nervous system due to accumulation of very long chain fatty acids (>C24). The juvenile form of ALD shows a rapidly progressive mental deterioration that may lead to dementia. Approximately 40% of patients with ALD initially present with symptoms that resemble psychiatric disorders. Adrenomyeloneuropathy (AMN), the adult and more chronic form of ALD, mainly involves the spinal cord and peripheral nerves but may also affect the cerebral hemispheres.

Cognitive function was assessed in five patients with various clinical phenotypes of ALD. One patient had AMN and showed progressive spastic paraplegia, peripheral sensory neuropathy of the legs, and adrenal cortical insufficiency that required substitution with hydrocortisone. Three symptomatic female heterozygotes who had spastic paraplegia and impairment of vibration sense in the distal segments of the legs and one patient with an intermediate form between ALD and AMN who had evidence of cerebral, spinal, and peripheral nerve involvement were included in the study. Because of complex partial, simple partial, and generalized epileptic seizures he had been treated with antiepileptic drugs for 7 years. The present medication consisted of phenobarbital and carbamazepine. None of the other patients received any specific medication.

Assessments included the Wechsler Adult Intelligence Scale-Revised (WAIS-R), an Auditory Verbal Learning Test (VLMT), the Complex Figure Test (Taylor), a Trail Making Test, the Benton Visual Retention Test, a Controlled Oral Word Association Test, the Purdue Pegboard Test, and a computerized test of reaction time after different stimuli.

The patient with AMN and all of the female heterozygotes showed a decrease in performance in the Purdue Pegboard Test, which is a measure of psychomotor ability and which may add to predicting a lateralized lesion. The female heterozygotes also had long reaction times and showed additional deficits on the Trail Making Test and a slight but not significant impairment of the Digit Symbol of the WAIS-R, which is a test of psychomotor performance and which furthermore involves sustained attention and visuomotor coordination. Impairment of cognitive function was most marked in the patient with the intermediate form of ALD/AMN, involving memory, verbal, and psychomotor ability. However, individual subtests could be completed satisfactorily after the time limit had expired.

The pattern of neuropsychological performance implies that in the AMN patient and in all heterozygotes mainly complex motor sequences are impaired. Furthermore, it suggests an involvement of the upper limbs while there is no apparent clinical manifestation. Diminished speed may contribute to but does not alone account for the impaired performance. In the intermediate form of ALD/AMN, in consistency with evidence of multiple lesions on the computed tomogram, multiple areas of cognition are impaired. These include constructional, executive, verbal, and memory functions.

P-4-18

Earlier onset of psychostimulant use and the D2 dopamine receptor gene *Taq*I A1 RFLP predict preferential psychostimulant use in polysubstance abusers

A.M. Persico[a], G. Bird[a], F.H. Gabbay[b] and G.R. Uhl[a,c]

[a]*Molecular Neurobiology Branch, Addiction Research Center, NIDA/NIH, P.O. Box 5180, Baltimore, MD 21224, USA,* [b]*Department of Medicine and Clinical Psychology, Uniformed Services, University of the Health Sciences, Bethesda, MD, USA and* [c]*Department of Neurology and Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, USA*

Key words: Dopamine D2 receptor; Cocaine; Amphetamine; Substance abuse; Alcoholism

Several lines of evidence suggest that D2 dopamine receptor (DRD2) gene variants may contribute to polysubstance abuse vulnerability (Smith et al., 1992; Persico et al., 1993; Uhl et al., 1993). Among drugs abused by humans, psychostimulants possibly display the most powerful and specific dopamine-enhancing activity in mesolimbic/mesocortical circuits important for behavioral reward and reinforcement.

