ELEVATED PLASMA ENDOGENOUS NITRIC OXIDE SYNTHASE INHIBITOR MAY INDICATE ABNORMALITIES IN NMDA DEPENDENT NITRIC OXIDE PRODUCTION IN SCHIZOPHRENICS

I. Das, N.S. Khan, B.K. Puri, S.R. Hirsch. *Department of Psychiatry, Charing Cross & Westminster Medical School, London W6 8RP, UK*

Nitric oxide synthesis can be inhibited by guanidino-substituted arginine analogues such as L-N^G-monomethylarginine (L-NMMA) and N^G,N^G-dimethylarginine (asymmetric dimethylarginine, ADMA) which is present in human plasma and urine. This raises the possibility that guanidino-substituted arginine analogues may exert a control mechanism on the brain nitric oxide synthase (NOS) and hence modulate nitric oxide (NO) metabolism which is also connected to NMDA subtype of glutamate receptor implicated in the pathophysiology of schizophrenia. Increased presence of an endogenous inhibitor of NOS in drug naive schizophrenic plasma samples was observed when schizophrenic plasma inhibited platelet NOS in vitro. We have investigated the plasma concentrations of ADMA and nitrate levels in drug naive schizophrenic patients and matched control subjects to see if endogenously produced NOS inhibitors is perturbed in schizophrenia.

Blood samples from 16 schizophrenic patients never exposed to neuroleptic treatment meeting DSM III-R criteria for schizophrenia were taken. Three of the above schizophrenic patients were treated with sulpiride 600 mg/day for 3 months. The main form of schizophrenia was paranoid but other types were also used. Nine healthy volunteers who had not taken any drugs for at least 2 weeks were used as controls. Plasma samples for ADMA were analyzed blindly by high-pressure liquid chromatography technique. Plasma ADMA levels in schizophrenic patients was elevated significantly compared to control subjects. Neuroleptic treatment in 3 patients seemed to have a lowering effect on ADMA levels. The cellular origins of methylarginines are not precisely known but the presence of free methyl and dimethylarginines in the brain were reported. Low CSF concentrations of cyclic guanosine 3'5'-monophosphate observed in schizophrenia may be related to the elevation of ADMA. The occurrence of these free methylarginines may have an important role in regulating the signal transduction through NMDA dependent NO metabolism in the brain, and suggest novel therapeutic targets.

FACTORS ASSOCIATED WITH SCHIZOPHRENIC RELAPSE: A RETROSPECTIVE STUDY

B. Payá, M. Sáenz, J. del Rio, J.L. Ayuso-Gutierrez. *Servicio de Psiquiatría, Hospital Universitario San Carlos, 28040 Madrid, Spain*

The study was a retrospective investigation of the factors associated with relapse in one hundred consecutive schizophrenic patients who had suffered a clinical exacerbation and were admitted to San Carlos Hospital in Madrid. Reports of patients and significant others, and information from the medical records were used to determine whether patient had been compliant with treatment. A self-report scale predictive of drug compliance in schizophrenics was also used to assess subjective response to drug therapy.

We have recorded the following variables:
Illness variables
Marital status
Socioeconomic level
Level of family support
Therapeutic regimen prior to admission
Medication side effects
Patients' attitude toward health and illness
Incidence of stressfull life events
Alcohol and drug abuse comorbidity

This study offers preliminary evidence that sociodemographic factors and illness variables were unrelated to compliance, while treatment variables, especially side effects of medication, were associated with improved compliance. Noncompliant patients had significantly lack of feeling of illness and insight into it, and had more alcohol and drug abuse comorbidity. The compliant patients had higher incidence of adverse life events.

INFLUENCE OF GENDER AND FAMILY HISTORY ON THE AGE AT ONSET OF SCHIZOPHRENIA

D.G. Dikeos, G.N. Papadimitriou, E.G. Daskalopoulou, D. Vassilopoulos [1], C.N. Stefanis. *Department of Psychiatry, University of Athens, Athens 11528, Greece; [1] Department of Neurology, University of Athens, Athens 11528, Greece; Clinical and Molecular Neurogenetics Unit, Eginition Hospital, Athens 11528, Greece; University Mental Health Research Institute, 74 Vas Sofias ave, Athens 11528, Greece*

Family, twin and adoption studies have demonstrated that genetic factors play an important role in the pathogenesis and clinical expression of schizophrenia. Gender and family history have been suggested to influence the age at onset of the disease. In order to investigate this issue, 42 patients from 20 multi-affected families and 15 sporadic cases were personally examined. As age at onset was considered the age at the first appearance of clinical symptomatology, while the genetic loading for the familial cases was calculated on the basis of the number of affected and non-affected first-degree relatives.

For the familial cases, no difference was found between males and females concerning the age at onset (probands: males 21.5 yrs, females 22.1 yrs, $p > 0.1$; other family members: males 27.9 yrs, females 31.2 yrs, $p > 0.1$). Regarding the sporadic cases however, a difference was observed (males 20.6 yrs, females 25.2 yrs, $p < 0.05$). Additionally, among all the familial cases, the age at onset was found to be negatively correlated with the genetic loading only in females ($r = -0.37$, $p < 0.05$) and not in males ($r = -0.09$, $p > 0.1$).

These results support the hypothesis of the existence of two clinical subtypes of schizophrenia: one with common age at onset for both sexes and positive family history, and another with later age at onset for women and negative family history. The observation that, regarding the familial cases, the genetic loading influences the age at onset only in women, should be further evaluated in a larger sample of patients in relation to other clinical variables.

REDISCOVERING PROPFSCHIZOPHRENIE

G.A. Doody, D.G.C. Owens, E.C. Johnstone. *University Department of Psychiatry, The Royal Edinburgh Hospital, Morningside Park, Edinburgh, Scotland, U.K. EH10 5HF*

Emil Kraepelin first introduced the term 'Profpschizophrenie' in 1919. It was then defined as a sub-type of dementia praecox characterised by dull intellect, negative symptomatology and poor outcome. However, the negative symptomatology referred to by Kraepelin varied from that with which we are familiar with today.

Current research suggests that cognitive impairment is an integral component of schizophrenia. There is also evidence that the point prevalence of schizophrenia in individuals with mild learning disability is three times that seen in the normal population. Yet many studies of schizophrenia continue to exclude individuals with a premorbid history of mild learning disability. This study aims to redefine the psychopathology of schizophrenia as it occurs in patients with a premorbid I.Q. in the mildly learning disabled range (50–70).

57 subjects have been seen in three age and sex matched groups; subjects with a dual diagnosis of premorbid mild learning disability and schizophrenia (obtained from a National register, N = 21), sub-

https://doi.org/10.1016/0924-9338(96)89335-7 Published online by Cambridge University Press