an early litter (that is, at an early maternal age) descent when the litter size is maximal have smaller litters than do the females that were taken from a late litter (or late maternal age) descent where the litter size had been minimal. Here again is evidence of a compensatory mechanism influencing litter size.

It is clear by the evidence now available that the characteristics of the offspring occurring in the maternal-age descents in the middle of the age distribution do not significantly change between the F_1 and F_{10} generations—it is only the offspring of the two extreme maternal-age classes which deviate, and this deviation is counter to the trend of maternal-age selection.

The obvious reason for such compensatory changes as those enumerated in the preceding pargraphs is to keep the species in equilibrium. If there were no such compensatory mechanism, it would be relatively easy for a species to drift into chaos. This would necessarily be so for any character that may be partially influenced by parental age and other factors. If the practice were continued for many generations for females to have their first child (or litter) earlier and earlier, irreparable damage to the species might be the result. Similarly, the practice of bearing young long after the normal reproductive period has been exceeded might also produce disastrous results.

The present experiment indicates quite convincingly that, unless the insult has not been too great for too many generations, a compensatory mechanism corrects for a deviation from the norm, and this variation takes place counter to the trend of selection.

In genetics there is a concept that a species is in equilibrium until a mutation occurs "to upset the applecart," after which a new equilibrium is established by incorporating into, or by discarding from descent, the new mutation. We no longer have to make the assumption that the species is in equilibrium (homeostasis). There is evidence, such as the present data, to prove that a mechanism actually exists. The nature of this mechanism is still in doubt, and we do not know how to influence it.

It is not my intention to review the literature dealing with equilibrium or homeostasis. To me it is not clear whether biological or genetic equilibrium is involved. To some investigators these two phenomena may be absolutely dependent on each other. This may be true, but certainly more data are needed for final analysis. The field of genetic homeostasis has recently been covered by Lerner (*5*).

Since so many types of biological characteristics, such as age of first litters, litter spacing, litter size, and various types of tumors, are kept in equilibrium, this mechanism must be of extreme biological importance. A species could probably not be kept in equilibrium unless the individuals who make up the species are also in equilibrium at least during the reproductive period.

The various types of cancers which arise in the mammalian body have, at least, one characteristic in common. Cancer arises because the organism has lost control of a definitive part. Perhaps during the aging process the mechanism that keeps the individual in equilibrium is disrupted, and as a result of this loss of control of all the parts cancer of one or more elements is able to originate and to grow at the expense of the rest of the body.

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15 January 1957

Auditory and Aversion Thresholds of Rats for Bands of Noise

In the context of animal behavior theory, stimuli are often described as having both drive and cue value (*1*). Drive value refers to the ability of a stimulus to motivate behavior, and cue value refers to the ability of a stimulus to serve as a signal to the animal by virtue of its distinctiveness. In general, these two aspects of stimuli have been studied independently within the framework of two separate psychological disciplines, namely, learning theory and psychophysics. As a result of this, there are few studies comparing the cue and drive properties of stimuli, although it is obvious that the two properties are not unrelated in the case of most stimuli.

The purpose of the present study (*2*), then, was to develop a technique for comparing the drive and cue properties of a specific stimulus dimension—in this case, noise. More specifically, this research compares the auditory thresholds of rats for bands of random noise with the aversion thresholds of rats for the same bands of noise. The auditory thresholds were taken to represent the minimal cue value of white noise, and the aversion thresholds the minimal drive properties of white noise. Thresholds were obtained for a number of different frequency bands of noise so that both the shape of the functions and the distance between them could be compared. The following bands of noise were used: 250 to 500, 500 to 1000, 1000 to 2000, 3000 to 4000, and 4000 to 5000 cy/sec.

