Table 1. Linear regression equations and $\Delta p$H/min. for the normal subjects and the two groups of patients who differed significantly from the normals as well as from each other.

| Subjects | $n$ | Hydrolysis rate | Regression equation | $\Delta p$H/min |
|---|---|---|---|---|
| Patients | 10 | Slow | $Y = 7.917 - 0.0075X$ | − 0.0075 |
| Normals | 10 | Normal | $Y = 7.906 - 0.0097X$ | − 0.0097 |
| Patients | 7 | Fast | $Y = 7.922 - 0.0116X$ | − 0.0116 |

drolysis range, it is interesting to note in passing that one is presently considered by the clinical staff to have an organic lesion as indicated by electroencephalographic examination, and five are considered by the clinical staff to have neurotic depressions. Sixteen patients were evaluated clinically as schizophrenic.

These preliminary data do not contradict my general hypothesis that acetylcholine-chloinesterase imbalance may be a biochemical concomitant of the so-called "functional psychoses." A disturbance in enzymatic kinetics which may be reflected in excessive cholinesterase activity or deficient enzyme activity may be responsible for the maladaptive behavior which characterizes those that comprise the schizophrenic syndrome group. Since some pharmacological agents are now available whose effects on the acetylcholine-cholinesterase cycle are well known, experiments will be conducted to determine the behavioral changes that follow pharmacological manipulation of the kinetics of this enzyme system and its substrate. Specifically, it is predicted that marked behavioral changes should accompany the administration of an anticholinesterase—that is, diisopropyl fluorophosphate—to an individual whose hydrolysis rate for acetylcholine is too rapid, as compared with normal values; moreover, the administration of cholinergic blocking agents should produce marked behavioral changes in those individuals who manifest slow hydrolysis of acetylcholine by erythrocyte cholinesterase.

Although several investigators have previously focused attention on the role of acetylcholine-cholinesterase balance in schizophrenia and manic depressive psychosis, one may infer from their work that the hypothesis tested was limited to the role of deficient acetylcholine levels. Thus Fiamberti (*9*) has reported improvement in some schizophrenic subjects when intravenous injections of acetylcholine were administered. Rountree et al. (*10*) increased acetylcholine levels by administering diisopropyl fluorophosphate to schizophrenics and manic depressives without noting significant improvement in all subjects. The findings of the present study suggest that the administration of anticholinesterases or parasympathomimetic drugs could be effective only for those patients who manifested a rapid rate of hydrolysis of acetylcholine by the erythrocyte cholinesterase. If we can assume that the slopes obtained from the samples are reliable estimates of regression for populations, then we can deduce that, approximately, only half of a functionally psychotic population, selected at random, could be favorably affected by the pharmacological stimulation of a pronounced cholinergic effect. The remaining half, manifesting slow hydrolysis, would require cholinergic blocking agents.

It is not necessary, at this time, to consider whether or not this biochemical mechanism is the invariable concomitant of the functional psychoses. The next step requires that studies be undertaken to determine whether predictable behavioral changes result from systematic variations of enzymatic kinetics produced by appropriate pharmacological agents.

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**References and Notes**

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17 April 1958

## Measurement of Observing Responses in Human Monitoring

The variables involved in visual monitoring and vigilance tasks need description and analysis, especially the observation, detection, and control response variables. In the usual study, control responses are measured, and then detection of a signal and observation of the display are inferred. Recently, however, Holland (*1*) has shown that direct measures of observing responses can be obtained. His subjects worked in a dark room and were required to detect and report deflections of a pointer on a dial. The dial could be seen only when the subject illuminated it for a short time by depressing a key. Each key depression was defined as an observing response. A second key was depressed by the subject to record signal detections and to reset the pointer. Holland found that, under fixed-interval schedules of pointer deflections, after each detection, observing responses ceased for a time and then resumed in an accelerated manner until the next detection. This resulted in scallop-shaped records of the subject's observing rate which were analogous to those obtained in other operant conditioning experiments with infrahuman subjects (*2*).

