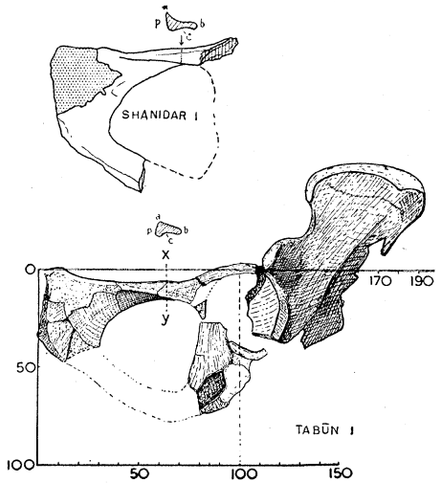

Fig. 2. Left pubic bone of Shanidar I and left innominate bone of Tabūn I, each with a cross section of the superior pubic ramus along the line *x-y*. Explanation of abbreviations in Fig. 1. [Lower figure modified from McCown and Keith (*1*, Figs. 49g and 53)]

unique shape of pelvis, whereas the Skhūl specimens combine a nearly modern skull morphology with an essentially modern shape of pelvis. The pelvic differences impress me as having as much significance as the skull differences. Together they amount to a fundamental difference.

So long as the skulls from Mount Carmel were mainly the subject of discussion, interpretations of their variations took two courses: (i) "the Mount Carmel people were in the throes of evolutionary change" (*1*, p. 14), or (ii) "the Mount Carmel population arose . . . as a result of hybridization of a Neanderthaloid and a modern type, these types having been formed earlier in different geographical regions" (*7*, p. 258). In view of the new evidence, neither of these explanations seems completely logical. To my way of thinking it is simpler and more reasonable to strip the Mount Carmel remains of the role of a "population," and especially a hybrid population, and to recognize their two components as fundamentally distinct. There is no reason now to regard the Skhūl specimens as anything other than representatives of an early variety of modern man. The Tabūn-Shanidar specimens then become representatives of the local Neanderthal variety, which probably went on to extinction. All this does away with the need for setting up hypothetical types and for assuming that the whole lot of the Mount Carmel skeletons represents a single breeding population.

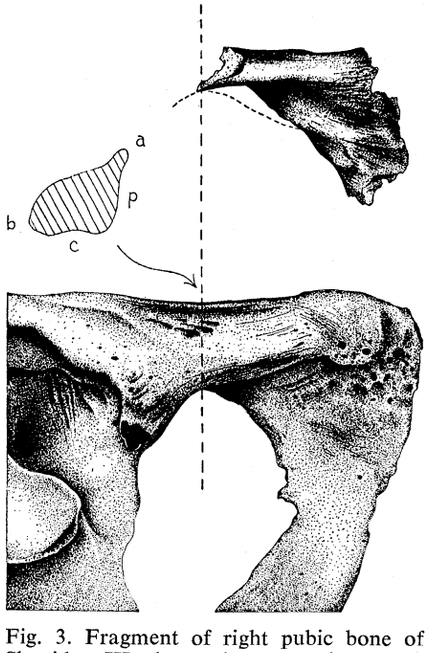

Fig. 3. Fragment of right pubic bone of Shanidar III shown in comparison with the corresponding part of a modern specimen (male). Explanation of abbreviations in Fig. 1.

It may be objected that spatial separation is required to maintain the distinctiveness of human varieties and that the Mount Carmel caves did not afford such separation. In general this is a valid objection, but as yet there is no proof that the recovery of two different varieties of man from a cultural layer which accumulated over thousands of years in the Mount Carmel caves necessarily means actual physical contact between these varieties. I have stated elsewhere (*8*) my reasons for doubting that the Skhūl and Tabūn remains represent a breeding population. The fact that these remains were separated stratigraphically most likely means that the distinct varieties which they represent were separated in space; in other words, separate occupation of the caves at different times by these distinct human varieties could have taken place while they were living in the surrounding area as breeding isolates. The concept of contemporary breeding isolates is well established, but the nature of the isolates in this instance cannot be clearly discerned. Incidentally, such an explanation often has been precluded in the past by the dubious assumption that all remains of ancient man have to be fitted into a straight evolutionary line.

To recapitulate, then; the evidence here presented forces consideration of the possibility that an early variety of modern man lived side by side, so to speak, with a Neanderthal variety during Mousterian times in the area now designated as the Near East.

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22 January 1960

Fusion of Complex Flicker II

Abstract. Flicker waveform has been found to have a slight but specific effect upon fusion threshold. A depression of threshold amplitude of about 30 percent occurs if a second harmonic of near-threshold amplitude is added to the fundamental. The magnitude of the depression depends critically on the relative phase of the two components of the waveform.

