due to the unusual patterns of touch and pressure and vestibular stimulation that result; similar illusions were experienced by subjects in the present study. In both cases, these illusions represent the organism's attempt to impose order on its relation to the environment despite restricted and abnormal patterns of sensory afflux.

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1. The contact forces provide a consistent representation of apparent posture but one that is alternative to that provided by the vestibular input [J. R. Lackner and A. Graybiel, *Aviat. Space Environ. Med.* **49**, 484 (1978); *ibid.*, p. 798].
2. The relationship between the subject's apparent posture and sound localization is predictable from the classical studies of auditory localization by H. Wallach [*J. Exp. Psychol.* **27**, 339 (1940)].
3. With eyes closed, different subjects' apparent orbits vary in diameter from about 45 to 180 cm; with eyes open, from about 8 to 32 cm. The heavier the subject, the larger the diameter of his apparent orbit. The subject can switch from experiencing one form of motion to experiencing the other by simply having his eyes open or closed.
4. The experimental apparatus is described in A. Graybiel and E. F. Miller, II, *Aviat. Space Environ. Med.* **47**, 893 (1976).
5. When we mention g levels, we are referring to the magnitude of the resultant gravitoinertial force vector in G^* units [see J. L. Patterson and A. Graybiel, in *Environmental Physiology*, N. S. Balfour, Ed. (Mosby, St. Louis, 1974), pp. 163–275].
6. The slow phase of the subject's nystagmus is compensatory for the direction of experienced motion; for example, when the subject experiences leftward motion his eyes drift right and beat left. The amplitude and frequency of the nystagmus depend on the subject's experienced velocity in his orbit, not on his true rotary velocity.
7. Further aspects of these mechanisms are discussed by J. R. Lackner [in *Handbook of Sensory Physiology*, R. Held, H. Leibowitz, H.-L. Teuber, Eds. (Springer-Verlag, New York, 1978), vol. 8, pp. 805–845].
8. These illusions are described in A. Graybiel and R. S. Kellog [*Aerosp. Med.* **38**, 1099 (1967)] and in R. S. Johnston and L. F. Dietlein, Eds. [*Biomedical Results from Skylab* (SP-377, NASA, Washington, D.C., 1977)].
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Fluorine Is a Major Constituent of the Marine Sponge *Halichondria moorei*

Abstract. *Fluorine constitutes about 10 percent of the dry weight of the marine sponge* Halichondria moorei. *The fluorine occurs as potassium fluorosilicate, which is a potent anti-inflammatory agent. A closely related sponge living in the same habitat does not contain any fluorine. The habitat was found to be free of fluorine except for the small amount naturally present in seawater.*

Many marine organisms accumulate iodine, bromine, and chlorine (*1*, *2*). Reports of fluorine accumulation by marine organisms are rare and mostly confined to its occurrence as fluorite (CaF_2) or fluorapatite [$Ca_5(PO_4)_3F$] in calcareous skeletal tissue. Some mollusks and brachiopods, such as the gastropod *Archidoris britannica*, are known to contain up to 3 percent (dry weight) fluorine (*1*, *3*), probably in the form of fluorite spicules (*4*). However, until now there has apparently been only one report of fluorine incorporation by sponges, that of Bowen and Sutton (*5*), who noted its presence in *Dysidea crawshayi* or in its symbionts without detailing its concentration or form. We report that specimens of the marine sponge *Halichondria moorei* Bergquist found off Auckland, New Zealand, contain fluorine at remarkably high concentrations (up to 11.5 percent of dry weight).

