of schizophrenia or to provide a biochemical basis. Most of the observations which support the neurodevelopmental hypothesis can be explained on the basis of genetically determined abnormalities in membrane phospholipid metabolism which can be attenuated or exacerbated by various environmental events. The phospholipids provide the main structural basis for all neuronal membranes and influence the behaviour of all membrane-bound and membrane-associated proteins such as receptors, ion channels and ATPases. The phospholipids also modulate the actions of all neuronal cell signalling systems, and the fatty acids they contain provide many of the second messengers which are activated as a result of receptor occupancy. The phospholipids provide a unique site where genes and environment interact: basic phospholipid structure depends on the enzymes involved in their synthesis and breakdown, whereas those enzymes depend on the environment for the supply of the fatty acids which are major components of the phospholipids. The phospholipid hypothesis proposes that in schizophrenia there are reduced rates of incorporation into phospholipids and increased rates of loss from phospholipids of the long chain polyunsaturated fatty acids (LCPS) which make up about 20% of the dry weight of the brain. Because phospholipids are so important in the brain, such defects could lead to abnormal brain morphology and synaptic remodelling, abnormal susceptibility to viral infections and perinatal hypoxia, insults which are known to interfere with phospholipid metabolism, and the onset of overt symptoms around or soon after puberty when phospholipid metabolism is known to change. This concept provides novel proposals for improved treatment of schizophrenia.

Wed-P40

P50 IN DEFICIT AND NON DEFICIT SCHIZOPHRENIA

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Sensory gating impairments have been found in schizophrenia, with prevalence estimates as high as 90%. Schizophrenic patients show a diminished suppression of the auditory - evoked P50 potential to the second (test) of two paired click stimuli as compared with control subjects. The P50 suppression measure was calculed as the ratio of the test amplitude to the conditioning amplitude (C/T ratio). In order to investigate the relationship between P50 suppression and negative symptoms, we have compared P50 measures between 19 deficit and 32 non deficit schizophrenic patients. The 51 patients were all neuroleptic-treated at the time of the testing and the Schedule for the Deficit syndrome (Kirkpatrick et al., 1989; Ribeyre et al. 1994) was used to classify patients as either deficit or non deficit subtypes.

P50 measures were obtained at vertex during a conditioning-testing paradigm.

P50 amplitudes, latencies and C/T ratio were similar for both deficit and non deficit subgroups. These results suggest that sensory gating impairment is not related to the clinical subtype of schizophrenia.

Wed-P41

ACTIVE ^{3}H-DOPAMINE UPTAKE OCCURS IN PLATELETS AND IN ARTIFICIAL NEURONAL CELL LINES OF HUMAN ORIGIN BUT NOT IN LYMPHOCYTES

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As lymphocytes have been proposed as a peripheral model of dopamine reuptake in brain neurones, which might play a role in several psychiatric diseases, kinetic and pharmacological properties of ^{3}H-dopamine uptake by native human lymphocytes were investigated.

Our results suggest that the transport of ^{3}H-dopamine measured with lymphocytes after separation over Ficoll-Paque™ or Percoll™ is mainly generated by platelets which are always part of freshly prepared lymphocyte suspensions.

The investigations were extended to well defined cell lines in order to compare the pharmacological properties of native and artificial cells without any influence of contaminating cells such as platelets in lymphocyte suspensions. The artificial cell lines MOLT-3 and EBV-transformed lymphoblasts were not able to transport ^{3}H-dopamine which is consistent with our hypothesis that native lymphocytes do not exhibit a dopamine uptake. The investigation of the human neuroblastoma cell line IMR-32 demonstrated a GBR-12909 and cocaine-sensitive specific transport of dopamine, whereas dopamine transport in platelets is performed by a imipramine-sensitive serotonin transporter.

Our results do not support the existence of a dopamine transporter in human lymphocytes and demonstrate the possibility of verifying experiments conducted with crude native cells by the use of artificial, but homogeneous cell lines.