The frequency at which a flickering light appears to fuse into steady light has appeared to depend mainly on the average luminance and the amplitude of the fundamental Fourier component of the flicker waveform, and very little on its other components (*1*). However, recent results with a waveform whose second harmonic was much stronger than its fundamental (*2*) seemed to yield flicker fusion which depended on the amplitude of either the fundamental or the second harmonic, whichever was above threshold (*3*). This experiment was designed to check whether the threshold for flicker fusion is indeed not depressed when two components are summed, both components being near threshold.

The subject was seated with his head held fixed by a chin rest. A Sylvania R-1131/c glow modulator transluminated a ground glass screen placed 10 inches from his eyes. The luminance could be varied without change of color by special circuitry provided by H. S. McDonald of Bell Telephone Laboratories. Only one average luminance was used in the experiments, namely 200 ft-lam. The screen subtended about 1° at the subject's eyes and was seen in a white surround of 40 ft-lam, subtending about 10°. The average d-c lamp luminance could be modulated in one of three modes selected by the subject by switch. These modes were: a sinusoid of frequency f, a sinusoid of frequency $2f$, and the two components summed. The experimenter set the frequencies and the relative phase of the components (see Fig. 1). The subject could vary the amplitude of modula-

tion in each mode independently. First, the subject set the amplitudes of f and of $2f$ to just exceed the threshold separately. He then left these settings undisturbed while he adjusted the amplitude of the sum of the two components according to the same criterion. He reset this amplitude for each of a set of phase differences selected by the experimenter. By switching back and forth among the three modes, the subject could compare his setting with those he had made for the sinusoidal modes. It was hoped in this way to compensate for possible shifts in threshold criteria during a run through a complete set of phases. Each subject made four such runs.

It should be noted that, above 15 cy/sec, equating the degree of flicker near threshold seems to be a straightforward task, uncomplicated by doubts about the comparability of flickers of different frequency. Under the given conditions, all flickers above about 15 cy/sec appeared to be of the same frequency. This is an effect noted by Bartley in an early paper (*4*).

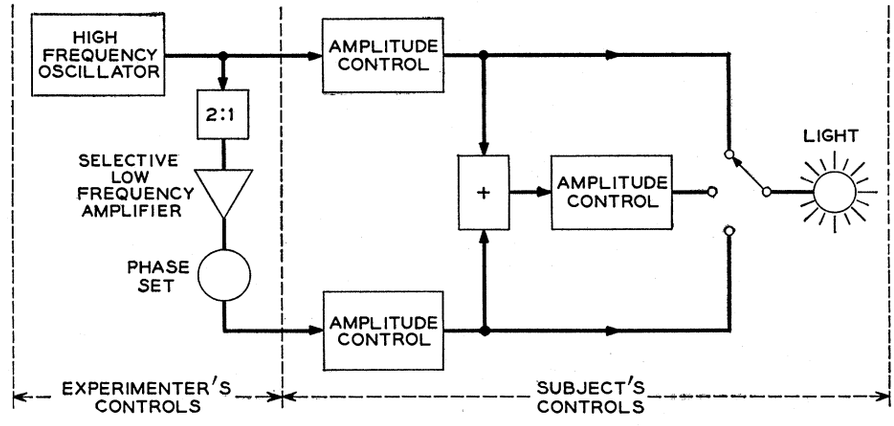
The average settings of five subjects are plotted in Fig. 2, curves *A* and *B*. Each point therefore is the average of 20 settings. Standard deviations are indicated for only one point in each curve. The deviations were very nearly the same at all phases.

When the two flicker components were combined, all observers perceived the flicker more readily. They found it necessary to reduce the component amplitudes by 30 percent, on the average, to bring the percept as near to threshold as either component alone. They also found it necessary to reduce the amplitude by different amounts for different relative phases of the components. Thus, waveform does affect threshold. The reason this was not previously observed (*1*) is that only the fundamental was near threshold amplitude in the waveforms used. This result also conflicts with the conclusion I drew (*3*) from Brown and Forsyth's work (*2*): "as well as one can tell from the data, in the fusion region the observer responds independently to whichever component is above threshold." In Brown and Forsyth's data there were only two or three points for which both components were near threshold. Fortuitously, the positions of these points may have missed indicating the slight depression of threshold to be expected.

