cognitive impairment. Characteristics of the frail person and the care situation were assessed and - if an informal caregiver was available - burden measures and the CES-Depression Scale were applied.

Results: The care of the frail old people (n = 306, attrition: 39%; mean age: 80.2 years; female: 68.6%) was provided mostly by family caregivers (n = 262; mean age: 61 years; female: 73%). Both the burden experience and the depressive symptoms were higher among the female than among the male caregivers. Multiple linear regression analyses confirmed that caregiver's gender was one of the strongest predictors of burden experience as well as of depression. Structural equation modeling suggested that burden mediates depression; it further proposed that there should be separate models for female and male caregivers.

Conclusion: The results provide a basis for the development of strategies to reduce or even prevent serious distress and psychiatric disorders among informal caregivers. Furthermore, they point to the need for gender-specific interventions in this field.

S02.05

Sex differences in the occurrence of late-life dementia

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Background and Aims: As a result of the higher life expectancy of women, age-related illnesses such as dementia occur with quite different frequencies in men and women. The present contribution provides a survey of sex-related differences in the prevalence, incidence, diagnostic distribution and duration of late-life dementia.

Methods: Review of epidemiological studies.

Results: In western industrialized countries, more than 70% of the dementia patients are women; less than 30% are men. Since women with dementia are on the average older and more frequently widowed than male dementia patients, the consequences are correspondingly different. Women are in greater need of care in an old-age home, whereas men have better chances of being cared for in a home environment. Epidemiological studies indicate a more frequent incidence of vascular dementia among men and of degenerative dementia among women. Furthermore, the results give rise to the suspicion that the incidence among women is higher in the most advanced age groups and that some risk factors are more closely associated with the occurrence of a dementia in women than in men.

Conclusions: There are considerable sex differences in the prevalence, incidence, duration, the lifetime risk and the consequences of late-life dementia. The risk of contracting the illness possibly increases with age more steeply for women than for men. This could be an indication that the illnesses are at least partly determined by different risk factors or that there are sex-risk-factor interactions.

S03. Symposium: ANTIPSYCHOTICS: MODE OF ACTION HIGHLIGHTS

S03.01

Antipsychotics: Mode of action highlights

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Dopamine D2 receptor blockade is the main mode of antipsychotic action. The optimal occupancy of D2 receptors seems to be crucial to balancing efficacy and adverse effects such as extrapyramidal symptoms or hyperprolactinaemia. Partial D2 receptor agonism, different pre- and postsynaptic D2 receptor antagonism, serotonergic antagonism and modulation, and neurotrophic effects contribute to differentiated antipsychotic efficacy, less side effects, favourable effects on the negative and cognitive symptoms of schizophrenia, etc. In addition, neurotrophic effects of the 2nd generation antipsychotics increase neuronal plasticity and synaptic remodelling in the striatum, in the prefrontal cortex and hippocampus, which may normalise glutamatergic dysfunction and structural abnormalities postulated by the neurodevelopmental disconnection hypothesis of schizophrenia. We demonstrate these mechanisms using various antipsychotics and serotonin manipulations in animal models of schizophrenia (MK-801).

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S03.02

The complexity of using D2-dopamine antagonists in the treatment of patients with schizophrenia

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Schizophrenia is a complex disorder and the view that schizophrenia is caused by hyperdopaminergic activity is an oversimplification. In fact, there are clinical evidence in accordance with a hypodopaminergic condition. Thus, untreated patients show motor disturbances in line with a decreased dopamine activity in the extrapyramidal system, likewise cognitive deficits and negative symptoms.

In our research we have explored the evidence of schizophrenia as a hyper- or hypodopaminergic condition. With Positron Emission Tomography (PET) we have not seen any evidence of increased D2-dopamine receptors in the brain of never medicated patients. The major dopamine metabolite homovanillic acid (HVA) was lowered in CSF in line with a decreased dopamine turnover in the brain. Tyrosine is precursor to the synthesis of dopamine and for that aim we have made transport studies in an in vitro model with fibroblasts to determine tyrosine kinetics. The results demonstrated that tyrosine transport is lower in patients with schizophrenia in comparison to healthy controls. Tyrosine kinetics measured with PET demonstrated dysregulation of tyrosine transport into the brain.

We have found evidence of schizophrenia as a hypodopaminergic condition. This fact is a problem realizing that our antipsychotics are D2-dopamine antagonists, thus decreasing dopamine activity even further. The concept of schizophrenia as both a hypo- and hyperdopaminergic condition may explain why clozapine, a week D2-antagonist, works more efficiently than other antipsychotic compounds. It should be recognized that positive symptoms are, at least partly,

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