Wed-P42

INFLUENCE OF SEVERITY AND DURATION OF PSYCHOTIC STATE ON THE LEVEL OF MIDDLE MOLECULES

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It is known, that various toxic conditions are accompanied by increased level of middle molecules (molecular wheight 500–5000 Dalton) in blood plasma. It is considered, that the increase of middle molecules (MM) concentration in plasma in schizophrenia proves endotoxicosis hypothesis.

It was studied the level of MM in plasma in schizophrenia. There was examined 14 patients: 10 patients with paranoid schizophrenia (F 20.0, ICD-10) and 4 patients with postschizophrenic depression (F 20.4). Patients with organic or somatic pathology were excluded.

In schizophrenic patients with acute episode, characterized by severe paranoid and hallucinosis symptomatology (6–7 CGI score, less than month duration) the MM plasma concentration has exceeded 3–4 time the normal level. In psychotic patients with less severe states (4–5 CGI score) the duration of which was more than month, the MM concentration was less increased and exceeded the normal level by 1.5–2 times.

In all patients with postschizophrenic depression (3–4 CGI score, state duration more than month) the MM level did not exceed norm.

Control MM level was 0.45 ± 0.06 g/l.

It was found the tendency to negative relationship between MM plasma concentration and duration of psychotic symptomatology and positive relationship between MM plasma concentration and severity of psychotic symptomatology.

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We suppouse, that the chronification of patient"s psychotic state is followed by the decrease of MM level.

Wed-P43

ZOTEPINE ENHANCES NORADRENALINE LEVELS IN RAT FRONTAL CORTEX MICRODIALYSATES: FURTHER SUPPORT FOR ANTIDEPRESSANT ACTIVITY

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Zotepine is an antipsychotic drug with a marked atypical profile that not only has efficacy for positive and negative schizophrenic symptoms but combines activity in animal models predictive of antidepressant activity (Needham *et al.*, 1997; *Biol. Psychiat.* **42,** 175–176S) with antidepressant properties in patients (Fleischhacker *et al.*, 1989; *Psychopharmacol. Bull.* **25,** 97–100). Since zotepine inhibits ^{3}H-noradrenaline (^{3}H-NA) uptake by rat frontal cortex synaptosomes (Needham *et al.*, 1997), we studied the effects of zotepine and comparator antipsychotics on extracellular NA in the frontal cortex using *in vivo* microdialysis. In freely-moving male CD rats (250–350 g), basal levels of cortical NA were 31 ± 3 fmol/20 µl. Zotepine (0.5, 1.0 or 1.5 mg/kg, ip) evoked biphasic, dose-related rises in cortical NA with peaks at 60 min (+94% to +171% above basal values; $p < 0.001$ by ANOVA with *post hoc* Dunnett's *t*-test) and at 240 min (+142% to +212%; $p < 0.001$) post-zotepine. The increases in NA were sustained for up to 120 min beyond the initial peak. Clozapine (10 mg/kg, ip) increased NA levels by 72% ($p < 0.05$) but only for 20 min. Neither ziprasidone (3 mg/kg, ip) nor olanzapine (1 mg/kg, ip) had any action on cortical NA. The antidepressant, desipramine (a NA uptake inhibitor; 0.3 mg/kg, ip), elevated NA levels 5-fold ($p < 0.001$), an effect which declined over 240 min. Zotepine's elevation of cortical NA probably occurs via NA uptake inhibition. Clozapine's weaker action may derive from α_2-adrenoceptor blockade. This action of zotepine may contribute to its antidepressant profile and its reported superiority *vs* clozapine in improving some cognitive deficits in schizophrenic patients (Meyer-Lindenberg *et al.*, 1997; *Pharmacopsychiatry* **30,** 35–42).

Wed-P44

COGNITIVE AND EMOTIONAL SIDE EFFECTS AND THE EFFICACY OF CLASSICAL AND ATYPICAL NEUROLEPTICS IN ACUTE SCHIZOPHRENIA

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The importance of cognitive emotional side effects of neuroleptics is underestimated in general, but according to the statements of many patients, it is a reason for their noncompliance.