The experimental results reported here suggest that the perceived flicker amplitude depends upon the peak-to-peak light amplitude for the flicker waveform. To check this hypothesis, the results are compared in Fig. 2 with the threshold variation expected from changes in the peak-to-peak amplitude as the relative phase of the two components is varied. (The phase angle is defined as the lead of the positive-going zero-crossing of the low-frequency component with respect to that of the high-frequency component, in degrees of the high-frequency cycles.) Curve *A* shows the fraction of either component used to set flicker at threshold for various relative phases of 20 cy/sec sinusoidal flicker combined with 10 cy/sec; curve *B* shows the same for 40 cy/sec combined with 20 cy/sec; curve *C* shows the fractions to be expected were the flicker threshold determined only by the peak-to-peak amplitude of the waveform when the components are combined. It should be noted that curve *C* was computed on the basis of *equal* component amplitudes. Equal amplitudes were assumed because each component had been set at its particular threshold—that is, equal "sensation levels" of the two components are assumed. The fractions by which the combined amplitudes were reduced were almost what the peak-to-peak hypothesis might lead one to expect. However, the phase dependence is quite different from that predicted. It is true that the curve for high frequency (curve *B*) comes fairly close to *C* and does have a rise in the 270° region as predicted, but note that the rise is not significant compared with the indicated standard deviations.

Generally, curve *B* comes closer to *C* than *A* does, and this may indicate that at still higher frequencies the peak-to-peak prediction may be borne out more accurately. To check this, more intense light sources will have to be used.

The form of curve *A* clearly indicates on-versus-off asymmetry in the human flicker detection mechanism. Unlike curve *C*, which has a peak for every 180° of lead of the low-frequency component, curve *A* has a peak every 360°. The waveform of the light intensity modulation is inverted every 180° of phase lead. The 360° periodicity of *A* therefore shows that the peak-to-peak amplitude alone does not determine flicker threshold, but rather that the same waveform may be seen more readily in one polarity than when inverted. Of course, the difference is small, and observable only for wave-



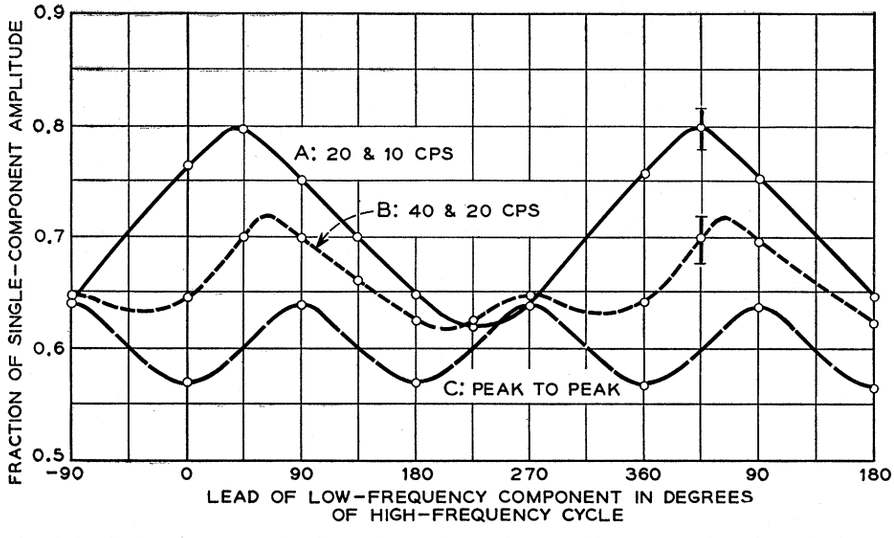


Fig. 1 (top). Apparatus used. Fig. 2 (bottom). Fusion amplitude as a function of phase difference between components.

forms having relatively weak fundamentals.

The information now available provides a fairly precise description of the time sequence of events in the retina during flicker fusion. Under the specific conditions mentioned above, flicker fusion thresholds do depend on waveform, contrary to previous opinion (*1*), and not upon one component alone (*3*, *5*).

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1 February 1960

Is Reserpine Tranquilization Linked to Change in Brain Serotonin or Brain Norepinephrine?

Abstract. Reserpine, when administered to animals stressed by exposure to cold, does not induce sedation or appreciably lower brain serotonin, but markedly lowers brain norepinephrine. Reserpine in cold-exposed hypophysectomized rats elicits sedation and releases both amines equally. The results support the view that the tranquilizing action of reserpine is not related to brain norepinephrine loss but rather to change in the level of brain serotonin.

The tranquilizing action of reserpine, originally linked to the release of brain serotonin, is now often ascribed to the loss of brain norepinephrine. From studies based on bioassay, Kärki and Paasonen (*1*) concluded that Raunescine, in doses which release norepinephrine but not serotonin in the brain, has a sedative effect in rats. But, using fluorimetric methods, we found that various sedative doses of Raunescine lower serotonin and norepinehrine levels to the same extent (*2*). Pletscher *et al.* (*3*), on the basis of studies in mice with two benzoquinolizine derivatives, proposed that the sedative action of reserpine is associated with loss of brain norepinephrine. They reported that in 1 hour the potent tranquilizer, Ro 4-1284, releases more brain norepinephrine than does the weak tranquilizer Ro 4-1398, while the two drugs release serotonin to the same extent. However, we found that whereas in 20 minutes Ro 4-1284 releases much more serotonin than does Ro 4-1398, in 1 hour the difference in serotonin levels disappears because the action of the former compound is brief and brain serotonin forms rapidly (*2*). Thus, the results with Raunescine and the benzoquinolizines do not make it possible to associate sedation with either one of the amines.