Generally speaking, observing responses refer to the relation, through time, between sense-organ orientation and displays. The visual sense is most commonly employed by humans in monitoring tasks. While Holland's technique insured that the observing response permitted observation of the display, the depression of a key may or may not be the same as actual head and eye movements involved in monitoring tasks. The experiment described in this report was designed to obtain a measure of observing responses which, while not eye movements, is assumed to be highly correlated with them. These measures were compared with those obtained by Holland.

Five male employees of the Research and Development Division of Electric Boat served as subjects, and each was given ten 30-minute sessions on a fixed, 1-minute interval schedule. As in Holland's study, the subjects worked in a dark room and had to detect deflections of a pointer from a null position. Detection was recorded and the pointer was reset when the subject pushed a button; the pointer remained deflected until the button was pushed. A continuous light source fixed atop elastic headstraps worn by the subject permitted him to observe the dial and pointer. The presence of the light on the dial was defined as an observing response. These observing responses can be thought of not as movements but as fixations of "holding responses" where the light is held on the dial. The light source was a 2.25-v flashlight bulb (lighted by a 1.5-v battery) fixed in the rear of a tube 10 in. long and 3/4 in. in diameter. This tube was fixed to the elastic headstraps. At a normal viewing distance of 28 in., the circle of light was 3 in. in diameter and had an intensity of 3 ft-ca.

Before each session the subject sat in a comfortable position with his eyes on the dial. The tube was then adjusted by the experimenter so that the light fell on the dial behind which was a light-sensitive germanium diode. When the light fell on the dial, a recording pen was deflected. The pointer deflections and resets were also recorded.

Each subject was instructed to detect as many signals as he could and to reset the pointer as quickly as possible. At the end of each session each subject was told the number of signals he had detected and his reset times. No mention was made of the experimenter's interest in the observing responses, and subjects were told only that they could use the light to illuminate the dial.

Inspection of the records of the tenth session shows marked consistency of observing behavior within subjects but great differences between subjects. Data showing a portion of each subject's responses on session 10 are presented in Fig. 1.

The magnitude of deflection away from the "no-response" base line depended upon the proximity of the light to the dial, and it can be seen that there was both intra- and intersubject variability.

Two of the subjects, *S*-2 and *S*-3, exhibited behavior much like that reported by Holland—that is, the observing responses increased as signal time approached. The record of one subject, *S*-3, corresponds almost exactly to those presented by Holland.

The observing responses of the other three subjects, *S*-1, *S*-4, and *S*-5, were relatively continuous and unlike those obtained by Holland. This was particularly true of *S*-1.

While Holland found that the temporal manner of signal presentation controlled the observing behavior of subjects, the results of the present experiment indicate that this behavior differed between subjects under identical experimental conditions. Some subjects moved their head and eyes away from the display immediately after a signal and then fixed their eyes on the display again as the signal time approached. Other subjects apparently fixed their eyes on the display in a fairly continuous manner. The differences from Holland's results may be due to the measurement of a different response or to differences between subjects. It is also possible that the relatively continuous observing shown by *S*-1, *S*-4, and *S*-5 was due to the ease of the observing response. It has been shown (*3*) that there is no scallop in the observing rate curves for fixed-interval schedules when Holland's technique is used and when the key tensions are very light. However, the delays after detection and before responding increase with key tension.