Acoustically, the apparatus for both threshold studies was the same, consisting primarily of a noise-generating system and a heavy Celotex enclosure 2 ft wide, 3 ft deep, and 6 ft high lined with fiber-glass insulation. The noise-producing system included a white noise generator, electronic switch, audio amplifier, attenuator, two UTC-4C variable band-pass filters, and a horn-type loudspeaker mounted inside the Celotex enclosure. Two test cages were used in the study; one for the determination of auditory thresholds and one for the determination of aversion thresholds. Both cages had the same over-all physical dimensions (7 in. wide, 10 in. deep, and 7 in. high); when in use (one at a time), they were mounted at the midline of the cabinet on steel rods. The sound field within each cage was relatively uniform (± 1½ db for all frequency bands).

Auditory thresholds were determined by means of a classical shock-avoidance technique. Six animals were first trained to turn a small wheel located at one end of the cage whenever a noise stimulus was presented. This was accomplished by giving the animal an electric shock by means of a shock grill floor if it did not turn the wheel within 2½ seconds of the onset of the noise. Whenever the animal responded within the 2½-second period, the noise was turned off and no shock was administered; if the animal did not respond within the 2½-second period, the noise continued and electric shock was administered until the rat turned the wheel. After the animal had been trained to respond to the cue or signal value of the noise, it was possible to determine the auditory threshold by varying the noise stimulus in 5-db steps around the threshold and recording the number of times the animal responded to each intensity. At the lowest intensi-

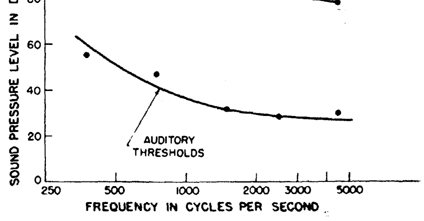

Fig. 1. Auditory and aversion thresholds of rats for bands of noise.

ties of noise used, the animals never responded, while at the higher levels they responded nearly 100 percent of the time. As in psychophysical studies on human subjects, the threshold was defined as the point at which the animal responded 50 percent of the time to the noise stimulus.

The auditory thresholds obtained through this procedure are shown by the lower line in Fig. 1. As can be seen, the threshold decreases as frequency increases within the frequency ranges studied, and the function is quite comparable to threshold functions of rats which have been obtained for pure tones (*3*).

Aversion thresholds for the same bands of noise were obtained by determining the intensity of noise that the animals avoided 75 percent of the time in a simple spatial preference situation. These thresholds were determined in a cage so designed that when the animal was at one end of the cage silence prevailed, but when it moved to the opposite end a specified level of noise came on and stayed on as long as it remained there. If the noise was intense enough, the animal soon learned to avoid the noisy end of the cage and remain at the silent end.

To obtain the aversion thresholds, the relative avoidance of the noisy end was determined for five intensities at each band. These ranged, at all bands, from 65 to 105 db in 10-db steps. Six animals were run at each of these bands of noise, and each animal was tested for its relative avoidance of the noisy end for each of the five intensities during separate 50-minute test periods. Each animal was given a single test period each day, and the order in which it received the noise intensities over the 10-day test period was randomly determined. Any preference for one end of the cage was balanced out by giving the animal each intensity at both ends of the cage on succeeding days.

The noise-aversion thresholds were determined by plotting the animal's avoidance of the noisy end of the cage during the last 30 minutes of the 50-minute trial as a function of sound level. The aversion threshold was defined as the intensity of noise the animals avoided 75 percent of the time, and these points were determined visually for each level from the afore-mentioned functions.

The aversion thresholds for the five bands of noise studied are shown by the upper line in Fig. 1. The form of the aversion-threshold function is much the same as that obtained for the auditory thresholds in that the threshold decreases as frequency increases. The chief difference between the two functions is that the aversion thresholds are some 40 to 50 db higher than the auditory thresholds.

