ferent familiarization procedures (*4*). Three-month-old infants were exposed for 4½ minutes to a cross or a circle, whichever form was preferred in initial exposure periods when both forms were presented simultaneously. During subsequent periods of exposure to both forms, the infants showed a decrease in fixation of the familiarized form. A greater effect of the familiarization period was shown when the two stimuli differed in color as well as form. No significant effect was shown as a result of exposure to the initially nonpreferred stimulus.

Evidently, incidental visual experiences can be retained by infants over 2 months of age, at least for a short period of time. This satisfies the third prerequisite given above for a possible developmental influence of early visual explorations. To what extent and under what conditions this influence actually occurs are questions for further study. The determination of changes in visual preferences following various types of experience will be useful in such studies, since the technique can be used at an age when other response measures are not available.

ROBERT L. FANTZ
Psychology Department, Western Reserve University, Cleveland, Ohio

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2 September 1964

Crown Gall and Tomatine

I object strenuously to the presumption tacit in the title of the report "Isolation of an antihistaminic principle resembling tomatine from crown gall tumors," by B. A. Kovacs, J. A. Wakkary, L. Goodfriend, and B. Rose (17 April, p. 295), that the principle isolated was intrinsically related to crown gall.

My objection was communicated to Kovacs and in reply he cited, among other facts, the isolation of a presumably similar principle from a variety of oak galls. These are not crown gall and in my opinion weaken rather than strengthen the assumption to which I objected.

In the report only one type of crown gall was cited, that on tomato; the substance isolated, which was not purified, was said to "resemble tomatine," an alkaloid known to be synthesized by healthy tomato plants. Crown gall tissue is an exuberant growth of whichever of the hundreds of possible hosts is involved, and as such may be expected to produce quantities of host-specific metabolites which are not necessarily disease-specific. Identification of the isolated substance with "tomatine" rests on reasonable presumptive grounds. Analogy with similar alkaloids produced in other galls such as those on oak leaves has some basis. The presumption, however, that the principle is intrinsic in crown galls appears to have no basis other than coincidence.

Unless the substance in question can be isolated in identifiable form from tissues of taxonomically unrelated hosts affected by the same disease, in this case crown gall, its demonstration carries no evidence of relation to the disease. The critical experiment by which Stanley established the crystalline nature of tobacco mosaic virus was the isolation of physically identical and biologically active crystals from tobacco and spinach.

This sort of report can only serve to becloud our understanding of the processes of tumefaction exemplified by crown gall.

PHILIP R. WHITE
Jackson Laboratory, Bar Harbor, Maine

17 July 1964

White objects to what he thinks is a tacit presumption that the principle isolated from crown gall tumors, stimulated by infecting tomato stalks with *Agrobacterium tumefaciens*, is a characteristic of crown gall tumors per se. We should like to point out that although no such assumption was made, the fact that the principle is found in large quantities in crown gall indicates that the two must be related but does not necessarily indicate that the principle may not be found elsewhere. Furthermore, we do not think, as does White, that any issue has been beclouded.

It should be noted, as was already pointed out in a personal letter to him, that a similar principle has been found in crown gall tumors of the roots of apple trees, as well as in different forms of oak galls.

We stated in the paper, and would like to reiterate now, that whereas the principle resembled tomatine, it was not identical with it. Consequently, his contention that the principle has nothing to do with crown gall tumors hangs in mid-air.

Finally, since in all the experiments the starting materials used for the isolation of active principle were crown galls of tomato, we do not see how the wording could be changed unless White thinks that crown galls should be called something else.

B. A. KOVACS, J. WAKKARY
L. GOODFRIEND, B. ROSE
Division of Immunochemistry and Allergy, Royal Victoria Hospital, Montreal 2, Canada

16 September 1964

Intrauterine Ring

In his letter concerning the uses of the intrauterine ring for contraceptive purposes (7 Aug., p. 536), Josef Novak presents no facts to support his claim that it produces "adverse effects" in what he calls a "considerable" percentage of cases. Furthermore, it is difficult to believe that there are any figures to support his contention that it is more likely that a couple will conceive while using the intrauterine ring than while using other forms of contraception; yet that is what he is claiming when he says, "There are other more reliable" forms of contraception available. The comparison of reliability need not even include the many pregnancies that occur when couples who have adopted other forms of contraception fail to use them consistently; it need present only the rate of conception of couples using the ring, compared with that for each of the other contraceptive methods. If Novak has figures to support his statement, he should present them to the scientific community.

