bodies indicate that at least two 7*S* molecules in close proximity on the cell surface are required to fix a C′1a molecule. Furthermore, the generation of such doublets must be a random process, that is, the presence of a 7*S* molecule at a particular site on the cell surface does not influence the probability of doublet formation. If the process of doublet formation were directed rather than random, the slope of the 7*S* dose-response curve would approach unity. Thus, under conditions where the number of antibody-binding sites is relatively large, one would expect only a small proportion of the 7*S* antibody molecules to form doublets and, therefore, to be capable of binding C′1a. Since, on the other hand, each molecule of 19*S* antibody is capable of binding one molecule of C′1a, whole antiserum will behave like the 19*S* fraction, provided that the number of antibody binding sites is large. This result has been obtained even with antiserums in which the ratio of the number of molecules of 7*S* antibody to the number of molecules of 19*S* antibody was more than 100. It can be predicted from these results that the number of C′1a molecules fixed by a given amount of 19*S* antibody should be independent of cell concentration, provided that the number of antibody binding sites is not limiting and that the antibody in combination with antigen has a low tendency to dissociate. Under similar conditions, the number of C′1a binding sites generated by a given amount of 7*S* antibody will decrease with increasing cell concentration. Experimental results have been obtained which are in agreement with these predictions.

Earlier evidence indicated that relatively few sensitized sites on the cell surface were required to initiate the lytic process. Rapp presented evidence that fewer than ten molecules of 19*S* hemolysin per cell were required for sensitization (*3*, p. 145). On the basis of probability this observation was at variance with the conclusion of Weinrach *et al.* that two 19*S* antibody molecules in close proximity on the cell surface are required for sensitization (*6*). Weinrach *et al.* also proposed that four 7*S* antibody molecules are required to establish a potentially lytic site on the cell surface. The experiments on which their conclusions were based, however, suffered because the extent of lysis as a function of antibody concentration was not independent of complement concentration (*1*). More recently Humphrey and Dourmashkin have shown that as few as two 19*S* antibody molecules suffice to sensitize an erythrocyte (*7*). They presented evidence that several hundred molecules of 7*S* antibody are required to sensitize an erythrocyte to the lytic action of C′. Statistical considerations led them to postulate that either a single molecule of 19*S* antibody or two molecules of 7*S* antibody are sufficient to initiate the lytic process. Based on the evidence given in this report, we propose that on cell surfaces a single molecule of 19*S* antibody suffices to fix C′ while doublets are required for 7*S* antibodies.

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5. We are indebted to the following individuals for supplying some of the reagents: Dr. L. Muschel (*S. typhosa* and rabbit antiserum to *S. typhosa*), Dr. W. Rosse (human I "cold agglutinin" and *S. typhosa* somatic antigen and its corresponding rabbit antibody), and Dr. T. Ishizaka and Dr. K. Ishizaka (IgG and IgM fractions of human antiserum to A substance).
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2 August 1965

Dulcin and Saccharin Taste in Squirrel Monkeys, Rats, and Men

Abstract. *In a taste-preference comparison of sweetening agents, men reacted positively to two nonnutritive sweeteners, dulcin and sodium saccharin; rats preferred only saccharin and squirrel monkeys, only dulcin.*

The mechanisms regulating taste preferences may also be mechanisms of reinforcement in the conditioning situation (*1*).

Sodium saccharin is reported by humans to be about 675 times as sweet as sucrose, and dulcin is about 200 times as sweet as sucrose. These are the sweetest substances known to man (*2*). Sodium saccharin has been used as an incentive for rats in the conditioning situation; dulcin has not been so used. The increasing importance of the squirrel monkey as a laboratory animal warrants systematic study of preferences for sweeteners on this animal and comparison of the resulting data with that from similar work on other laboratory subjects.

Preferences for dulcin and sodium saccharin in four male squirrel monkeys (*Saimiri sciureus*) were studied and compared to data obtained from five male albino rats and three male humans. Three additional male squirrel monkeys provided information about the reinforcing properties of dulcin.

The Richter two-bottle preference test (*3*) was used to determine taste functions in the animals. Two drinking tubes were suspended from the wall of the animals' cages; one contained distilled water and the other a sapid solution made with distilled water. Intake was recorded every 24 hours at which time the contents were reversed to compensate for position preferences. Every 48 hours the concentration of the sapid solution was increased to provide an ascending concentration series.

Information on the reinforcing properties of dulcin for squirrel monkeys in a lever-pressing situation was collected from three squirrel monkeys. The animals were trained to press a bar, on a

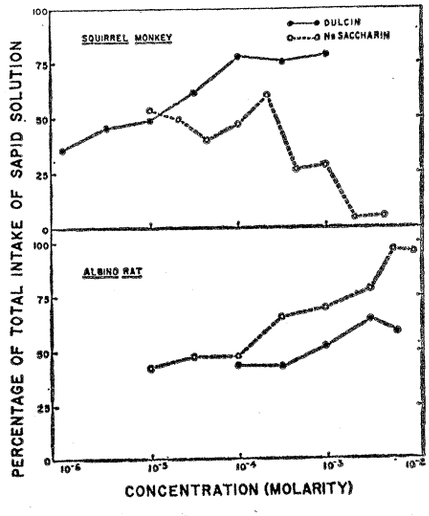

Fig. 1. Averaged preference-aversion curves for dulcin and saccharin for four squirrel monkeys and five albino rats.

fixed-interval schedule of 30 seconds (occasion for reinforcement of a response occurs 30 seconds after the previous reinforced response), for a 5-second presentation of a drinking tube containing various concentrations of dulcin. The different concentrations were presented in a Latin-square fashion to preclude order effects. The squirrel monkeys were subjected to two series of four concentrations each. The first series consisted of the following molar concentrations: 10^{-6}, 10^{-5}, 10^{-4}, and 10^{-3}. The second series was run to provide a finer scale with which to examine the critical portion of the reinforcement curve. The molar concentrations used were 1.8×10^{-4}, 3×10^{-4}, 5.6×10^{-4}, and 1.8×10^{-3}. Each session lasted 30 minutes; at the time of testing the monkeys had been deprived of fluids for 16 hours.

