ing the above derivations, each neuron in the optic nerve provides one independent sample over unit time τ with stochastic signal properties common to the ensemble of visual afferent neurons. In the case of the rats in my experiments, where sampling times on C_1 and C_2 are equal, the difference of magnitude in the sample space for contralateral stimulation (through C_1) compared to ipsilateral stimulation (through C_2) results from the difference in the number of neurons in the two afferent channels, and is equivalent to a difference of total sampling time between T_1 and T_2 in the equation for the coherent detector. The unit signal-to-noise ratio (S/N) is a common parameter for each of all neurons in the ensemble.

Demonstration that the brain functions as a parallel coherent detector carries several important implications. (i) It lends impressive support to the proposed concept of the neuronal collective as a basic neuronal process for communications in the networks of the brain; this follows from the definition of the neuronal collective as a subset of neurons characterized by a temporally coherent discharge pattern (*4*). (ii) Only in a coherent detector, does a change in mean output depend upon the signal value alone and the variance of the output on the noise value alone; thus a response threshold point can be set for the expected value of a signal independent of noise (*2*). (iii) Evolution has provided at least the mammalian brain with the most efficient stochastic signal detection scheme known.

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3. In our experimental series, stimulus intensity was 11 lu/m^2 (within the range of normal illumination for rats); a standard stimulus repetition rate of 16 flashes per second is used as a matter of convenience to maintain comparability with other experiments involving human subjects. In the latter experiments, this repetition rate is presented since it is a frequency range that elicits good discrete responses from the brain yet avoids confounding the visual evoked response with changes in the fundamental or second harmonic of normal brain alpha frequency. In the course of developing the standard experimental technique, other flash and filter frequencies were tested to ensure that the brain processes of interest were not uniquely associated with a particular stimulus repetition rate [for example, A. Trehub, *Electroencephalogr. Clin. Neurophysiol.* **19**, 182 (1965).] Other experimental work with our standard stimulation frequency has yielded high positive correlations between signal detection efficiency and filtered brain output, has confirmed previous findings regarding the modulation of bioelectric output in the brain, and has related very closely to differential attack behavior described in completely independent work [J. Isgur and A. Trehub, *Electroencephalogr. Clin. Neurophysiol.* **31**, 96 (1971); A. Trehub, *ibid.* **30**, 113 (1971); R. Bandler and J. P. Flynn, *Science* **171**, 817 (1971); A. Trehub, *ibid.* **173**, 1041 (1971)]. The information presented above bears on the question of whether the present derivations concerning signal-to-noise ratio and mode of detection in the brain might be unique to the stimulus repetition rate with my standard technique. The range of implication and generality of previous findings with this technique suggest that the present conclusions are not limited to a particular frequency of stimulation.
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Phenothiazine Effects on Auditory Signal Detection in Paranoid and Nonparanoid Schizophrenics

Abstract. *The differential effects of phenothiazine medication on auditory signal detection performance were compared in two types of schizophrenic subjects and in normal subjects. With increasing phenothiazine dosage a decrease in efficiency of signal detection performance occurred among nonparanoid schizophrenics and an increase in efficiency occurred among paranoid schizophrenics. These and related findings were interpreted in terms of differences in neuropsychological response and information processing characteristics in the two types of schizophrenics. The primary deficit in information processing in nonparanoid schizophrenics may be related primarily to their hypersensitivity to sensory stimuli, whereas in paranoids it may be related primarily to their impaired focusing of attention. Phenothiazines appear to decrease sensitivity to stimuli in nonparanoids but increase the ability to focus attention in paranoids. The possibility of treatment regimens which take into account the differential effects of phenothiazine medication was suggested.*

