

(for example, DBA/2) closely resembled the patterns obtained after turpentine stimulation of haptoglobin in other strains.

The fact that AKR and C3H strains may be stimulated to produce serum haptoglobins by nonspecific agents indicates that the normal deficiency or absence of this protein in these strains is not due to a lack of the genetic information required for haptoglobin synthesis, and suggests the possibility that the transient appearance of haptoglobin in C3H and AKR mice may be a result of unknown environmental stimuli. In contrast, deficiency of liver catalase in the C57BL/6 strain has been shown to be under genetic control (4).

The relation between the formation of spontaneous tumors and haptoglobin levels was studied in AKR and C3H mice. One hundred AKR female mice, born on the same day, were obtained as weanlings and, at age 3 months, were found uniformly to have no demonstrable haptoglobin. Two of 13 mice at age 5 months were found to have low levels of haptoglobin. At age 9½ months, when over 50 percent of the mice had died of leukemia, serum haptoglobin levels were estimated in the remaining 22 mice, which were then killed and autopsied (Table 1). In this group, 10 out of the 22 mice had definite histological evidence of leukemia. The haptoglobin values could be divided into three groups: (i) markedly elevated (> 100 mg of hemoglobin bound per 100 ml), (ii) moderately or slightly elevated (20 to 100 mg

of hemoglobin bound per 100 ml), and (iii) absent (> 15 mg). Of ten mice with markedly elevated serum haptoglobin, seven had definite histologic evidence of leukemia, an increased spleen weight (> 150 mg), and large thymus. Of seven with moderately elevated serum haptoglobin levels, three had definite leukemia. Five animals without demonstrable haptoglobin had no leukemia. There is thus a strong tendency for elevated haptoglobin levels, elevated spleen weights, and positive histological diagnosis for leukemia to occur together.

All animals with leukemia had elevations of serum haptoglobin. On the other hand, seven animals had elevated serum haptoglobin levels, and had not yet developed histologic signs of leukemia. On the presumption that these animals will develop leukemia, the data suggest the possibility that elevation of serum haptoglobin precedes any of the present diagnostic criteria for leukemia in AKR mice.

In contrast to the elevations in serum haptoglobin that occurred when leukemia developed in the AKR mice, haptoglobin levels in C3H mice did not rise even when mammary tumors were pronounced. C3H mice having definite tumors and low or absent haptoglobins could be stimulated by turpentine to produce an elevated level of haptoglobin. It appears, therefore, that with respect to stimulation of haptoglobin synthesis, the two host-tumor situations are unlike.

The data indicate that there is a

notable distinction between the serum haptoglobins of mice and men. In man, differences in types of haptoglobin are striking. Mice seem to differ only with respect to quantitative levels. These differences in haptoglobin levels may serve further to characterize strains of mice.

ANDREW C. PEACOCK

ALBERT H. GELDERMAN

RAY H. RAGLAND, HAROLD A. HOFFMAN
National Cancer Institute,
Bethesda, Maryland 20014

References and Notes

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2. M. F. Jayle and J. Moretti, *Prog. Haematol.* **3**, 342 (1962); C. B. Laurell and C. Grönvall, *Advan. Clin. Chem.* **5**, 135 (1962); C. Lambant, J. Moretti, M. F. Jayle, *Biochim. Biophys. Acta* **97**, 262 (1965).
3. The amount of haptoglobin was estimated from guaiacol-stained electrophoretic separations by using a 6 percent polyacrylamide gel [method of K. G. Queen and A. C. Peacock, *Clin. Chim. Acta* **13**, 47 (1966)]. The lowest level of serum haptoglobin surely detected binds 15 mg of hemoglobin per 100 ml. Subsequently, many haptoglobin levels were determined by the method of P. H. Tarukosi, *Scand. J. Lab. Clin. Invest.* **18**, 80 (1966), and quantitation was estimated from photographs of earlier gels (most of which were negative).
4. W. E. Heston, H. A. Hoffman, M. Rechcigl, Jr., *Genet. Res.* **6**, 387 (1965); M. Rechcigl, Jr., and W. E. Heston, *Biochem. Biophys. Res. Commun.* **27**, 119 (1967).

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Dichoptic Viewing and Temporal Discrimination: An Attempted Replication

Robinson's observation (1) that dichoptic presentation of visual stimuli allows correct discrimination of order at interstimulus separations of only 5 msec is of particular import. No previous investigation has implied such rapid, veridical processing of successive stimuli by humans. If valid, this observation would demand a reorientation of theory regarding the relation of stimulus input to the temporal processing mechanism. It would also follow that dichoptic presentation may be adapted to facilitate other perceptual capabilities.

To test the observation, a replication study was conducted with the use of procedures described by Robinson. A three-channel Scientific Prototype tachistoscope was fitted with stimuli (a square and a triangular luminous patch, each subtending 1 degree of visual arc) and a red circular fixation patch. The placement of the stimuli as well as the luminance were approximately the same as Robinson reported. Opal dif-

Table 1. Serum haptoglobin and autopsy data, AKR mice.

Thymus enlargement	Lymph nodes enlargement	Spleen weight (mg)	Organs with histologic leukemia
<i>Serum haptoglobin markedly elevated</i>			
Great	Great	750	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	670	Thymus, lymph nodes, spleen, liver
Great	Great	610	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	600	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	465	Thymus, lymph nodes, spleen, liver, kidney
Great	Slight	450	Thymus, lymph nodes, spleen, liver, kidney
Great	Normal	130	Thymus
Slight	Slight	150	None
Slight	Slight	150	None
Slight	Normal	120	None
<i>Serum haptoglobin moderately elevated</i>			
Great	Slight	275	Thymus, lymph nodes, spleen
Normal	Normal	100	Thymus, lymph nodes, spleen, liver, kidney
Moderate	Slight	128	Thymus
Slight	Slight	130	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None
<i>Serum haptoglobin not detectable</i>			
Slight	Slight	120	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None

fusing glasses and polarizing sheets also covered the stimuli. Orientation of polarizers at the viewer allowed dichoptic viewing with the square stimulus presented to one eye and the triangular stimulus presented to the other.

