



Fig. 2. Excitability change in cuneate tract terminals produced by acoustic stimuli. Sample records from the superficial ulnar nerve in response to microelectrode stimulation at a depth of 1.2 mm in the cuneate nucleus. (A) Testing stimulation (alone). (B) Testing stimulation preceded at 50 msec by conditioning acoustic stimulation.

cuneate cells (1, 4), while the P wave has been postulated to be due to prolonged depolarization of the presynaptic terminals of cuneate tract fibers (4, 5, 7). Brief flashes or clicks generated similar N and P waves on the surface of the cuneate nucleus (Fig. 1). In response to photic and acoustic stimuli, however, the N wave (10 msec latency) was more prolonged and the P wave reached its peak at 55 msec and lasted about 80 msec. When a P wave was evoked in the cuneate nucleus in response to conditioning photic or acoustic stimuli, it depressed the test P wave evoked by an ipsilateral cutaneous volley. This P wave depression reached its maximum at conditioning-testing interval of about 50 msec and lasted over 200 msec (Fig. 1). This was similar to the effects on the P wave by conditioning stimulation of the adjacent forelimb nerves (7), the contralateral sensorimotor cortex (7), or remote skin areas in the other limb (11).

Another evidence for a visual and auditory influence on the cuneate nucleus was observed by the method of excitability testing (5, 12). Microelectrode stimulation within the cuneate nucleus evoked an antidromic response in the superficial radial nerve consisting of an initial spike complex conducted antidromically over the faster cutaneous nerves and a second spike complex that is analogous to the dorsal root reflex (5). Conditioning photic or acoustic stimuli caused an increase in the initial spike complex and a depression in the secondary spike complex (Fig. 2), with a similar time course for both effects. This time course was also similar to that observed during the P wave interaction just described. These changes and their time courses are suggestive of presynaptic inhibition (5, 11).

A third line of evidence was observed from the effects of photic and

acoustic conditioning stimuli on the test mass discharge in the contralateral medial lemniscus evoked by stimulation of the ipsilateral forepaw. Photic and acoustic stimuli depressed the test discharge in the medial lemniscus.

A fourth line of evidence was provided from observations that conditioning photic and acoustic stimuli also inhibited spontaneously firing cuneate neurons as well as those driven by peripheral cutaneous stimulation. The latter influence was demonstrated by a decrease in the probability of discharge, a decrease in the number of spikes per discharge, a lengthening of initial spike latency, or a combination of these effects.

Convergence and interaction between visual, auditory, and somatic sensory stimuli have already been demonstrated in cortical "polysensory" areas of the cat (13), monkey (14), and man (15). Little is known about these interactions at subcortical levels (16), and nothing is known about them at the level of the first somatic sensory relay.

Although we have demonstrated modulatory influences of photic and acoustic stimuli on the cuneate nucleus, we have no precise information about the pathways involved. These influences were present but attenuated when the cats were under pentobarbital anesthesia. The persistence of auditory inhibition in decerebrate preparations rules out the necessity for reflex stimulation through the somatosensory cor-

tex. Recently, Chu (17) demonstrated that the pyramidal tract was not essential for auditory and visual facilitatory and inhibitory effects on the spinal cord. We cannot, however, rule out a role for the brainstem reticular formation which can receive a multisensory input (18) and can exert modulatory influences on the gracile and cuneate nuclei (8, 9).

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Comparative Ability of Hycanthone and Miracil D to Interact with DNA

The report of Hartman *et al.* (1) on the mutagenic activity of the antischistosomal agent hycanthone in *Salmonella* concludes with the comment that while published reports are available on the interaction of the related compound, miracil D, with DNA and its effects on bacterial metabolism, comparable information on hycanthone is lacking. It is the purpose of this brief note to summarize the data on the latter agent which have been recorded recently in rather scattered fashion.

In standardized test systems, hycanthone exhibited activity equivalent, on a molar basis, to miracil D in increasing the melting temperature and relative viscosity of DNA—two measures of their ability to complex with this

macromolecule. Both compounds inhibited the growth of *Bacillus subtilis* in vitro and of mouse leukemia L1210 in vivo and interfered at equivalent concentrations with DNA and RNA synthesis in these tumor cells in vitro.

In addition to these data from our laboratories (2), Waring has recently adduced elegant evidence for the capacity of hycanthone to intercalate between the base pairs of DNA on the basis of measurements of the sedimentation coefficient of circular duplex DNA of bacteriophage ϕ X174 (3). Wittner *et al.* (4) have demonstrated pronounced activity of hycanthone against RNA synthesis, but not DNA or protein synthesis, in HeLa cells.