Figure 1 illustrates the squirrel monkeys aversion to sodium saccharin. Dulcin, on the other hand, was preferred by these animals. The aversion threshold (set at 25 percent, or less, of total intake) for sodium saccharin was about $5 \times 10^{-4}M$. The preference threshold (set at 75 percent, or more, of total intake) for dulcin was about $10^{-4}M$. The rats showed a clear preference for the sodium saccharin beginning about $3 \times 10^{-4}M$ and only a suggestion of a preference for dulcin (65 percent of total intake) at only one value, $3 \times 10^{-3}M$. The solubility of dulcin limited the extent of the ascending series, however, $6 \times 10^{-3}M$ was presented, and the earlier suggestion of a preference was contraindicated.

Figure 2 shows that a concentration of $1.8 \times 10^{-4}M$ provided about the same incentive as the $10^{-6}M$. The next step, 3×10^{-4}, generated a noticeably higher rate which progressed with increasing concentration. The reinforcing concentration of the dulcin appeared to increase the preference threshold value by about half a log dilution. The individual curves were very similar to the average curve.

Three human subjects provided data for thresholds of reported sweetness for sodium saccharin and dulcin. The subjects were given an ascending series with a "water break" between the two series. Two glasses, one containing the sapid solution and the other water, were presented simultaneously to the subject. The subject tasted the contents of one of the two glasses, rinsed, tasted the other, and reported the taste quality. The order of tasting the solutions in each pair was randomly determined.

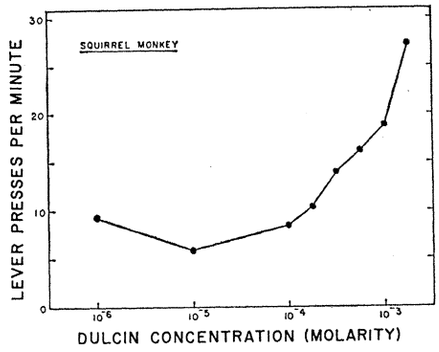

Fig. 2. Combined rates of lever-pressing for three squirrel monkeys maintained by dulcin reinforcement.

One minute was allowed for each judgment, and a 2-minute intertrial period was observed.

The reports of sweetness of the three individual subjects were in perfect agreement. The subjects reported that saccharin tasted "like water" at $10^{-5}M$ and "sweet" at $3 \times 10^{-5}M$. The report of "sweet" continued for all higher concentrations. Similarly, the subjects reported that $3 \times 10^{-4}M$ dulcin was "like water" and $10^{-3}M$ dulcin and higher concentrations, "sweet." Subject N.K. later reported both dulcin and sodium saccharin pleasant above threshold; D.A. considered the highest concentration of dulcin and sodium saccharin "sickeningly sweet"; B.N. reported only the highest concentrations to be too sweet to be pleasant.

Our data indicated that squirrel monkeys have a strong preference for dulcin and an aversion for sodium saccharin above a certain concentration. Rats, on the other hand, preferred the saccharin and were indifferent to the dulcin. Dulcin is not only preferred to water but may be used to maintain operant behavior in squirrel monkeys. Saccharin will do the same for rats (*4*).

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Adrenaline and Noradrenaline: Relation to Performance in a Visual Vigilance Task

Abstract. *Concentrations of adrenaline and noradrenaline in the circulating blood were measured in blood samples taken from subjects as they performed a visual vigilance task or viewed movies, both under identical conditions. For those subjects whose vigilance performance deteriorated it was concluded that the concentration of circulating adrenaline decreases as a function of time in a vigilance task but not under "relaxed" conditions, such as watching motion pictures.*

The typical decrement in signal-detection performance which occurs in many "vigilance tasks" (*1*) is related to various physiological changes, which suggests decreasing arousal of the cortex (*2*) and of the sympathetic-autonomic nervous system (*3*).

Arousal, both cortical and autonomic, is correlated with activity within the ascending reticular activating system (ARAS) of midbrain and diencephalon (*4, 5*). It has been postulated (*6*) that when the cortex is aroused, this activating system serves a "vigilance function," making the cortex responsive to neural "cues" or signals as they arrive by way of classical sensory tracts. Perhaps the deterioration of detection performance frequently found in vigilance tasks results from decreasing ARAS activity. If so, sources of activation should show a quantitative decrease throughout the course of a vigilance task.

As the reticular activating system is normally excited by the direct action of circulating biogenic stimulants, particularly adrenaline (*5*), the hypothesis of this experiment was that circulating adrenaline decreases in human subjects when their detection performance deteriorates during a vigilance task.

Illumination of a 32-mm, circular aperture was continuously cycled from dim (2 sec) to brighter (1 sec) every 3 seconds. Occasionally a "signal," defined as a still greater brightness, was generated during the 1-second part of the cycle, and the task was to report the detection of such signals by pressing a hand-held response button.

Subjects were 16 males ranging in age from 20 to 34. One week prior to serving in the experiment each subject undertook a psychophysical test aimed at determining the signal brightness which he could detect in 90 per-