The procedure of presenting the stimuli to the subjects differed somewhat in that counterbalancing was incorporated. Half of the presentations were made with square to the right eye and triangle to the left, and the remaining trials in reverse order. Also, half of the subjects began with the square to the left eye and half with the square to the right eye. Eight of the twelve subjects had previous experience serving as subjects in a similar experiment. Nearly all of the subjects were research staff members with advanced academic degrees. Nine were men and three women, with an overall mean age of 33.

Each subject viewed 72 presentations of succession. The square was presented for 10 msec, immediately followed by a variable interstimulus duration of 0, 20, 40, 60, 80, or 100 msec of darkness and then by a 10 msec presentation of the triangle. On half of the trials the sequence was in reverse, that is, triangle-blank-square. Order and interstimulus durations were both randomized in six lists of 12, with each list containing two trials with each magnitude of interstimulus duration and one of these pairs in each order. Three lists of 12 trials were used for each counterbalanced condition.

As in Robinson's experiment, each subject was required to state after each presentation which stimulus was viewed first. All subjects were given preliminary trials to insure that they fully comprehended the task, and no subject failed to understand the instructions by performance on the preliminary trials.

The timers on the control unit of the tachistoscope were checked for accuracy at the factory on the day prior to testing. Claimed accuracy is ± 2 percent with lamp rise and fall times of 0.005 msec.

Results obtained are presented in Fig. 1, which describes the mean values for all subjects. Each mean is the percentage of correct responses for 144 trials at 12 trials per subject. This observation conflicts with Robinson's data

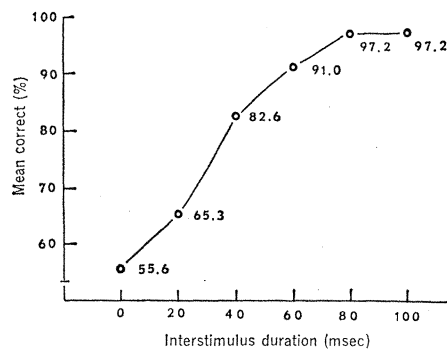


Fig. 1. Replication data with greater number of subjects ($n = 12$) for dichoptic viewing of two successive stimuli separated by a variable interstimulus duration. Duration of stimuli was always 10 msec.

which indicated 100 percent correct response by each of three subjects at only 5 msec interstimulus duration. It also conflicts with the observation that all subjects were able to perceive correct order at 10, 20, and 40 msec interstimulus durations with 100 percent accuracy.

The data afforded by one subject in the present study is of unusual interest. This subject responded correctly on every trial including the 12 trials with zero interstimulus duration (2). None of the remaining 11 subjects were 100 percent correct on the 20 msec interstimulus duration, and only one subject was 100 percent correct on the 40 msec interstimulus duration.

Comparison of mean errors made by presentation of stimuli to right eye or to left eye did not differ significantly. Order of the two sets of 36 trials did not differ significantly in mean errors.

It may be concluded from the present data that dichoptic viewing of successive stimuli does not enhance correct discrimination of successivity to the extent inferred from Robinson's study.

DONALD H. THOR

E. R. Johnstone Training and Research Center, Bordentown, New Jersey 08505

References and Notes

1. D. Robinson, *Science* **156**, 1263 (1967).
2. Since the original study this outstanding subject was retested. His errorless performance could not be replicated when extra caution was taken to avoid any visual or auditory cues that may have occurred due to switching of function-selector control knob during intertrial intervals.
3. I acknowledge the advice and assistance of H. H. Spitz, D. L. Hoats, and E. A. Holden, Jr., of the Johnstone Research Staff.

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Thor's replication (1) of my research in the perception of order (2) provides results in conflict with mine although one of his subjects performed as all three of mine did; that is, he was able to perceive order at interstimulus intervals as brief as 5 msec. His other subjects required greater temporal separations to discriminate the order of presentations. Since Thor and I used essentially the same equipment and since I provided him with a complete description of our apparatus modifications and procedures, it is unlikely that the disparity in our findings is artifactual.

Furthermore, since my earlier publication, other investigators (3), studying the minimum onset asynchrony sufficient for the perception of a delay, report better than chance (60 percent) discriminations at interflash separations as brief as 1 msec with dichoptic presentations. My own research in this area suggests that the variables responsible for the partial inconsistency are practice and individual differences.

Dichoptic viewing is ocularly fatiguing. Sustained fixation is impossible for some subjects and quite difficult for most. Highly trained subjects are those who have not simply been exposed to many dichoptic presentations but who have, as a result, acquired controlled fixation. In the absence of this, images blur, and reports of order degenerate to chance levels. Unpracticed subjects in our studies initially require intervals of 50 to 100 msec; after 2 weeks, about 30 to 50 msec, and, after 2 or 3 more weeks, less than 10 msec. For some subjects, however, practice appears to produce only marginal improvements. It should be noted also that the relative sophistication of subjects is irrelevant to successful discrimination. I have served personally as a subject and have been unable to maintain fixation under dichoptic viewing conditions for more than 1 or 2 minutes.

DANIEL N. ROBINSON

Electronics Research Laboratories, Columbia University, New York 10027

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