References and Notes

1. C. H. Park, D. E. Bergsagel, E. A. McCulloch, *J. Nat. Cancer Inst.* **46**, 411 (1971).
2. D. H. Pluznik and L. Sachs, *J. Cell. Comp. Physiol.* **66**, 319 (1965).
3. T. R. Bradley and D. Metcalf, *Aust. J. Exp. Biol. Med. Sci.* **44**, 287 (1966).
4. S. Abrahams, J. E. Till, E. A. McCulloch, L. Siminovitch, *Cell Tissue Kinet.* **1**, 255 (1968).
5. Adj. PC-5, in the 97th transplant generation, was obtained in ascitic form from Dr. Michael Potter, National Institutes of Health. In our laboratory, it was adapted for growth in the spleen and has been transplanted fortnightly by the intravenous injection of 10^6 to 10^7 tumor cells. The present experiments were carried out with cells from intravenous transplant generations 107 to 111. Dr. Potter also supplied us with additional plasmacytoma lines, MOPC 104E and MOPC 46B, which had been carried continuously by subcutaneous passage. These two tumors are maintained at our laboratory by subcutaneous passage. Plasmacytoma cell suspensions were prepared from the spleens or subcutaneous tumors of mice given previous injections of plasmacytoma cells by mincing with scissors and washing through a fine wire mesh screen with culture medium.
6. C. P. Stanners, G. L. Eliceiri, H. Green, *Nature New Biol.* **230**, 52 (1971).
7. Purchased from Philadelphia Blood Center, Philadelphia, Pa.
8. Purchased from General Biochemicals, Chagrin Falls, Ohio.
9. V. Demole, *Biochem. J.* **28**, 770 (1934).
10. F. J. Yourga, W. B. Esselen, Jr., C. R. Fellers, *Food Res.* **9**, 188 (1944).
11. J. J. Burns, H. M. Fullmer, P. G. Dayton, *Proc. Soc. Exp. Biol. Med.* **101**, 46 (1959).
12. S. S. Zilva, *Biochem. J.* **29**, 1612 (1935); P. G. Dayton and J. J. Burns, *J. Biol. Chem.* **231**, 85 (1958).
13. Purchased from J. T. Baker, Phillipsburg, N.J.
14. Obtained through the courtesy of H. J. Wehner of Hoffmann-La Roche Ltd., Montreal, Canada.
15. Purchased from BDH Chemicals, Toronto, Canada.
16. Purchased from Fluka, Switzerland.
17. H. M. Fullmer, G. R. Martin, J. J. Burns, *Ann. N.Y. Acad. Sci.* **92**, 286 (1961).
18. C. A. Nichol, *Fed. Proc.* **11**, 452 (1952); K. P. Misra, C. W. Woodruff, W. J. Darby, *ibid.* **16**, 393 (1957).
19. E. A. McCulloch and J. E. Till, in *Hemopoietic Cellular Proliferation*, F. Stohlman, Jr., Ed. (Grune & Stratton, New York, 1970), p. 15.
20. We thank Dr. David Osoba for performing these experiments.
21. G. E. Levenson, *Exp. Cell Res.* **62**, 271 (1970).
22. I. B. Chatterjee, N. C. Kar, N. C. Ghosh, B. C. Guha, *Ann. N.Y. Acad. Sci.* **92**, 36 (1961).
23. P. A. Loach, in *Handbook of Biochemistry, Selected Data for Molecular Biology*, H. A. Sober, Ed. (Chemical Rubber Co., Cleveland, 1968), p. J-27.

24. Supported by a grant from the Ontario Cancer Treatment and Research Foundation (197). We thank Mrs. A. Kaufman and Mrs. M. H. Park for their excellent technical assistance.

7 June 1971; revised 16 August 1971

The Brain as a Parallel Coherent Detector

Abstract. *Knowledge of the bioelectric signal-to-noise ratios in rat brain makes it possible to demonstrate for the first time that the brain functions as a coherent signal detector, an important class of detectors that are explicitly formulated within the statistical theory of communication. Within an afferent neuronal channel of a single modality, the brain functions as a parallel signal processor.*

In the visual system in the rat during photic stimulation the relative bioelectric signal-to-noise power ratio (S^2/N^2) for input at the contralateral eye as compared to the ipsilateral eye measured at either the dorsal lateral geniculate nucleus (LG) or at the visual cortex (VC) corresponds to the known decussation ratio of neurons in the optic nerve (*1*). A narrow band-pass measuring technique was used to define a signal channel (*1*). Signal-to-noise ratios were computed by subtracting the integrated filtered brain output obtained during a no-input condition (N) from the output obtained during a matched period of channel-tuned photic stimulation (S') and dividing the obtained value (S) by the output without input (N). In this procedure, the output without input is defined as background noise. Thus, signal-to-noise ratio $= (S' - N)/N = N$.

