dure could have given additional information about the ability of the subject to focus his attention. The way in which failures to respond are treated will generally have a considerable effect on computed values of the d' statistic.

Finally, Rappaport *et al.* indicate that "support was found . . . for the hypothesis that nonmedicated nonparanoid schizophrenic patients perform as efficiently as normal subjects under the difficult S/N [signal-to-noise] condition . . ." and, presumably on the basis of this finding, state in their abstract that "the primary deficit in information processing in nonparanoid schizophrenics may be related primarily to their hypersensitivity to sensory stimuli. . . ." Such a conclusion is consistent with the theory of one of the authors, Silverman (*3*), but does not seem to be borne out by their data. The fact that in the difficult signal-detection condition nonmedicated nonparanoid schizophrenics were found to be slightly (though not significantly) *hyposentitive* does not seem to provide very strong support for the interpretation that they are *hypersensitive* under such conditions.

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2. As is discussed by D. M. Green and J. A. Swets [*Signal Detection Theory and Psychophysics* (Wiley, New York, 1966)], estimates of the percentage of correct responses made can be obtained from d' values. A useful rule of thumb is that (except for percentages very close to chance or to 100) a 1-db change in signal level will lead to a 5 percent change in correct responses.
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Emmerich and Levine state that "the patients who received different dosages [of medication] also differed on whatever clinical variables the ward physician used to determine dosages." We would dispute this point, since each patient was interviewed and rated on the day of testing. Consequently, our assessment of clinical condition was considerably more current than the one on which the ward physician based his medication order. Furthermore, the rating scales that were used incorporated a wide range of clinical variables. The modified Brief Psychiatric Rating Scale (*1*) used contains 21 separate clinical items. From these a composite measure of overall mental disturbance was obtained. We found that at zero dosage and moderate drug dosages there were no significant differences in this measure between paranoid and nonparanoid schizophrenics. At the heaviest dosage paranoid schizophrenics showed a greater overall mental disturbance score than did nonparanoids, yet their d' scores were closest together—quite the opposite of what might have been expected if severity of mental disturbance were the major factor affecting their signal detection performance.

They also comment that there were no direct statistically significant effects within either group related to phenothiazine dosage. It is true that we based part of our interpretations on indirect evidence of a differential effect of chlorpromazine on paranoid and nonparanoid schizophrenics—the fact that with increasing dosage nonparanoids showed a decrease in signal detection performance while paranoids showed an improvement in performance. This led to the finding that signficant differences between the two groups of schizophrenics disappeared with increased medication, and this result could not be accounted for by differences in the clinical pathology displayed by each group. In fact, with the paranoids showing greater pathology than nonparanoids at the highest dosage level one would expect them to perform significantly worse. The fact that they did not makes it reasonable to suspect that medication enhances their ability to attend to and to detect auditory signals. Further, we have other evidence that, under four other signal-to-noise (S/N) conditions interspersed between the easy and difficult S/N conditions reported, the same results occurred consistently.

Emmerich and Levine's retrospective suggestion that both a "yes" and a "no" response button could have helped distinguish a true lapse of attention from an intentional "no" response has merit. It would not have been compatible with our methodological design, however. We would not have been able to calculate other desired signal detection measures had we employed a two-button method. For example, we were interested in calculating each individual's normally occurring response propensity in order to determine whether schizophrenics underrespond or overrespond compared to normals. These results have been reported (*2*).

Finally we do not indicate in our report that the data directly reflect hypersensitivity of nonparanoid schizophrenics to auditory stimuli. In fact our hypothesis was quite conservative inasmuch as we stated (*3*) that we expected "nonparanoid schizophrenics would perform at least as well as normal subjects" where signals were difficult to detect. The hypersensitivity hypothesis has been put forward by Silverman (*4*) and was based upon averaged evoked potential data, which need not necessarily correlate highly with psychomotor response data such as we reported where in the latter situation attentional, cognitive, and motivational considerations can influence subject output. The hypersensitivity hypothesis was used primarily to predict a differential response to phenothiazine medication by nonparanoid and paranoid schizophrenics and this it appeared to do.

