Scale (AIMS). 12 patients had never received antipsychotic medication and none had dyskinesia. Dyskinesia was found in 10–45% of patients who had received medication.

308 elderly individuals in Madras, India, were also examined for dyskinesia, using the AIMS. Dyskinesia was found in 15% of normal subjects (N = 101, mean age 63 years), 15% of first degree blood relatives of younger schizophrenic patients (N = 103, mean age 63 years), 38% of never medicated patients (N = 21, mean age 65 years) and 41% of medicated patients (N = 83, mean age 57 years).

We conclude that dyskinesia in elderly schizophrenic patients is an integral part of the illness and not associated with antipsychotic medication.

Results from a one-year follow-up of the 21 never treated patients will also be presented.

COMPARATIVE STUDIES OF ABNORMAL INVOLUNTARY MOVEMENTS IN NEVER-TREATED VS TREATED POPULATIONS WITH SCHIZOPHRENIA

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There is an important question to answer: is tardive dyskinesia due to neuroleptics only, or does schizophrenia itself represent a risk factor for these abnormal movements? A number of studies have been conducted in Casablanca to answer this question, some of them in collaboration with the Department of Psychiatry of Portland, Oregon, USA.

Some preliminary results of a ongoing study can be presented:

Methods and patients: 61 never medicated schizophrenics (G1), 45 treated schizophrenics (G2), and 25 normal controls (G3) were included, matched for sex, age and duration of illness. The mean age for the 3 groups was G1: 29.8 ± 6.5 years; G2: 28.9 ± 5.7 years; G3: 28.6 ± 3.7 years.

The mean duration of illness for G1 was 6 ± 5.0 years; G2: 5.3 ± 3.9 years.

The clinical assessment used the Abnormal Involuntary Movement Scale (AIMS), Each examination was videotaped and assessed in two ways: open and blind.

Results: The mean global score of AIMS for the open assessment was for G1: 3.5 ± 2.7, for G2: 3.2 ± 3.5 and for G3: 0.4 ± 0.7.

For G1, there was a positive correlation with age. The abnormal movements observed were firstly in the limbs, followed by the orofacial area, and by the trunk.

THE LONGITUDINAL ASSOCIATION OF COGNITIVE DYSFUNCTION WITH TARDIVE DYSKINESIA IN SCHIZOPHRENIA

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Though the subject of much controversy in a historical context, there is an increasing body of contemporary evidence that in schizophrenia the contribution of spontaneous, disease-related involuntary movements to tardive dyskinesia appears to have been underestimated. We have been studying correlates of such movement disorder among features of the illness in neuroleptic-treated populations. In younger outpatients, we found those with orofacial dyskinesia to evidence an increased ratio of minor physical anomalies of the head to those of the periphery, indicating an association with a relative predominance of early craniofacial dysgenesis, and greater neuropsychological impairment on frontal lobe testing; severity of movement disorder was associated both with this anomalies distribution index and with extent of neuropsychological impairment. In older inpatients followed longitudinally over 10 years, those with persistent orofacial dyskinesia showed poorer function in more basic cognitive domains than did those consistently without such movement disorder, though in neither group did that function change over the decade; the only patients to show significant deterioration in these cognitive domains were those evidencing the *de novo* emergence of orofacial dyskinesia, and this deterioration occurred only over the time-frame in which their dyskinesia developed. Orofacial dyskinesia emerging during long-term neuroleptic treatment in schizophrenia appears intimately related to features of the illness for which that treatment was prescribed; it would seem to reflect, at least in part, the neuroleptic-induced precipitation or enhancement of motor patterns intrinsic to the disease process.

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S17. Special aspects in the treatment of opioid addicts

Chairmen: M Gastpar, P Baumann

NEW ASPECTS IN THE PHARMACOKINETICS AND METABOLISM OF METHADONE

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Methadone (MTD) is a racemic drug, but (R)-MTD accounts for nearly all opioid effects of the racemate. However, most countries have introduced racemic MTD for maintenance treatment of opioid addicts. Plasma level monitoring of MTD has been introduced, but an optimal concentration range cannot be agreed upon, as almost all studies did not measure the plasma levels of the enantiomers. In situations of comorbidity, such as depression, comedications may be necessary, but little is known of their interactions with the stereoselective metabolism of methadone and their clinical consequences. We have conducted several studies on the metabolism of MTD in patients:

A. In Germany, until recently, only (R)-MTD has been used. For economic reasons, the racemic form is presently being introduced into this country. In a collaborative study, 22 patients under (R)-MTD treatment were switched to a double dose of (R,S)-MTD. Under racemic treatment, the (R)/(S)-ratios ranged from 0.63 to 2.40, and there was a significant decrease ($p < 0.005$) in the mean serum concentration/dose ratios of the active (R)-enantiomer before and after the change was measured (3.97 vs 3.33). This suggests self-induction of MTD metabolism, as already observed during maintenance therapy with racemic methadone. As a consequence, this may necessitate, in some patients, a dose adjustment.

B. 6 and 7 addicts treated with racemic MTD were comedicated with fluvoxamine and fluoxetine, respectively. Fluvoxamine (50–250 mg/day) addition resulted in a significant increase in the plasma concentrations of both enantiomers, while only those of (R)-MTD were increased by fluoxetine (20 mg/day). These results suggest that CYP2D6 (inhibited potently by fluoxetine) preferentially metabolizes (R)-MTD, and CYP1A2 (inhibited by fluvoxamine) contributes to the metabolism of both MTD enantiomers.