Interest was first aroused when an extract of *H. moorei* was shown to have potent anti-inflammatory activity. The active constituent was isolated and identified as potassium fluorosilicate (K_2SiF_6), also known as the mineral hieratite. (These findings were especially interesting in light of a report that the Maoris believed that the application of this sponge to wounds promoted healing.) Examination of *H. moorei* extracts for anti-inflammatory activity was carried out by inducing edema in rat paws with carrageenan (*6*). This test was used as a guide to fractionation during the isolation of the anti-inflammatory constituent. Upon being collected, the sponge was frozen and ground cryogenically. The pulverized organism was extracted sequentially with aqueous ethanol, water, and dilute ammonia, and each extract was separated from the insoluble material by centrifugation (32,000g). Each of the extracts displayed some anti-inflammatory activity, but the extract with ammonia was the most potent and, because of its low salt content, the most easily fractionated. Highly purified active material (0.83 percent of dry weight) was separated from this extract by successive diafiltration (Amicon UM05 membrane, with a 500-dalton cutoff), gel permeation chromatography (Sephadex G10), and high-pressure liquid chromatography on octadecyl silica. Powder x-ray diffraction analysis of this material, supported by atomic absorption and emission spectroscopy data, revealed that it contained about 33 percent potassium fluorosilicate. By comparison with an authentic sample, potassium fluorosilicate was established as the anti-inflammatory constituent of *H. moorei*.

Studies on the mechanism of action of potassium fluorosilicate (*7*) have shown that the compound probably exerts its anti-inflammatory activity by means of some counterirritant mechanism (*8*). Intraperitoneal administration of potassium fluorosilicate (50 mg/kg) causes mice to writhe.

Subsequently a more comprehensive study of the occurrence of fluorine in *H. moorei* and its habitat was recently undertaken. Fresh samples of *H. moorei* were collected near Auckland from Westmere Reef in Waitemata Harbour and at Takapuna. Potassium fluorosilicate was readily identified by x-ray diffraction as a major constituent of freeze-dried *H. moorei* from both locations. No other fluorine-containing substance was identified in the samples by this technique. The sponges were shown to contain 11.5 percent (Westmere Reef sample) and 9.7 percent (Takapuna sample) fluorine (equivalent to 22.2 and 18.7 percent potassium fluorosilicate), respectively, on a dry weight basis by analysis with a fluoride ion-specific electrode (detection limit, 0.1 percent) of extracts made with 1 percent sodium carbonate solution. Analysis of both the suspended and bottom sediments of the Westmere habitat detected no fluorine.

A second sponge, *Hymeniacidon perleve* Montagu, collected from Westmere Reef and from nearby Mill Bay in Manakau Harbour, was subjected to the same forms of analysis, but no fluorine or potassium fluorosilicate was detected. This sponge has a comparable growth pattern, occupies a similar habitat, and belongs to the same taxonomic order (Halichondrida) as *H. moorei*.

Since electron microscopy studies of *H. moorei* have shown it to be free of algal and bacterial symbionts (*9*), and since there are no unusual fluorine sources such as volcanic activity and industrial pollution in the immediate vicinity of the collection sites, it must be concluded that the fluorine in *H. moorei* is obtained from the low concentration (1.3 μg/ml) naturally present in seawater (*10*).

It is apparent that most sponges require little or no fluorine for their life

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processes. However, our research establishes that *H. moorei* is a remarkable exception, since this sponge accumulates and maintains a quantity of potassium fluorosilicate equal to about 5 percent of its wet (living) weight. The slight solubility of potassium fluorosilicate in water (0.77 g/liter at 0°C; 1.77 g/liter at 25°C) and in some other hydrous systems (*11*) indicates that most of it must be present in *H. moorei* in the solid state. Whether it constitutes an essential part of the skeletal tissue along with the amorphous silica also shown to be present by x-ray diffraction has yet to be determined quantitatively. Conventional procedures for separating spicules from sponge tissue involve solubilizing the tissue with aqueous oxidants and are, of course, unsuitable for the quantitative analysis of a water-soluble compound such as potassium fluorosilicate. In our qualitative examination of *H. moorei*'s spicules, we found nothing to distinguish them from the common siliceous spicules. Electron microscopy studies showed them to be very similar to *H. perleve*'s spicules and typically siliceous. In addition, several treatments of a sample of *H. moorei* with sodium hypochlorite solution produced a residue rich in spicules that appeared to be identical to those in the intact organism.