I question also his claim that this method is not cheap. It does not entail the frequently repeated cost incurred for every other form of contraception except the highly unreliable rhythm method. The total cost for contraception is the cost of the insertion of the ring. In private practice, this fee is not much higher than the fee charged

for prescribing a diaphragm; in public clinics, the total cost to the public is lower, for the ring itself is less expensive than a diaphragm, and there is no cost for spermicidal agents. Obviously, there is some additional cost when a woman decides to have the ring removed so that she may attempt to conceive. Only if she changes her mind in this way as frequently as every third month, however, can the costs even approach the costs of using and then abandoning drugs that prevent ovulation.

Finally, I object to the gratuitous comments Novak makes about how the ring may be presumed to function. As yet no evidence has been accumulated to support his contention that the ring prevents or disturbs nidation but does not prevent fertilization.

EVE JONES
5833 Dorchester Avenue, Chicago, Illinois

22 September 1964

Electroencephalographic Data: Baseline Crossings

In a recent report (*1*) MacIntyre *et al.* describe a method of analyzing electroencephalographic data in terms of baseline crossings, a technique also used in other laboratories. Two important points need to be clarified: (i) the full spectrum of EEG activity is *not* "recorded with equal emphasis given to all durations independent of amplitude"; and (ii) plots of pulses per minute as a function of pulse width, as in their Fig. 2, should be interpreted with caution, taking into account characteristics of the system of analysis.

One characteristic of the system is shown by plotting the *maximum* number of pulses per minute as a function of pulse width. The maximum number of pulses per minute is equal to 30,000 msec divided by the pulse width in msec, assuming that the EEG recording is above the "baseline" 50 percent of the time (depends on discriminator level). Since more pulses per minute are possible at short pulse widths than at long, the plot rises sharply (reciprocal function) at short pulse widths.

When empirical data of mixed frequencies are analyzed, the higher frequencies are favored since they are more likely to cross the baseline, provided they have sufficient amplitude. Thus, many potentially long pulse widths are sacrificed whenever a shorter pulse width occurs first. This results from a fundamental characteristic of the analysis system, namely, that the pulse widths are determined sequentially and are therefore mutually exclusive. This system characteristic may be the source of their report that waves of less than 10 msec "actually comprise 85 percent of the total distribution." The quantity of data having 4- to 20-msec pulse widths would be about 40 percent when computed in terms of percent of maximum possible pulses per minute or in terms of time.

Even more important, expressing the data as percent of maximum possible pulses emphasizes that the sum of these measures over all pulse widths equals 100 percent, provided that all the data fall in one or another of the pulse-width classes. This results from the system characteristic that, given exhaustive classes, the sum of the products of pulse widths and number of pulses equals the total analysis time. Since the area under the curves in this sense is constant, another interpretation of the curves in Fig. 2 is possible. Whenever one part of the curve rises (increase of pulses of a particular width), another part or parts of the curve must fall (decrease of pulses of other widths). The decrease between the "eyes open" and "eyes closed" distributions in the 4- to 20-msec wave widths may result directly from the increase of 36- to 68-msec wave widths, and in this sense may be an artifact of the measuring procedure. Additional support for such an explanation is that the short wave widths were of small amplitude and thus generally could not cross the "baseline" when large-amplitude waves of alpha frequency were in progress during the "eyes closed" condition. Thus, the baseline-crossings technique is not independent of amplitude (with respect to different pulse durations) and the scores in the various wave-width classes are not independent of each other.

The baseline- crossings method may be useful in analyzing EEG data. If it is used, I suggest plotting the results as percent of maximum possible pulses for each wave width, as an aid to avoiding interpretation pitfalls. The need for data reduction in EEG has been met in a variety of ways. We have found another on-line approach (*2*) to be useful in reliably detecting small EEG effects (*3*).

ROBERT M. CHAPMAN
Institute for Behavioral Research and *Walter Reed Army Institute of Research, Washington, D.C. 20012*

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26 June 1964

The assumption of equal emphasis given to all durations independent of amplitude is in reference to analysis in the time domain. Thus, to consider a pulse as made up of a short-duration, small-amplitude width superimposed on a large pulse of long duration has no meaning in the time-domain analysis. The only parameter that is meaningful in this analysis is the time between the successive crossings of the baseline. It is this value which is recorded with equal emphasis regardless of the pulse height between these crossings.

In suggesting plotting the results as percent of maximum possible pulses, Chapman has brought up one of several alternatives that have to do with the choice of presentation of data rather than with the recording. While the reported data were plotted as a histogram of the number of pulses versus pulse width, these data have also been expressed in terms of the total time of analysis occupied by pulses of specific duration (number of pulses multiplied by the average duration) whether or not a change in specific duration is dependent on the total distribution.

Chapman's comment correctly points out that any data-reduction system must be interpreted with close regard to what data are emphasized and what data are eliminated.

WILLIAM J. MACINTYRE
Western Reserve University, Cleveland, Ohio

5 October 1964