On the basis of these data, it is possible to describe more fully the relationship between the drive and cue values of auditory stimuli for albino rats. For all practical purposes, those stimulus intensities which fall between the auditory and aversion thresholds can be described as having primarily cue value, while those falling at and above the aversion threshold can be considered to have both drive and cue value. This information may serve as a reference for experimental psychologists who wish to select auditory stimuli which are sufficiently intense to serve as distinct cues without being aversive, or to those who wish to select stimuli which are clearly aversive.

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20 November 1956

Antibodylike Factor in Serums of Ragweed-Sensitive Individuals Shown in vitro

Numerous attempts to demonstrate specific antibodies in serums of allergic individuals by *in vitro* methods have been reported in the literature. Although some workers have claimed that they have been able to detect an antibodylike factor by techniques such as the inhibition of complement fixation (*1*) and the clumping of allergen-coated collodion particles (*2*) and erythrocytes (*3, 4*), the results of other workers are contradictory or inconclusive.

In the present study (*5*) the highly sensitive hemagglutination technique, as described recently by Stavitsky and Arquilla (*4*), was shown to lend itself to the clear-cut demonstration of antibodylike factors in serums of untreated and treated ragweed-sensitive individuals (*6*). Rabbit erythrocytes were used for sensitization with a ragweed extract. To 0.1 ml of a 1/1 suspension of rabbit erythrocytes in saline, 3 ml of a 0.5-percent saline solution of water-soluble ragweed extract (WSR) (*Ambrosia artemisiaefolia*) and a bis-diazotized benzidine solution in phosphate buffer was added. All serums, prior to testing, were absorbed with nonsensitized erythrocytes to remove nonspecific agglutinins.

The method was standardized with two precipitating antibody-antigen systems: WSR-rabbit anti-WSR, and BSA-rabbit anti-BSA (bovine serum albumin). Typical hemagglutination patterns are presented in Fig. 1. The high sensitivity of the method as claimed by Stavitsky and Arquilla (*4*) was confirmed (for example, the titer of the rabbit anti-WSR serum was 1/600,000,000). Furthermore, the specificity of the hemagglutination reaction was demonstrated by the inhibition of the test with an excess of the specific antigen. By the use of erythrocytes sensitized with ragweed, positive results were obtained with four serums of treated, and with twelve serums of untreated, ragweed-sensitive individuals in dilutions as high as 1024 and 512 respectively. Thirty normal human serums gave negative results. The positive reactions were shown to be specific for ragweed as demonstrated by the inhibition of the tests with excess water-soluble ragweed extract and not with other antigens, such as bovine serum albumin, grass pollen, and wormwood.

Heating serums of untreated, allergic individuals containing reagin at 56°C for as long as 11 hours did not change their hemagglutination titer, although their skin-sensitizing ability was destroyed. Positive hemagglutination tests were obtained only with serum fractions (separated by starch electrophoresis from two serums of untreated ragweed-sensitive individuals) that also possessed skin-sensitizing activity. However, these findings cannot be taken as evidence that the hemagglutination factor is identical with the skin-sensitizing antibody that is commonly found in allergic serum.

On the basis of these experiments, it seems reasonable to conclude that serums of individuals who are allergic to ragweed contain an antibodylike factor or factors that are demonstrable *in vitro*. These studies would suggest that this system behaves very much like an ordinary

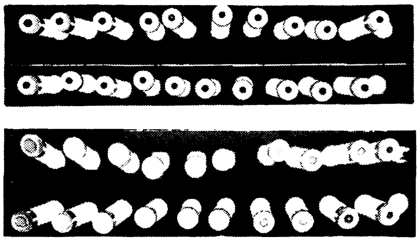

Fig. 1. Hemagglutination patterns. Each row represents tubes containing serum in halving dilutions. The concentration of serum decreases from left to right. (Top pair) Controls using normal human serum. No hemagglutination is observed in any tube. (Middle pair) Allergic serum. The patterns represent a gradual decrease in the extent of hemagglutination. (Bottom pair) Rabbit antiserum. The patterns represent positive results.