Among normal and emotionally disturbed human subjects and among animals individual differences have been noted in response to stimuli of different intensities (*1*, *2*). It also has been observed that drugs of the phenothiazine class, so commonly used in the treatment of severe emotional disturbances, reduce both sensory sensitivity and central nervous system hyperarousal (*2*, *3*). The above findings have been reported for visual and gustatory stimuli. We now report an examination of the effects of different dosages of phenothiazine medication on the ability of paranoid and nonparanoid schizophrenics to detect auditory signals under different signal-to-noise (S/N) conditions. It has been hypothesized that these two types of schizophrenics modulate sensory stimulation in rather different ways (*4*, *5*). The acute paranoid, who scans his environment extensively and responds to many ordinarily irrelevant stimuli, appears to have a primary difficulty in focusing attention. He appears "wide open" to extraneous stimuli. It has been reported that phenothiazine medications significantly reduce the range of environmental stimuli to which the paranoid schizophrenic responds (*5*). The acute nonparanoid schizophrenic, on the other hand, does not extensively scan his environment and is therefore not as overloaded by irrelevant peripheral cues. It has been reported that the sensory peculiarity of the nonparanoid schizophrenic stems from his hypersensitivity to stimuli of low and ordinary intensities and from his attenuated response to very strong stimulation (*2*, *6*). Phenothiazines are reported to reduce significantly his sensitivity (*5*).

It was hypothesized that, if a signal detection is used to measure sensory responsiveness (d'), increased dosages of phenothiazine medication would be associated with opposite changes in d' in paranoid and nonparanoid schizophrenics (*7*, *8*). For the nonparanoid, an increased dosage was expected to impair sensitivity to stimuli and hence lower d'; in paranoids it was expected to improve ability to focus attention. It also was hypothesized that, without medication and under conditions where auditory signals were difficult to detect (low S/N ratio), nonparanoid schizophrenics would perform at least as well as normal subjects. With medication nonparanoids should perform less efficiently than normal subjects. Under S/N conditions where signals were of higher intensity nonparanoid schizophrenics, either on or off phenothiazine medication, would be expected to perform less efficiently than normals. Paranoid schizophrenics would be expected to perform consistently worse than nor-

mals under the difficult S/N condition, especially without phenothiazine medication (*6*).

The signals to be detected were different decibel levels of a 1000-hz tone of 150-msec duration, presented through Permoflux earphones (model PDR-15M). Each time a subject heard a tone he was instructed to press the microswitch he held in his hand. A tone could appear every 2 seconds. Its occurrence, however, was determined randomly, and the probability of its occurrence during each 2-second interval was 0.5. Analyses of responses were made for conditions where the S/N ratios were −17 and −22 db. Signals were presented against a background of continuous white noise.

The order in which the S/N conditions were presented was randomized. At the end of testing each subject had had the opportunity to respond to 250 signal-plus-noise presentations and to approximately 250 intervals of noise only under each S/N condition.

At the beginning of each testing session several signals were presented consecutively until the subject made about eight successive button presses. Thereupon the experimenter placed the stimulus apparatus into the random presentation mode. The use of this procedure ensured that at the outset the subject was attending and responding as required. The subject was also instructed to observe three small lights mounted at approximately eye level on the wall directly in front of him. He was told that a white light would flash during each 2-second interval to alert him to attend and listen for a tone. This flash lasted 200 msec and occurred simultaneously with the tone interval whether or not a tone was present. He was told that if a tone appeared and he pressed the switch, a green light would flash immediately, indicating he had made a correct response. On the other hand if he had made an incorrect choice, a red light would flash. There were two incorrect choices: making a response when there was no tone (a commission error) and not making a response when a tone was present (an omission error).

All tests were made while a subject sat upright in a comfortable recliner type chair inside an IAC (Industrial Acoustics Company) acoustical room. Before an initial orientation and practice run, an audiometric examination was given to eliminate any subject with hearing deficits (that is, if he showed more than a 20-db decrease at either 500, 1000, or 2000 hz).

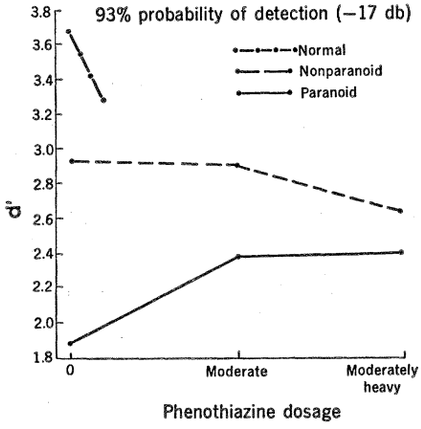

Fig. 1. Sensory responsiveness (d') as a function of dosage at −17 db. The terms moderate and moderately heavy refer to phenothiazine dosages equivalent to 100 to 300 mg and 400 to 800 mg of chlorpromazine, respectively. Normal subjects on medication received 50 mg of chlorpromazine.