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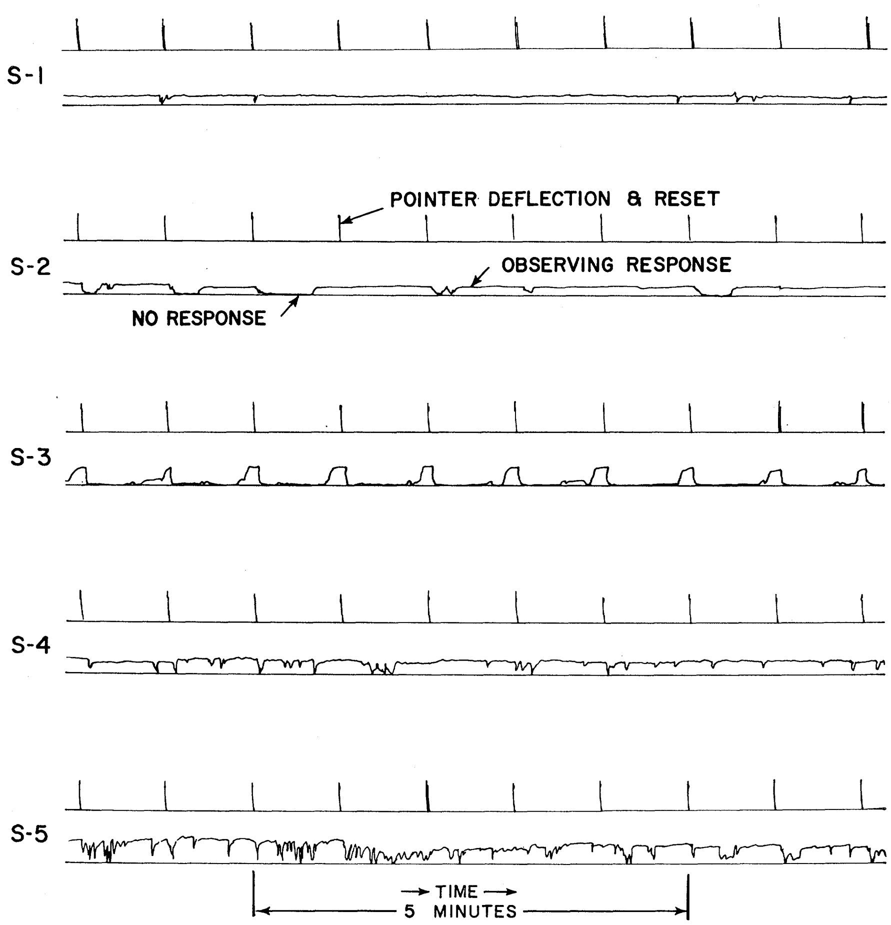


Fig. 1. Characteristic response records of each subject for a 1-minute fixed-interval schedule of pointer deflections. The records were obtained on the last (tenth) session.

**References and Notes**

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6 March 1958

## Common Strontium Content of the Human Skeleton

The geochemical and biogeochemical behavior of the element strontium is important in understanding the movement of fission-product strontium-90 into man (*1*). Several investigators (*2, 3*) have analyzed human bone from different locations for strontium. The availability of a large collection of bones from the study of world-wide fallout of strontium-90 made convenient the examination of this parameter in greater detail. This report (*4*) is concerned with (i) the distribution of strontium among the different bones in an individual skeleton, (ii) the distribution of strontium in the population of a single city, and (iii) the extension of information on geographical variation. Samples consisted of a variety of bones from eleven individuals, whole-skeleton ash from 133 New York City cadavers, and composites from 16 localities, each representing equal weights of bone ash from 4 to 38 individuals.

The analyses were performed by an emission spectrographic technique modified from that of Turekian and Kulp (*2*). The standards used to define the working curves were actual samples of bone ash which were analyzed by the isotope dilution method (accurate to within 5 percent). All samples were run in duplicate and are reported as parts of strontium per million. The reproducibility of these analyses is estimated to be about ± 10 percent.

The average strontium content of additional samples from previously investigated areas (*2*) was found to be about 30 percent lower. In order to check this discrepancy, some of the original samples were reanalyzed by the present method. The new analyses were also about 30 percent lower in each case. Synthetic standards similar to those used by Turekian and Kulp (*2*) were analyzed, using the present working curve defined by isotope dilution analyses of bone ash. The results indicate that a matrix dif-