Contrary to findings of many other workers are those of Sheppard and Zimmerman (*4*), who reported that the subcutaneous injection of small doses of reserpine (0.1 mg/kg) into female guinea pigs causes in 20 minutes a rise of 75 percent in brain norepinephrine level, and in 2 hours a rise of 45 percent in heart norepinephrine level. After 2 hours they found a small decline in brain serotonin level. These authors measured norepinephrine fluorimetrically by a procedure in which filters are used for isolating the activation and fluorescent light bands. Because of the relatively wide spectral bands of filters, the validity of the values thus obtained is contingent on proof that the method for norepinephrine determination is specific.

This is especially relevant in view of the presence of reserpine and its metabolites in the body. However, no evidence is offered for the specificity of the method. The experiments were repeated in this laboratory (*5*) with a fluorescence spectrometer, which permits the use of narrow spectral bands. With methods of proved specificity we have shown that the administration of 0.1 mg of reserpine per kilogram to female guinea pigs at no time causes a rise in brain or heart norepinephrine levels. Brain levels of norepinephrine and serotonin decline at the same rate and to the same extent.

A study of the phenomenon, noted by Garattini and Valzelli (*6*), that administration of reserpine to cold-exposed rats causes no sedation and no decline in the level of brain serotonin, led us to discover that, in animals subjected to stress, administration of reserpine considerably depletes the amounts of norepinephrine in the brain but does not elicit sedation or appreciably change the content of brain serotonin.

Rats (males, Sprague-Dawley, weighing 150 to 180 gm) after 4 hours' exposure to cold (4°C), were injected intraperitoneally with 1 mg of reserpine per kilogram. The animals were then kept in the cold for an additional 4 hours, during which time they gave no evidence of sedation. The rats were then decapitated, and the brains were analyzed for norepinephrine and serotonin by fluorimetric methods (*7*). As shown in Table 1, the reserpine released considerable amounts of brain norepinephrine but affected brain serotonin levels only slightly. Exposure of rats to cold for 8 hours without reserpine administration resulted in no change in the amine levels. Reserpine given to rats at room temperature (22°C), or to rats exposed only briefly to cold, elicited marked sedation and released both amines. Experiments with rabbits gave similar results.

A close association between the appearance of sedation and the release of brain serotonin was shown by experiments in which rats were exposed to cold for 4 hours, given reserpine, and then brought to room temperature. The levels of brain serotonin then slowly declined, and evidence of sedation appeared only when the serotonin level had declined by about 50 percent.

The possibility that "stress," produced by exposure to cold, prevented the decline in brain serotonin and the sedative action of reserpine was tested by administering the drug to cold-exposed, hypophysectomized rats. Under these circumstances, reserpine elicited sedation and released both amines. Hypophysectomized rats exposed to cold for 8 hours without reserpine showed no change in brain amine levels.

These studies suggest, but do not prove, a causal relation between the release of serotonin and the tranquilizing actions of reserpine. Other lines of evidence also indicate that the sedative action of reserpine is associated with changes in brain serotonin rather than changes in brain norepinephrine. For example, studies from our laboratory show that small doses of Su 5171 (dimethylaminobenzoyl methylreserpate) release relatively little brain serotonin in rabbits; the animals give no evidence of sedation, despite a marked decline in brain norepinephrine (*2*). Finally, recent reports indicate that the norepinephrine loss induced by reserpine does not lower sympathetic discharge from the central sympathetic system (*8*) and may even increase the outflow (*9*).

Table 1. Brain levels of serotonin and norepinephrine (± standard error) in rats exposed to cold stress. The animals were given 1 mg of reserpine per kilogram, intraperitoneally. Figures in parentheses refer to number of experiments. The brains of three animals were pooled in each experiment.

Treatment	Serotonin content (μg/g)	Norepinephrine content (μg/g)	Sedation
None	0.45 ± 0.02 (15)	0.49 ± 0.02 (15)	
Reserpine at 22°C	0.16 ± 0.02 (15)	0.16 ± 0.02 (15)	Yes
Brief (2 min) cold-exposure followed by reserpine at 4°C	0.19 ± 0.02 (4)	0.19 ± 0.03 (9)	Yes
Long (4 hr) cold-exposure followed by reserpine at 4°C	0.36 ± 0.02 (9)	0.23 ± 0.03 (9)	No