All schizophrenic subjects were drawn from the patient population at Agnews State Hospital. A patient was classified as a paranoid schizophrenic on the basis of his having one or more of the following characteristics: delusions of persecution, delusions of grandeur, ideas of reference, plus two or more of the following characteristics: hallucinations; autistic or unrealistic thinking; unpredictable behavior; fairly constant attitude of hostility or aggression; excessive religiosity with or without delusions of persecution; expanded delusional system of omnipotence, genius, or special ability; or systematized hypochondriacal state. Schizophrenic patients not evidencing these characteristics were classified as nonparanoid. Severity of patient pathology was assessed by the Brief Psychiatric Rating Scale (*9*) before testing.

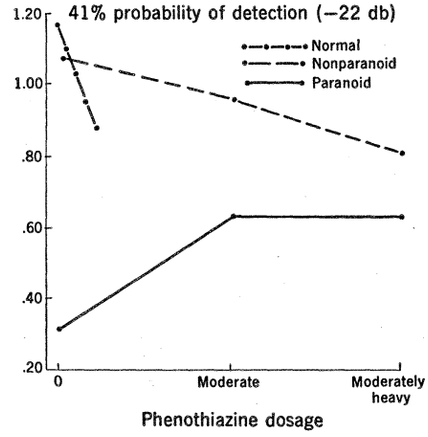

Fig. 2. Sensory responsiveness (d') as a function of dosage at −22 db. The terms moderate and moderately heavy refer to phenothiazine dosages equivalent to 100 to 300 mg and 400 to 800 mg of chlorpromazine. Normals on medication received 50 mg of chlorpromazine.

Paranoid (PA) and nonparanoid (NP) patients' signal detection data were grouped in terms of three levels of phenothiazine medication: (i) zero medication (7 PA, 9 NP); (ii) moderate medication, the equivalent of 100 to 300 mg of chlorpromazine (5 PA, 9 NP); and (iii) moderately heavy medication, the equivalent of 400 to 800 mg of chlorpromazine (17 PA, 15 NP). The actual medications administered were chlorpromazine, trifluoperazine, and thioridazine. The dosage for each patient had been determined by the ward physician, and was based on clinical impressions of the patient's condition. Each patient had been on medication at least a week.

Among the 22 paranoid patients on medication (7 of whom were tested when not on medication as well) there were 10 males and 12 females whose ages ranged from 21 to 58 with a median of 33 years. Sixteen of these patients were hospitalized for less than 6 months, six for more. Among the 24 nonparanoid patients on medication (nine of whom were tested off medication) there were 10 males and 14 females whose ages ranged from 20 to 58 with a median of 29 years; 21 patients were hospitalized for less than 6 months, three for more. All patients had received at least a high school education, except for one in each group who had not.

For patients who could be tested both on and off medication, the drug sequence was randomized. Patients who were tested first on drugs were required to wait up to 3 weeks while off drugs before they were retested. Their urines were examined weekly for phenothiazine metabolites by the FPN test (*10*). Subjects were tested before the 3-week period if the FPN test was negative. Patients who were tested first when they were not taking drugs were retested a week later when they were taking drugs. For purposes of comparison, data obtained from normal subjects tested off and on medication (chlorpromazine, 50 mg administered once) were used.

Among the nine normals tested both on and off medication (a total of 16 were tested off medication) there were eight males and one female whose ages ranged from 20 to 44 years, the median

being 26 years. All had at least some college education. These were selected from hospital and research staff.

The measure d' is used to indicate signal detection efficiency. Its theoretical origin is described by Swets *et al.* (*7*) and by Swets and Green (*8*). This measure has been used to make inferences regarding the sensitivity of peripheral and central sensory mechanisms for detecting and responding to stimuli independently of such factors as the set, motivation, and attitude of the subject. It can be obtained from published tables provided that the conditional probabilities of responding when signal and noise are present and when noise alone is present are known.

