

presented as well as an evaluation of the effect of psychotherapy at month 12 after the individual onset of the study.

S14.02

PHARMACOKINETICS OF METHADONE AND LAAM, AND THEIR CLINICAL RELEVANCE

C.B. Eap*, P. Baumann. *Département Universitaire de Psychiatrie Adulte, Hôpital de Cery, CH-1008 Prilly, Switzerland*

Our knowledge on the pharmacokinetics and pharmacogenetics of methadone and other opioids has considerably increased during the past few years. In particular, it has been demonstrated that isozymes belonging to the cytochrome P450 superfamily play a major role in their metabolism. These isozymes can be inhibited, or induced, by specific compounds. These data allow to explain, and possibly avoid, the majority of metabolic interactions involving methadone. It is also well known that there is a large variability in the activities of these isozymes, a variability which is both genetically and environmentally controlled. We recently demonstrated that a therapeutic response (i.e. no consumption of illicit opiate) was significantly associated with a (R)-methadone (the pharmacologically active form of methadone) blood concentrations of 250 ng/ml (Eap et al., *Drug and Alcohol Dependence*, in press). To obtain this concentration, due to interindividual variabilities in methadone concentrations for the same given dose corrected for the weight of the patient, theoretical doses of methadone could be as low as 55 mg/day and as high as 921 mg/day in a 70 Kg patient. Therapeutic drug monitoring of the active enantiomer could be useful in patients in methadone maintenance treatment who continue to use illicit drugs, and this stresses the importance of individualizing methadone treatment. With regard to levo-alpha-acetylmethadol (LAAM), although few data are presently available on its pharmacokinetics, some possible consequences of the known involvement of cytochrome P450 enzyme(S) in its metabolism will be discussed.

S14.03

USE ABUSE AND DEPENDENCE FROM BENZODIAZEPINES IN METHADONE MAINTAINED PATIENTS – THEORETICAL AND PRATICAL ISSUES

G. Forza*, E. Levarta, F. Schifano. *Addiction Treatment Unit #1, Local Health Unit #16, Padova, Italy*

Ninety-two out of the 550 patients in methadone maintenance (range: 20–90 mg/die) for at least three months in Addiction Treatment Units of Padova at the date of 1.1.97 were randomly selected. They had been studied with the means of a clinical interview and SCL-90 questionnaire. Fifty-eight patients (63.0%) reported a BDZ usage in 1996. We defined as "problematic BDZ users" those patients who showed at least one of the following characteristics: 1) a reported daily diazepam-equivalent dosage larger than 60 mg (14 pts); 2) a use of BDZs to get the "high" or to "boost" the effects of methadone itself (17 pts); 3) a self-administration characterized by binges in some circumstances (7 pts); and 4) i.v. usage in some circumstances (4 pts). Due to the overlap of these criteria, we identified a subgroup of 26 patients (28.3% of the total sample, 44.8% of BDZ users). With respect to the others, these last pts showed a significant higher prevalence of concurrent administration of BDZs with alcohol (63.2% vs. 20.8%, $p = 0.011$), and/or with cocaine (26.3% vs. 0%, $p = 0.011$), and a significant higher lifetime prevalence of cocaine (69.6% vs. 43.3%, $p = 0.049$), amphetamine (52.2% vs. 3.4%, $p < 0.001$) and hallucinogens (34.8% vs. 5.0%, $p = 0.001$) abuse/dependence. On a toxicological basis, this group

is therefore characterized by a poly-substance abuse/dependence. On a psychopathological basis, problematic BDZ users showed, with respect to the others, a profile more disturbed at the SCL-90 (GSI: 1.12 ± 0.81 vs. 0.59 ± 0.51 , $p = 0.003$), in particular with respect to the Hostility subscale (1.12 ± 0.98 vs. 0.41 ± 0.42 , $p = 0.001$). These pts had often been involved in anti-social behaviours as assaults, fights or robbery during BDZ intoxication, and they showed a higher prevalence of present judiciary troubles (47.8% vs 14.0%, $p = 0.003$). This group of patients is therefore characterized by an impulse dyscontrol or even a frank antisocial personality disorder.