These similarities between the two closely related antischistosomal com-

pounds, added to the observation (1) that both are mutagenic in an *Escherichia coli* T4 bacteriophage system, make it even more desirable that a persuasive explanation be found for the qualitative difference between them in mutagenicity for *Salmonella*.

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Height, Weight and Age at Menarche and the "Critical Weight" Hypothesis

Frisch and Revelle (1) have concluded that menarche occurs at a critical body weight, perhaps triggered by a feedback from the metabolic mass of the body to appropriate regulatory systems. They based their conclusions on the lack of differences in mean weight at menarche among girls when divided into four menarcheal age groups, as opposed to a steady increase in mean height from the youngest (< 12.0 years) through the oldest (> 13.9 years) age category.

We have investigated this more intensively in 70 normal girls, 42 of Caucasian ancestry from Philadelphia, and 28 of mixed European (largely Spanish), and American Indian background from Guatemala City. All of the subjects were well nourished and free of disease at related clinical examinations; they were taking part in longitudinal growth studies and had attained menarche in the interval between successive annual examinations. We estimated height and weight at menarche by interpolation.

The Philadelphia girls attained menarche at a mean age of 12.4 years and at an estimated mean height of 153.5 cm and weight of 47.1 kg. For the Guatemalan girls, the corresponding means were 12.3 years, 146.1 cm, and 39.8 kg. These means differed significantly between the two samples ($P < .001$). The range of variation in weight was a striking 22 kg for each group if one Guatemalan and one Philadelphia girl with weights of 60 and 61 kg, respectively, are excluded.

These data were standardized around their subsample means for age, height, and weight by converting to T-scores (2) and treated as a single sample.

Multiple regression analysis expressed age (A_m) as a function of height (H_m) and weight (W_m) at menarche, as given in the equation

$$A_m = 39.3 + 0.38 H_m - 0.17 W_m$$

The regressions of age on both height and weight are significant, the former at the .01 and the latter the .05 level. The coefficients of partial correlation are, for height and age at a constant weight, +.68, and for weight and age at a constant height, -.26; both coefficients are statistically significant.

The results indicate that, far from a critical and unvarying weight at menarche, there is not only a striking range of absolute variation, but also a significant regression of age upon weight if height is held constant. At a constant height girls who menstruate earlier are heavier than those menstruating later. At a constant weight, the early maturers are shorter. When considered together, therefore, early menarche is associated with shorter, heavier girls, and later menarche with taller and lighter girls.

The rather complex interrelation among the height, weight, and age at menarche, and the failure to consider them, could very well lead one to suspect the weight and age to be unrelated. For our sample, the regression of age upon weight, without considering height, is, at +.13 (T-score units), not significantly different from zero. On the other hand, the relationship between height and weight at menarche ($r = +.64$) is significant and positive.

Thus, weight at menarche is related to height, as is obvious, since taller girls weigh more than shorter ones.

Taller girls also reach menarche later. But, at a constant height, weight and age at menarche are significantly related in a negative direction. Weight is therefore related to height and to age in opposite directions.

The results of the directionally opposite relationships of weight to the height and age at menarche are to obscure the latter, unless the height covariance is accounted for. By merely comparing mean weights at menarche of various age groups, Frisch and Revelle have been led to conclude that the weight is constant over age. The more detailed analysis of our data in contrast reveals that the two are related and that the "critical weight" hypothesis is an artifact arising from failure to consider the interrelationships of all three variables.

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References and Notes

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The mean weight at menarche found recently by Johnston, Malina, and Galbraith for Caucasian girls from Philadelphia is about the same, 47.1 kg, as we found (47.8 ± 0.51 kg) for Caucasian girls from Berkeley, Boston, and Denver who had menarche three decades ago (1). However, the mean age of menarche of the Philadelphia girls, 12.3 years, is 7 months earlier than the mean age of menarche, 12.9 ± 0.1 years, of the girls of three decades ago. This appears to support our critical weight hypothesis and our explanation of the secular trend to an earlier menarche (1, 2). (We assume that standard errors of Johnston *et al.*, which are not given, are in a similar range as ours.)

Different racial groups have different weights and heights at menarche, as was found by Johnston *et al.* for the Philadelphia and Guatemalan girls, and as we noted from the significant difference in weights and heights at the time of maximum rate of growth, which precedes menarche (3); for example, the mean weight for Japanese girls is 33 kg (4), and that for American girls is 39 kg (5).