Within various double-blind studies on the efficacy and tolerance of classical and atypical neuroleptics in our hospital we applied a neuro-psychological test battery in order to record the influence of the substances on cognitive and emotional functions.

The results of these investigations were compared quasi-experimentally. The results showed that not only the serotonergic antagonistic atypical neuroleptics clozapine, olanzapine, risperidone and zotepine, but especially also the substituted benzamides remoxipride and amisulpride caused significantly less cognitive emotional side effects than the classical neuroleptics.

The discribed results also found their expression in the contentment with medication of the investigated patients.

The results shall be discussed in context with the problems of methodological measuring.

Wed-P45

PSYCHOPHARMAKOLOGISCHE BEHANDLUNG UND PRÄVALENZ VON EPS BEI PATIENTEN MIT 15JÄHRIGEM VERLAUF EINER AFFEKTIVEN-, SCHIZOAFFEKTIVEN-, SCHIZOPHRENEN- BZW. WAHNHAFTEN PSYCHOSE

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Einleitung: Das Vorkommen von extrapyramidal motorischen Nebenwirkungen (EPS) wird bei bis zu 90% der mit Neuroleptika (NL) behandelten Patienten beschrieben, das von irreversibel auftretenden Spätdyskinesien bei bis zu 40% der Fälle (Möller 1996). Im Rahmen der Münchener 15 - Jahres - Katamnesestudie werden bei Patienten mit der Diagnose einer affektiven-, schizoaffektiven-, schizophrenen- und einer (nicht schizophrenen) paranoiden Psyhose zum Follow-up-Zeitpunkt die gegenwärtige psychopharmakologische Medkation und das Ausmaß unwillkürlicher Bewegungsstörungen nachuntersucht.

Material und Methoden: Bestimmung von EPS und Spätdyskinesien durch: Extrapyramidale Symptom-Skala (Simpson, Angus 1970) und AIMS (abnormal involuntary movement scale).

Ergebnisse: 35% der nachuntersuchten Patienten mit einer funktionellen Psychose erhalten 15 Jahre nach dem ersten stationär psychiatrischen Aufenhalt keinerlei psychopharmakologische Medikation. NL werden von 44% der Patientem eingenommen. 31% der nachuntersuchten Fälle zeigen EPS, ein Drittel davon weisen EPS auf, obgleich sie keine NL einnehmen. 30% der Patienten weisen tardive Dyskinesien auf, 2/3 davon nehmen NL ein. Ausmaß von EPS und Spätdyskinesien bei den betroffenen Patienten werden angegeben.

Diskussion: Bei Betrachtung der Patientem mit EPS zeigt sich, daß die Patienten ohne NL-Einnahme aber mit einer sonstigen psychopharmakologischen Behandlung Lithium erhalten, von welchem bekannt ist, daß es eine neuroleptikainduzierte EPS verstärken une auch selbst EP-Symptome verursachen kann. Die Patienten mit EPS und ohne jegliche psycho-pharmakologische Medikation sind im Durchschnitt um ca. 10 Jahre älter, als die Gruppe mit EPS und NL-Einnahme.

Wed-P46

PHARMACOTHERAPY OF ANXIETY IN SCHIZOPHRENIA

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Nearly 75% of all persons are more of less anxious, which indicates that anxiety normally belongs to human being. At low grade it helps in quick reactions and in "planing" of adaptive activities. But, when anxiety last longer or appear more frequently with hard bearing intensity, we speak about pathological anxiety. In schizophrenia we are faced with syndromes of psychotic anxiety which is very often "intertwine" with other psychopathological features of schizophrenia.

In this research, 80 schizophrenics have been tested (57 male, 23 female) average age of 28–39 years (± 6.3) who were treated in Department for Psychosis of Day Hospital during 1996. The group was divided in two subgroups with 40 patients each who were treated with different pharmacotherapy. First, experimental