comparisons of the three pairs of means were all significant at $P < .01$. The interaction was not statistically significant. When the medium flash was preceded by the tone indicating the occurrence of a bright flash, the subjects pressed the "bright" switch on 97 percent of the trials. They pressed the "dim" switch on 90 percent of the trials, when the medium flash was preceded by the tone signaling the onset of the dim flash.

The data show that the potentials evoked by the same physical stimulus undergo a modification leading to the appearance of markedly different waves shapes in trials in which the occurrence of a different stimulus is signaled. When the medium stimulus intensity is preceded by a signal indicating the occurrence of a bright flash, the resulting evoked potential is more similar to the VEP obtained to a bright flash. The potentials evoked by the medium flash when a dim flash is expected closely resemble the VEP's elicited by the dim flash.

Of particular interest is the fact that our results were significant only at the vertex and not at the occipital. The occipital visual evoked response is often regarded as related to, or concomitant with, the specific processing of visual information and differs considerably from the responses recorded at the vertex, which are somewhat nonspecific and reflect a more advanced stage of information processing.

Our results demonstrate that the wave shape of the electrophysiological response to a sensory stimulus is not solely determined by the physical stimulus, but reflects the activation of endogenous neural processes related

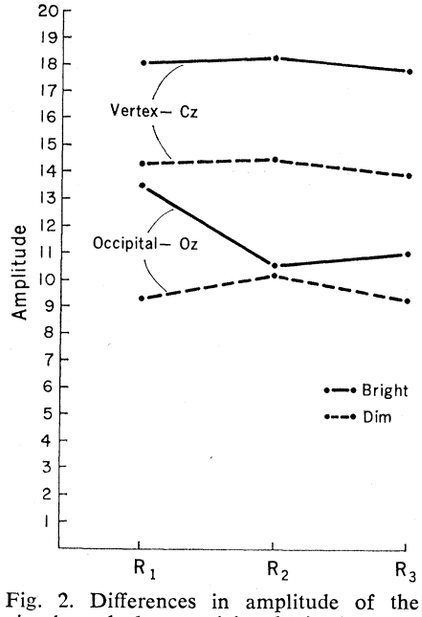

Fig. 2. Differences in amplitude of the visual evoked potentials obtained at Oz and Cz. During R_1, when the subject is presented with bright and dim stimuli, the amplitudes are different at both Oz and Cz. During R_2 and R_3, only stimuli of medium intensity are presented and the differences in amplitude are still apparent for Cz, but are no longer present at Oz.

to the past experience and present state of the organism.

It has been proposed that these endogenous patterns of neural activity may reflect previous experiences and are in that sense released from memory rather than evoked (*8*). We have observed changes in visual evoked potentials to a positive discriminative stimulus during sensory conditioning and extinction (*6*). These changes suggested that in addition to the neuronal activity evoked by the flash, the wave shape of the evoked potential reflects the release of neuronal activity which is related to the past experience of the organism. Additional support for this approach comes from studies which show that when an expected event does not occur, a brain potential appears at a latency similar to that of potentials usually evoked by the expected stimulus. These brain events, called "emitted potentials," have been interpreted as reflecting memory processes corresponding to past stimuli (*9*). A possible implication of our observation is that the experience of a specific stimulus image is dependent on the establishment of those neurophysiological processes originally involved in the registration and coding of the stimulus.

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Tremor and Involuntary Movements in Monkeys: Effect of L-Dopa and of a Dopamine Receptor Stimulating Agent

Abstract. *Either L-dopa, in combination with 1-α-methyldopa hydrazine (MK-486), or 1-(2″-pyrimidyl)-4-piperonylpiperazine, an agent that stimulates dopamine receptors, relieves surgically induced tremor in monkeys and concomitantly evokes involuntary movements. These results indicate that tremor and involuntary movements are associated with a common mechanism and that the activity of the dopamine receptors is involved in the regulation of these dysfunctions.*

Abnormal involuntary movements have emerged as one of the most limiting side effects in achieving optimum therapeutic results with L-dopa (*1*). A model for studies of involuntary movements (IM) in animals could provide some insights on the mechanisms involved in the production of dyskinesias. In this report we describe the effects of L-dopa and of 1-(2″-pyrimidyl)-4-piperonylpiperazine (Trivastal), an agent that stimulates dopamine receptors (*2*), on the relief of tremor and on the production of IM in monkeys with ventromedial tegmental lesions. These studies show that the stimulation of dopamine receptors is associated in monkeys with the relief of tremor and the development of involuntary movements.

Green monkeys (*Cercopithecus sabaeus*) were used, and unilateral radiofrequency lesions were induced in the ventromedial tegmental region of the brainstem as previously described (*3*). Hypokinesia of the contralateral extremities appeared immediately afterward. In some monkeys a resting tremor (4 to 6 cycle/sec) developed 5 to 7 days later. The lesions were induced at least 1 month before the start of the experiments. Recordings of tremors were obtained by means of a transducer attached to the extremities

Table 1. Types of abnormal movements.

Type 1
Increased aggressiveness and threatening posture
Restlessness, chattering, irritability, hypersensitivity
Increased water intake
Type 2
Repetitive stereotyped movements of the mouth, tongue, and face, with (i) lip smacking, (ii) chewing, (iii) tongue rolling, (iv) cheek pouch manipulation, (v) biting
Striking hyperkinesia with apparent highly vigilant orienting behavior
Increased grooming activity, including prolonged repetitive grooming of the same body area
Monotonous side-to-side swaying of body
Repetitive hand movements, sometimes without visible purpose
Chorea-like movements
Unusual sitting or walking postures

Table 2. The effect of L-dopa or Trivastal (Servier, France) on tremor and on the development of IM in normal monkeys with ventromedial tegmental lesions (VMT). L-Dopa and MK-486 (Merck) were given intraperitoneally, MK-486 60 minutes before L-dopa. These drugs were given for 5 consecutive days to three normal monkeys and to three monkeys with lesions. The development of IM was usually observed in normal monkeys after 2 or 3 days of treatment; in monkeys with lesions, the disappearance of the tremor and the development of IM were usually observed 1 or 2 days after treatment. Trivastal was given intravenously to three normal monkeys and to three monkeys with lesions. The drug was tested six times in each monkey, once every fourth day. In all experiments, the disappearance of the tremor was observed 20 to 40 minutes before IM developed.

Surgical lesion	Drug	Motor impairment	Involuntary movements	
			Type	Duration (hours)
None	MK-486 (10 mg/kg) + L-dopa (100 mg/kg)	None	1	1 to 2
None	Trivastal (3 mg/kg)	None	1	1
VMT	None	Hypokinesia and tremor	None	1 to 2
VMT	MK-486 (10 mg/kg) + L-dopa (100 mg/kg)	Tremor stopped for 60 minutes	1, 2	3
VMT	Trivastal (3 mg/kg)	Tremor stopped for 3 to 4 hours	2	1 to 2