In accordance with empirical findings

$$(S^2/N^2)_1/(S^2/N^2)_2 = \psi_1/\psi_2 \tag{1}$$

where $(S^2/N^2)_1$ is the signal-to-noise power ratio at a given brain station (say, LG) when the signal is transmitted through a communications channel 1 (C_1), $(S^2/N^2)_2$ is the signal-to-noise power ratio at the given brain station (LG) when the signal is transmitted through a communications channel 2 (C_2), and ψ_1/ψ_2 is the ratio of the number of visual afferent neurons carrying a photic signal in channel C_1 compared to the number of neurons carrying the signal in channel C_2.

This signal processing property of the brain may now be formally compared with various signal detector schemes that are well known in statistical communications theory. The *coherent detector* is of particular importance in that it is theoretically the most efficient of the stochastic signal detection systems (*2*).

If, in a communications system, S/N is measured on a single sample during time unit τ (for example, seconds), and if upon integration over repeated samples T (τ) then

$$S/N = (aT)^{1/2}\,(\dot{S/N}) \tag{2}$$

where a is a scale coefficient and $(\dot{S/N})$ is (S/N) for the unit sample. Then it can be said that the system is functioning as a coherent signal detector (*2*). Other kinds of stochastic signal detectors will also yield an increase in signal-to-noise ratio as a function of T, but will do so with less efficiency; for example, for the square law detector, $S/N \approx (aT)^{1/4}\ \dot{S/N}$. If $(S/N)_1$ is the signal-to-noise ratio measured over time period T_1, and if $(S/N)_2$ is the signal-to-noise ratio measured over time period T_2—where $(\dot{S/N})_1 = (\dot{S/N})_2$, that is, $\dot{S/N}$ for the unit sample is the same for T_1 and T_2—and if the scale coefficient a is constant, then from Eq. 2

$$(S/N)_1/(S/N)_2 = (aT_1)^{1/2}\,(\dot{S/N})/(aT_2)^{1/2}\,(\dot{S/N})$$

$$(T_1)^{1/2}/T_2^{1/2} = (S/N)_1/(S/N)_2$$

$$T_1/T_2 = (S^2/N^2)_1/(S^2/N^2)_2 \tag{3}$$

Equation 3 states that for any given coherent detection system the ratio of sample time periods (T) is equal to the ratio of their respective signal-to-noise power ratios (S^2/N^2). Then any system satisfying Eq. 3 can be said to function as a coherent signal detector for T_1 and T_2.

Combining Eqs. 1 and 3

$$T_1/T_2 = (S^2/N^2)_1/(S^2/N^2)_2 = \psi_1/\psi_2 \tag{4}$$

On the basis of Eq. 4, we conclude that for photic stimulation within the context of our experimental paradigm (at least), the brain functions as a coherent signal detector (*3*).

On the basis of Eq. 4 by implication

$$\psi_1/\psi_2 \equiv T_1/T_2 \tag{5}$$

Since ψ refers to the number of neurons carrying a signal in a communications channel within the brain, and T refers to the number of repeated samples of a signal integrated over time T (τ), how is the equivalence of the ratios for ψ and T (expression 5) reconcilable? The equivalence of the ψ and T ratios becomes clear once we understand the general statistical concept of the sample space. In the common treatment of signal detection in communications theory, sample space is enlarged by summing repeated samples over time. This corresponds to the usual model of the serial information processor. However, sample space may also be enlarged by parallel processing during a single time unit. (Thus the probability of heads or tails for coins can be established by either tossing one coin n times, or tossing n coins one time.)

My results illustrate the operation of the brain as a parallel signal processor. In the experiments (*1*) underlying 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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References and Notes

1. A. Trehub, *Electroencephalogr. Clin. Neurophysiol.* **30**, 113 (1971).
2. C. W. Helstrom, *Statistical Theory of Signal Detection* (Pergamon, London, 1968); G. Raisbeck, *Information Theory* (M.I.T. Press, Cambridge, Mass., 1963).
3. In our experimental series, stimulus intensity was 11 lu/m² (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.
4. A. Trehub, *Biophys. J.* **9**, 965 (1969).
5. I thank P. Johnson, E. Pietskowski, and R. Glorioso for assistance.

25 June 1971; revised 6 August 1971

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-