S14.04

METHADONE SUBSTITUTION THERAPY (MST): PATTERN OF SERVICE CONFIGURATION ACROSS EUROPE

H. Ghodse*, A. Oyefeso. *Centre for Addiction Studies, Department of Addictive Behaviour & Psychological Medicine, St George's Hospital Medical School (University of London), London, SW17 0RE, UK*

Methadone substitution therapy (MST) programmes are largely regarded as physical facilities with resources dedicated to the treatment of opiate addicts using methadone. Consequently, there is no common protocol for administering MST across treatment settings. As protocols are determined by the programme's treatment philosophy, models of treatment delivery and expected outcomes can be different.

Given the increase in the transnational mobility of opiate addicts across EU members states and in order to ensure continuity in the care of this client group across the EU, there is a need to move towards the unification of core policies and practices in MST programmes.

This paper examines the pattern of configuration of MST services in 11 MST programmes in eight European countries. The structure and process of MST in a sample of treatment programmes in these countries were reviewed in a cross-sectional survey. Study variables included staffing establishment, treatment goals and philosophy; programme setting and intensity and national health policies.

The main findings of the study (i) There are different models of MST provision across Europe (ii) MST delivery is significantly determined by the prevailing national health policies and priorities.

The paper discusses the implications of these findings for optimising the requirement for patient-policy-programme matching across Europe.

S15. Multiple foci in the support of schizophrenic patients

Chairs: F. Müller-Spahn (CH), H.D. Brenner (CH)

S15.01

STATE OF THE ART IN PSYCHOPHARMACOLOGICAL THERAPY OF SCHIZOPHRENIA

F. Müller-Spahn. *Basle, Switzerland*

Conventional antipsychotics have been found to be efficacious in acute and long-term treatment of schizophrenia. However, between 20%–30% of all patients do not respond adequately to neuroleptic therapy. Their care requires most of the cost of treating schizophrenia. Most of them lack of beneficial effects against deficit

symptoms and may experience side effects due to the biochemical and anatomical nonselectivity of classic neuroleptics.

Unlike these conventional neuroleptics, atypical antipsychotics have shown superior efficacy in ameliorating negative symptoms in large double-blind multicenter trials with only a low incidence of EPS and minimal effects on prolactin. Six drugs are currently considered as first-line therapy in patients with negative symptoms, Clozapine, Risperidone, Olanzapine, Amisulpride, Quetiapine and Ziprasidone. Clozapine is still the only drug with clear efficacy in severely treatment-refractory schizophrenic patients.

It is still a matter of debate whether these drugs treat only secondary negative symptoms due to acute psychosis, EPS or depression or schizophrenia-specific primary deficit symptoms. The advantages of the new generation – atypical antipsychotics may at least partially be explained by their serotonin – dopamine antagonistic properties and their preferential action on mesolimbic dopaminergic pathways.

S15.02

NEW DEVELOPMENTS IN PSYCHOSOCIAL REHABILITATION OF SCHIZOPHRENIA PATIENTS

H.D. Brenner. *Sozial und Gemeinde Psychiatrie, Universitäre Psychiatrische Dienste Bern, 49 Laupenstrasse, CH-3000 Bern 10, Switzerland*

The contribution provides a critical outline of the current position of psychological interventions in the treatment and rehabilitation of schizophrenia patients. Four cognitive behavioral treatment approaches have emerged as preeminently effective or at least especially promising as adjuncts to pharmacotherapy, i.e. the training of social skills, cognitive training programs for the remediation of neurocognitive deficits, psychoeducative, coping-oriented interventions with patients and their families, and cognitive behavioral therapy of residual symptoms. These approaches are discussed with regard to their efficacy in reducing relapse rates, psychopathology as well as cognitive and social disability. Open questions and possibilities for the further development of these approaches are considered and prognostications are made concerning the future of psychotherapy research in schizophrenia, notably in the light of changing conditions in public health care systems.