The relation between d' and phenothiazine dose is shown in Figs. 1 and 2 for the "easy" and "difficult" signal detection conditions, respectively. Specific means, standard deviations, and numbers of subjects are shown in Table 1. In the easy condition, normal subjects at the −17-db level respond correctly 93 percent of the time (based on a measure of rights minus wrongs). In the difficult condition, normal subjects at the −22-db level respond correctly 41 percent of the time.

As was predicted, nonparanoid schizophrenics showed a decrease in d' with each increase in phenothiazine medication. In contrast, paranoid schizophrenics showed an increase in d' with each increase in phenothiazine medication. At the zero dose nonparanoid subjects showed significantly better signal detection performance than paranoid subjects at both −17 and −22 db. (For −17 db, $t = 2.017$, $P < .05$; for −22 db, $t = 2.537$, $P < .02$.) In comparison there were no significant differences at moderate and moderately heavy doses. There were no significant relations between severity of mental pathology in either group of schizophrenics and d'.

Nonmedicated normals evidenced a significantly higher d' score than nonmedicated nonparanoids at −17 db ($P < .01$, t-test). At −22 db, however, there was no significant difference between normals and nonparanoids when neither were on medication. Medicated nonparanoids performed significantly worse than nonmedicated normals under both S/N conditions (at least ($P <$ .05 in all comparisons except one, namely at −22 db for nonparanoids receiving only moderate medication). However, between normal subjects and paranoids (whether medicated or not) there was a significant difference under both S/N conditions. Paranoids showed greater impairment in signal detection performance (at least $P < .01$ in all comparisons). Among normal subjects no consistent overall drug effect was observed.

Table 1. Effects of phenothiazine dosage on signal detection performance (d') in nonparanoid and paranoid schizophrenic patients and in normal subjects.

Drug dosage	Detection performance (d')								
	Paranoid			Nonparanoid			Normal		
	No.	M	S.D.	No.	M	S.D.	No.	M	S.D.
	−17 db S/N condition (easy)								
None	7	1.879	0.892	9	2.934	1.031	16	3.759	0.434
Moderate*	5	2.374	0.963	9	2.896	1.341	9	3.261*	0.806
Moderately heavy†	17	2.414	1.112	15	2.626	1.140	—	—	—
	−22 db S/N condition (difficult)								
None	7	0.319	0.553	9	1.084	0.567	16	1.167	0.275
Moderate*	5	0.632	0.526	9	0.962	0.650	9	0.889*	0.267
Moderately heavy†	17	0.626	0.352	15	0.810	0.438	—	—	—

* The equivalent of 100 to 300 mg of chlorpromazine for patients and 50 mg for normal subjects.
† The equivalent of 400 to 800 mg of chlorpromazine.

Our findings support the hypothesis that phenothiazines have opposite effects on signal detection performance in these two types of schizophrenics. Support was found also for the hypothesis that nonmedicated nonparanoid schizophrenic patients perform as efficiently as normal subjects under the difficult S/N condition and more poorly under the easy S/N condition. This is in accord with the interpretations that nonparanoid schizophrenics are at least as sensitive as normal subjects under low stimulus intensity conditions and that under relatively strong stimulus intensity conditions, they "tune out" or attenuate the impact of incoming stimuli. Their showing a decrement in auditory signal detection ability when under the influence of phenothiazine medication is consistent with other sensory findings (*11*). Finally, the trend toward improvement in paranoid subjects with phenothiazine medication is consistent with the interpretation that phenothiazines enhance the ability of some schizophrenics to focus attention.

These differences in neuropsychological response characteristics and in responsiveness to phenothiazine medication would appear to have implications for treatment. Studies by Goldstein and others have shown that certain acutely paranoid patients when treated with phenothiazine medication and certain acutely nonparanoids *not* treated with phenothiazines show lessened thought disorder and improved focal attention (*12*). These findings and those reported here and by others support the idea that improved patient treatment regimens may emerge by selectively medicating certain schizophrenic patients and not medicating others (*13*).

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