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Conditioned Tolerance to the Hypothermic Effect of Ethyl Alcohol

Abstract. *Results from experiments with rats support the proposition that tolerance to the hypothermic effect of alcohol involves the Pavlovian conditioning of compensatory responses. Tolerance was substantially reduced when alcohol was administered in an environment that had not been associated with alcohol. Direct evidence of a conditioned hyperthermic compensatory response was found.*

In a series of investigations, Siegel (*1*) proposed an unconventional theory of tolerance (the reduced responsivity to a drug caused by repeated experience with it) to several effects of morphine. Siegel postulated that tolerance to morphine is the algebraic summation of its unconditioned pharmacological effects and a compensatory conditioned response to those effects. According to the theory, the manifestation of tolerance is tied to environmental cues that become associated with the administration of the drug. There is now considerable evidence in support of this theory as it applies to the analgesic and hyperthermic effects of small (5 mg/kg) doses of morphine (*1*). An important test of the generality of Siegel's theory involves its applicability to nonopiate drugs. In this report we present data to show that tolerance to the hypothermic effect of alcohol also involves Pavlovian conditioning, and we give direct evidence for the existence of a conditioned compensatory response.

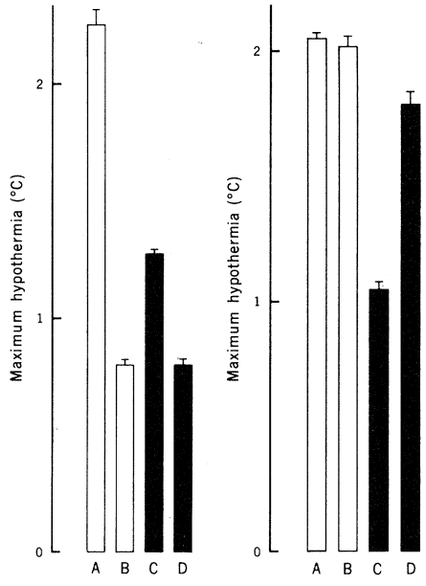

Fig. 1 (left). Peak hypothermic response (mean ± standard deviation) to alcohol in the first experiment. (Bar A) Initial response to alcohol (2.5 mg/kg). (Bar B) Diminished response after nine exposures to alcohol in the distinctive environment. (Bar C) Loss of tolerance during the first exposure to alcohol in the home room. (Bar D) Reinstatement of tolerance in the distinctive environment. Fig. 2 (right). Peak hypothermic response to alcohol (mean ± standard deviation) in the second experiment. (Bars A and B) Response to alcohol in the home (A) or distinctive (B) room when previous experience was with saline. (Bar C) Response of rats given nine injections of alcohol in the distinctive environment and tested for tolerance in the distinctive environment. (Bar D) Response of rats given nine injections of alcohol in the distinctive environment and tested for tolerance in the home environment.

In a preliminary experiment, in which within-subject comparisons were made, nine male Wistar rats (300 to 320 g at the beginning of the experiment) were used. They were caged separately in an environment that was maintained at 21° to 23°C with a photoperiodic cycle of 12 hours of light and 12 hours of darkness. Continuous access to water and laboratory chow was permitted. During tolerance acquisition (18 days), all animals received an intraperitoneal injection of alcohol (2.5 g/kg, 12.5 percent, weight to volume) in isotonic saline on alternate days. On such days, the rats were transported in a cage rack to a room made distinctive by dim illumination and the sound of static from a radio. They were weighed, had their rectal temperature taken as a baseline, and were injected with alcohol. Rectal temperature was again measured at 45, 60, and 75 minutes after the injection. On the days in which alcohol was not administered, the animals remained in their home room, where each was weighed, given an injection of isotonic saline as a control measure, and returned to its cage; no temperatures were taken.

On day 20 of the experiment, all the rats were subjected to the alcohol treatment and temperature measurement procedure, except that for the first time this was done in the home room, where the rats had never experienced the effects of alcohol. On day 22, all the animals were injected with alcohol in the distinctive room. (Days 19 and 21 were typical nonalcohol days.)

The results are displayed in Fig. 1, which shows the mean maximum hypothermia (maximum decrease from baseline) attained under the various experimental conditions. Bar A shows the hypothermia recorded during the first exposure of the rats to alcohol (during tolerance acquisition in the distinctive

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