Letter to the Editor

Tryptophan and Perceptual Schizophrenias

To the Editor:

Tryptophan (TP) metabolism has been reported to be abnormal in schizophrenics. The disturbance appears to be localized in the TP-nicotinic acid (NI) pathway since the urinary excretion of NI is found to be low in patients with this disorder (Price et al., 1959). Pollin et al. (1961) have shown that the administration of TP and a monoamine oxidase inhibitor modifies schizophrenic behavior. Contrariwise, the administration of NI seems to ameliorate schizophrenic symptomatology (Hoffer et al., 1957), although this issue is still controversial (APA Task Force Report, 1973, and Megavitamin Therapy, Hoffer and Osmond, 1976).

Manowitz et al. (1973) have recently reported that fasting plasma total TP is low in acute schizophrenics. This finding is consistent with our observations (Yaryura-Tobias et al., 1974) in subacute schizophrenics, who, in addition, display an abnormal response to a glucose load in a five-hour oral glucose-tolerance test (5-HOGTT). We also found that fasting serum free TP was significantly lower ($p<0.01$) in acute and subacute schizophrenics as compared with neurotics and controls before and during a 5-HOGTT (Chang et al., 1976).

An interrelationship between TP and glucose metabolism has been demonstrated in animal and human studies (Fernstrom et al., 1974), and glucose metabolism was found to be altered in psychotic patients (Yaryura-Tobias and Neziroglu, 1975). Our data showed significant intra- and intergroup differences between psychotics, neurotics, and a control population with respect to serum-free TP, free fatty acids, and insulin in the fasting stage and during some hours of a 5-HOGTT (Yaryura-Tobias et al., 1977). A clinico-bio-chemical correlation yielded lower fasting free TP values in schizophrenic patients ($N = 10$) with prominent symptoms of dysperceptions ($p<0.01$) when compared to schizophrenia with prominent paranoid symptoms (Chang et al., 1976).

Based on the assumption that a deficit in central TP metabolism per se may be a pathological factor in perceptual forms of schizophrenia and in the fact that TP is mostly metabolized via the kynurenic pathway in extra-CNS tissues, we have now carried out an open pilot study of the clinical efficacy of L-tryptophan in schizophrenic patients with prominent symptoms of dysperception (auditory and visual hallucinations, and changes in taste and smell). Informed consent was obtained from four outpatients who

participated in this study. L-tryptophan 1g t.i.d., nicotinic acid, 500 mg b.i.d., and pyridoxine HCI, 100 mg b.i.d., were orally administered to the patients during the treatment period. After three months on this regimen, a significant improvement in the perceptual symptomatology was observed in all the patients.

It has been shown, for instance, that NI supplementation can inhibit the major metabolic pathway of tryptophan by way of tryptophan pyrrolase, and thus, make more tryptophan available to the brain (Scherer and Kramer, 1972). Thus, the data obtained in this preliminary study are very encouraging and suggest an alternate means of therapy in this subgroup of schizophrenic patients, and possibly in others where an etiology related to an altered central tryptophan metabolism may be present. We are currently conducting experiments along these lines.

J.A. Yaryura-Tobias, M.D.
H.N. Bhagavan, Ph.D., FA.C.N.
F. Neziroglu, M.A.
North Nassau Mental Health Center
1691 Northern Boulevard
Manhasset, N.Y., 11030

REFERENCES

APA TASK FORCE REPORT NO. 7: Megavitamin and Orthomolecular Therapy in Psychiatry. American Psychiatric Association, 1973.

CHANG. A., NEZIROGLU, F., STEINER, H., and YARYURA-TOBIAS, J.A.: Tryptophan, Glucose, Insulin and Free Fatty Acids in the Blood of Psychiatric Patients. Academy of Orthomolecular Psychiatry Annual Meeting, Denver, Colorado, March, 1976.

FERNSTROM, J. D., MADRAS, B. K., and MUNRO, H. N.: Nutritional Control of the Synthesis of 5-Hydroxytryptamine in the Brain. In: Aromatic Amino Acids in the Brain. Ciba Foundation Symposium 22, Elsevier . Excerpta Medica, North Holland, 1974, pp. 153-173.

HOFFER, A., and OSMOND, H.: Megavitamin Therapy, Canadian Schizophrenia Foundation (Pub.), Regina, Saskatchewan, 1976.

HOFFER, A., OSMOND, H., CALLBECK, M. J., and KAHAN, I.: Treatment of Schizophrenia with Nicotinic Acid and Nicotinamide. J. Clin. Exper. Psycho. Pathol. 18:131-158, 1957.

MANOWITZ, P., GILMOUR, D. G., and RACEVSKIS, J.: Low Plasma Tryptophan Levels in Recently Hospitalized Schizophrenics. Biol. Psychiatry 6:109-118, 1973.

PRICE, J. M., BROWN, R. R., and PETERS, H. A.: Tryptophan Metabolism in Porphyria, Schizophrenia and a Variety of Neurologic and Psychiatric Diseases. Neurology 9:456-468, 1959.

POLLIN, W., CARDON, P. V., JR., and KETY, S. S.: Effects of Amino Acids Feedings in Schizophrenic Patients Treated with Iproniazid. Science 133:104-105, 1961.

SCHERER, B., and KRAMER, W.: Influence of Niacinamide Administration on Brain 5-HT and a Possible Mode of Action. Life Sciences 11:189-195, 1972.

YARYURA-TOBIAS, J. A., CHANG, A., NEZIROGLU, F., and BHAGAVAN, H. N.: Changes in Brain Tryptophan, Glucoseand Related Measures in Psychotics and Neurotics. Federation Proc. 36:1132, 1977.

YARYURA-TOBIAS, J. A., and NEZIROGLU, F.: Psychosis and Disturbance of Glucose Metabolism. J. Prevent. Med. 2:38-45, 1975.

YARYURA-TOBIAS, J. A., NEZIROGLU, F., and GURGONE, J.: The Relationship Between Tryptophan, Glucose and Insulin Levels in the'Mentally III. First World Congress of Biological Psychiatry, Buenos Aires, Argentina, 1974.