S15.03

MOTIVATIONAL EMPOWERMENT – A NEW APPROACH TO COGNITIVE REHABILITATION IN CHRONIC SCHIZOPHRENIA

M. Kuntze. *Basel, Switzerland*

Long-term course and prognosis of schizophrenic disorders are not only determined by the disorder *per se* but are also influenced by the individual's interaction with the symptoms. Psychopathology and motivational models, such as self-concept, self-expectancies, outcome-expectancies, and locus of control, are involved in coping which often results in a chronic course because of patient's resignation.

Our pilot study on the vocational rehabilitation of schizophrenia patients has shown that external control beliefs, uninfluenced by negative symptoms, predicted vocational outcome to the same extent as negative symptoms alone. External locus of control (by powerful others/by chance) correlated significantly with negative self-concept ($-.52/--.57$; $p < .001$), depressive-resigned coping ($.51/.61$; $p < .001$), and poor vocational outcome ($-.51/--.54$; $p < .001$).

In the present study, we aim at evaluating the impact of external locus of control, pessimistic outcome-expectancies, negative syndrome and depressive coping strategies on neuro-cognitive remediation in schizophrenia. Moreover, we intend to specify the concepts of depression, negative syndrome, and resignation. *Motivational Empowerment Training* will be applied to modify the patients' control beliefs, attributional styles, learned helplessness and self-image in such a manner that they are able to deal with their resources more competently and achieve an improved quality of life. *Motivational Empowerment Training* is a manual-guided cognitive-behavioral therapy supporting beneficial personal motives which may have a positive effect on the long-term course of schizophrenia.

- (1) Kuntze M., Kupper Z., Kunz B., Hoffmann H. (1999) Motivational empowerment in chronic schizophrenia. Poster "Third International Conference on Psychological Treatments of Schizophrenia". Oxford, UK.
- (2) Kuntze M (2000) *Motivational Empowerment Training – A manual-guided cognitive-behavioral therapy supporting beneficial personal motives in chronic schizophrenia patients*. Bern, CH.

S15.04

EVALUATION OF A NEW METHODOLOGY OF COGNITIVE-EMOTIONAL SOCIAL SKILLS TRAINING PROGRAMMES FOR SCHIZOPHRENIC PATIENTS

P. Zorn*, V. Roder. *Psychiatric Services, University of Berne, Department of Social and Community Psychiatry, Bolligenstrasse 111, CH-3000 Berne 60, Switzerland*

In the presented multicenter study, the effectiveness of three newly developed social skills training programmes (experimental groups), which include cognitive-emotional interventions and specific rehabilitation topics in residential, vocational and recreational areas, is compared with a conventional social skills training programme (control group) in terms of community functioning, cognitive abilities and psychopathology. These new programmes represent an extended scope of the social skills training subprogramme of the Integrated Psychological Therapy for Schizophrenic Patients (IPT). A sample of 143 patients with a diagnosis of schizophrenia or schizoaffective disorder (ICD-10) was selected. Treatment covered a 24-week interval, followed by a follow up of 48 weeks.

The results showed higher global treatment effects (effect sizes) in the experimental groups as compared to the control group on the factors that were obtained from a factor analysis over all dependent variables. All groups improved significantly in community and cognitive functioning. Therapy effects were more rapidly in the experimental groups. Furthermore the results indicated that psychopathology could be decisively reduced only by the new programmes. The obtained improvements were maintained at the follow up in all groups. Especially patients treated with the new programmes showed some further amelioration. Relapse rates and duration of hospitalisation diminished in experimental and control groups. In view of these effects, the new social skills training programmes could be included in standard treatment and might replace more conventional programmes in future.