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Fibrogenic Effect of Alcohol in Rat Liver: Role of Diet

Feinman and Lieber (*1*), in asserting a direct fibrogenic effect of alcohol on the livers of rats and baboons, make no reference to reports that show how diet can influence these results. Lillie *et al.* (*2*) reported that the cirrhosis induced in rats fed diets low in protein and choline was facilitated when the drinking water was substituted by a 20 percent ethanol solution. This type of alcohol-associated dietary cirrhosis was not only successfully prevented (*3*), but was also effectively reverted (*4*) by the inclusion of choline, methionine, and casein, singly or in combination. Best *et al.* (*5*) showed that, under carefully controlled dietary conditions, rats consuming a 15 percent aqueous solution of alcohol in place of water developed histological evidence of hepatofibrosis. This occurred when the alcohol calories were superimposed on a diet that contained lipotropic factors only sufficient to prevent liver damage when the diet alone was fed. With the addition of alcohol calories (27 percent of total caloric intake), fatty and fibrotic livers developed.

Neither histologically evident fibrosis nor abnormal accumulation of fat (determined by biochemically and histological methods) developed when additional choline, methionine, or casein was added to compensate for the additional calories derived from alcohol. Furthermore, when the alcohol-derived calories were replaced by isocaloric amounts of sucrose, fatty livers and hepatofibrosis resulted; but when additional lipotropic factors were given to these sucrose-fed animals, the livers remained normal.

We showed that not only hepatofibrosis but true cirrhosis (hepatofibrosis plus nodular regeneration of parenchyma and distortion of architecture) developed in rats consuming 37 percent of their caloric intake as alcohol or sucrose for 7 months, even though the basal diet alone did not produce liver damage (*6*). The addition of lipotropic factors and vitamins protected the liver against the alcohol or sucrose caloric load. In these experiments, cirrhosis or hepatic normality was documented by light and electron microscopy and by measurements of hydroxyproline in the alkali-soluble and -insoluble hepatic collagen fractions.

Although the results and interpretations of Feinman and Lieber were derived from experiments using totally liquid diets, we showed that when the diet provided abundant amounts of the protective factors (choline, protein, vitamin B_{12}, and folacin), previously cirrhotic rats regained completely all measured aspects of hepatic function and hepatic architecture reverted almost to normal despite the consumption of a liquid diet containing 36 percent of total calories as alcohol (*7*). The physiological and histological results were confirmed by measurements of hepatic collagen fractions. Similar results were obtained in cirrhotic rats when a sweetened alcohol solution in water was offered separately from the solid, adequately supplemented diet, even when the alcohol-derived calories were 50 percent of the total caloric intake (*8*).

We suspect that the animal diets used by Feinman and Lieber were not adequate to protect the animal livers from the caloric burden imposed by alcohol.

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It has been shown in a variety of species that the effects upon the liver imposed by ethanol are distinct from those arising from other dietary constituents or "caloric substitutes." Ethanol, as compared to isocaloric amounts of carbohydrates in diets of humans, causes hepatic fat accumulation and striking ultrastructural changes including marked alterations of the mitochondria; these changes occur despite massive dietary supplementation with choline, minerals, vitamins, and protein. These effects could be demonstrated whether diets were high or low in fat or high or normal in protein, and whether ethanol was given in addition to the diet or as isocaloric substitution for carbohydrates (*1*).

The lack of effect of choline in humans is not surprising in view of the resistance to choline deficiency found in man and other primates as compared to the rat; this resistance is possibly related to differences in hepatic choline oxidase activity (*2*). In the rat, Porta *et al.* (*3*) confirmed the steatogenic effect of alcohol that we described in that species (*4*); in this experiment they compared alcohol to isocaloric carbohydrate without the confounding simultaneous substitution of other dietary constituents. Even in the rat, choline afforded only partial protection against steatosis when ethanol was given for long periods (*5*) and no protection at all when one large dose of ethanol was given (*6*), a result confirmed by Hartroft *et al.* (*7*).

A second important consequence of substituting dietary alcohol calories for carbohydrate calories is the alteration in enzymic complement of hepatic endoplasmic reticulum in rats, baboons, and humans and the associated changes in drug metabolism (*8*). Finally, we reported (*9*) that when alcohol was isocalorically substituted for carbohydrates in otherwise adequate diets, hepatic collagen metabolism was significantly affected in rats and baboons. Collagen accumulated in the liver, and the evidence indicated that increased collagen synthesis was at least part of the mechanism responsible for this effect. The rats were fed liquid diets, but the baboons were given solid food with amounts of choline well above the requirement for that species (*10*).

We not only appreciate that dietary intake must be adequate to maintain normal liver function but have contributed to the clarification of the role of dietary fat in the development of alcohol liver injury both in man and rats (*11*), and to that of protein and choline, the latter of course in the rat (*12*). However, there are no diets known, no matter how superb by traditional nutritional criteria, that are "adequate" enough to fully protect the liver against the distinct effects of alcohol we have enumerated.

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