The hypothesis that DRD2 gene variants may influence patterns of drug choice was tested, contrasting DRD2 *Taq*I A, B, and D polymorphisms in subgroups of caucasian polysubstance users reporting distinct patterns of drug preference and in controls. Polysubstance users with a history of heavy daily preferential psychostimulant use display significantly greater *Taq*I A1 presence (26/60 = 43.3% vs. 33/119 = 27.7% in controls), as well as a markedly earlier onset of psychostimulant use. Opiate-preferring abusers, addicts with no drug preference and heavy polysubstance users, with lifetime daily use of six or more substances, do not differ from controls in DRD2 genotypes.

Our data are consistent with the hypothesis that DRD2 gene variants modulate patterns of drug use in polysubstance abusers.

References

Persico, A.M., Smith, S.S. and Uhl, G.R. (1993) D_2 receptor gene variants and substance abuse liability. Semin. Neurosci. 5, 377–382.

Smith, S.S., O'Hara, B.F., Persico, A.M. et al. (1992) Genetic vulnerability to drug abuse: the dopamine D_2 receptor *Taq*I B1 RFLP appears more frequently in polysubstance abusers. Arch. Gen. Psychiatry 49, 723–727.

Uhl, G.R., Blum, K., Noble, E. and Smith, S.S. (1993) Substance abuse vulnerability and D_2 receptor genes. Trends Neurosci. 16, 83–88.

P-4-19

Effects of S-12024 on brain electrical activity in patients with Alzheimer's disease

A. Franco-Maside, D. Vinagre, J. Caamaño, M.J. Gómez, X.A. Alvarez, L. Fernández-Novoa, B. Novo, R. Zas, C. Gorostiaga[a], E. Polo[a], M. García[a] and R. Cacabelos

Institute for CNS Disorders, Basic and Clinical Neurosciences Research Center, 15004-A Coruña, Spain and [a]I.R.I.S. Department of Psychiatry, Courbevoie, France

Key words: S-12024; Computerized EEG; Alzheimer's disease

S-12024 is a new compound with cognitive enhancing properties in animals and in healthy elderly subjects. Computerized EEG analysis has been shown to be a sensitive technique to evaluate central effects of drugs, and a valuable method for diagnostic and therapeutic assessment in dementia trials. In this study we have evaluated the effects of the repeated oral administration (28 days) of three different doses of S-12024 (0, 100 and 300 mg once daily) on brain electrical activity mapping in 35 ambulatory patients with dementia of the Alzheimer type. Patients were allocated to the three treatment groups after 1 month of pharmacological wash-out. Computerized EEG recordings were performed immediately before the administration of the first dose (T0) and 4 weeks after (T4). Relative delta, theta, alpha and beta power (%) were the evaluated parameters. No statistical inter-group differences were found in psychometric and brain mapping parameters in basal recordings (T0). The group of patients treated with placebo (0 mg of S-12024) showed a significant decrease in relative beta power in left temporal areas ($P<0.05$). Patients receiving 100 mg of S-12024/day showed a statistical increase of relative beta power in right central ($P<0.05$) and occipital ($P<0.05$) areas. A significant decrease in relative beta power in right parieto-temporal areas ($P<0.05$) was found in patients treated with 300 mg/day at 4 weeks of treatment. These results seem to indicate that the chronic oral administration of S-12024 activates fast frequencies in computerized EEG recordings in patients with Alzheimer's disease at moderate doses, with opposite effect at high doses. Therefore, S-12024 might be useful as a palliative treatment in Alzheimer's disease.

Supported by I.R.I.S. and EUROESPES Foundation.

P-4-20

Internal consistency of a new scale for the evaluation of benzodiazepine withdrawal syndrome

B.M. Cesana, A. Petracca[a], S. Chiroli, C. Borghi and G.B. Cassano[a]

Synthélabo Recherche, Milan, Italy and [a]II Cattedra di Psichiatria, Università degli Studi di Pisa, Pisa, Italy

Key words: Benzodiazepine; Withdrawal syndrome; Evaluation scales

Benzodiazepines (BZ) are widely used because of their efficacy and safety. However, there is increasing evidence that BZ