Alzheimer pathology: decline of glucose utilization, particularly in the hippocampus and enthorinal cortex; increased oxidative stress associated with the synthesis of advanced glycation endproducts (AGE); increased tau protein phosphorylation and neurofibrillary tangle formation; increased aggregation of beta-amyloid protein secondary to the insulin-degrading enzyme (IDE) inhibition. Therapeutic strategies targeted at restoring the balance in insulin metabolism in AD – applying nasal insulin or using thiazolidinedions – are currently in the phase of clinical trials.

P0017

A-Beta Plasma levels and long-term response to rivastigmine in Alzheimer's disease

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Cholinesterase inhibitors (ChEI) are currently the mainstream symptomatic treatment of patients with Alzheimer's disease (AD). To this end, the response to the treatment with ChEI is clinically difficult to predict. Several demographic, clinical and biological variables have been proposed as pre-treatment predictors of long-term therapy efficacy. The aim of this study was to confirm our initial observations of a significance of change in plasma levels of b-amyloid (Aβ) peptides after initial treatment with rivastigmine for predicting clinical response to ChEI. Fifty four carefully selected subjects (37 females) satisfying criteria for mild (N=25) or moderate (N=29) AD were included in the study. Rivastigmine was prescribed at the initial dose of 3 mg/day b.i.d.; the dose was escalated to the maximum tolerated one in at least 4-week intervals. The response to treatment was assessed using ADAS-Cog scale. The whole blood samples were collected twice: before the first rivastigmine dose and at the 2nd week on active treatment. Levels of Ab1-40 and Ab1-42 were measured in plasma using a commercially available ELISA. We confirmed that higher initial disease severity (higher ADAS-Cog scores) and the increase in the concentration of plasma Aβ1-42 peptide following 2 weeks of treatment with an initial dose of rivastigmine increased the chance of a clinically meaningful response to ChEI therapy in AD patients after 2 years of follow-up. To conclude, a change in plasma Aβ1-42 level might constitute a novel biochemical predictor of long-term rivastigmine treatment efficacy in AD.

P0018

APOE, CYP46, PRNP and PRND: Genetic polymorphisms in Alzheimer's disease and mild cognitive impairment

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Background: The only widely confirmed sporadic AD genetic risk factor is carrying the apolipoprotein E ϵ4 allele. The results of numerous studies on various other genes are highly inconclusive. Genetic studies in mild cognitive impairment (MCI) are scarce.

Objective: To assess the influence of APOE, CYP46, PRNP, PRND genetic polymorphisms on the risk of AD and MCI.

Material & Methods: To date, over 100 subjects with AD, amnestic form of MCI and cognitively healthy age-matched controls have been recruited for the study (ongoing recruitment). To increase the homogeneity of the studied population subjects with prominent comorbid vascular risk factors, family history of dementia or satisfying criteria for non-AD neurodegenerative dementias have been excluded from the study. RFLP and sequencing techniques were employed to assess polymorphic sites in the CYP46, PRNP, PRND and APOE genes.

Results: As expected, the proportion of APOE ϵ4 carriers was significantly higher in the AD group compared to controls. No statistically significant influence of polymorphisms in the CYP46, PRNP and PRND genes on the risk of AD or MCI was observed. However, the odds ratio for PRNP codon 129 homozygosity was over fivefold higher in the AD group compared to other study groups.

Conclusions: The significance of APOE genotype as an AD risk factor seems to be beyond controversy. The role of other genes putatively involved in the pathobiology of neurodegenerative disorders seems vague at most. Studies on much larger populations are required to estimate true significance of those genetic variants in the etiology of AD.

P0019

Prevalence of Dementia with Lewy Bodies in a communal psychogeriatric inpatient population

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Objective: Data on the prevalence of Dementia with Lewy Bodies (DLB) derive mostly from neuropathological data or community studies. There exist only limited data about the prevalence in the communal geriatric psychiatry service with 3% in a Chinese and 28% in a British study.

Method: We applied the recently revised consensus criteria for DLB, One Day Fluctuation Assessment Scale (ODFAS) and Unified Parkinsons Disease Rating Scale (UPDRS) retrospectively (chart review) (n=58) and prospectively (n=54) on demented patients in a communal psychiatric service in Basel, Switzerland.

Results: Prevalence in the prospective group was 19% and 5% in the retrospective group. The odds ratio between both groups is 5.1. If gender is considered odds ratio for women is 2.4 and for men 6.8.

Conclusions: Our study shows that in communal geriatric psychiatry a high prevalence of DLB is encountered and that prospective use of DLB diagnosis criteria in combination with scales for fluctuation and parkinsonism enhances the detection rate of DLB.

P0020

Risk factors in Alzheimer's disease evolution for patients with MCI

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Background and Aims: The MCI syndrome is precociously present in over 50% of the patients that develop Alzheimer's Disease (AD) in the following three years. The evolution rhythm can be precipitated by the intervention of some risk factors.

Methods: Retrospective study with 30 patients with their case histories and current AD diagnosis confirmed by CT and DSM IV, evolution stage medium to serious. The aim was emphasize risk factors:

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- repeated social psychotraumatic factors;
- depressive disorder and prolonged treatment with anticholinergic antidepressants;
- cerebral hypoxia, metabolic disfunction;
- ischemic cerebral vasculary alterations.

A correlation was made between the observed risk factors with the rapidity in the evolution of the disease in identical treatment conditions (donepezil, rivastigmine).

Results: The evolution from MCI to AD of the patients in the lot showed three ways :

- rapid, under 1 year (6 patients, 20%);
- medium, over 2 years (15 patients, 50%);
- slow, over 3 years (9 patients, 30%);

For the entire lot the weight of risk factors was :

- psychotraumatic (50%);
- depression (67%);
- prolonged antidepressant treatment (57%);
- cerebral hipoxia and metabolic dysfunction (33%);
- vascular (63%).

Conclusions: The rhythm for settlement of cognitive deterioration is proportional with the number of risk factors.

The social impact at family level was significantly important in the forms with rapid evolution.

The rapid evolution automatically associates depression, prolonged antidepressant treatment, hipoxia and vascular component and requires profilactic strategies.

P0021

Effect of memantine treatment at patients with moderate - severe Alzheimer's disease treated with Donepezil

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Objective: To investigate the behavioral and cognitive effects of memantine in moderate to severe patients with Alzheimer disease receiving donepezil.

Method: Study was a 24 weeks prospective, randomized, parallel group. 43 patients were enrolled in the study, 21 continued treatment with donepezil and 22 were randomized to donepezil and memantine treatment. Patients were at least 50 years old, receiving ongoing therapy with donepezil for at least 6 months (10 mg / day). Average age for both groups was 72.5 years. There were no significant imbalances between the treatment groups in demographic and baseline clinical characteristics. Cognitive, ADL, and global measures were collected at baseline and at the end of weeks 4, 8, 12, 18 and 24. Behavioral measures were obtained at baseline, at the end of week 12 and at week 24. Mean baseline MMSE scores were 15.2 for donepezil group and 14.9 for donepezil − memantine group. Mean baseline NPI scores were of 15.8 for the donepezil group and 16.4 for the donepezil − memantine group.

Results: Patients treated with donepezil − memantine had significantly lower NPI total scores than patients treated only with donepezil. Analyses of the 12 NPI domains revealed significant effects in favor of memantine on agitation / aggression, eating / appetite, and irritability / lability. Memantine - treated patients showed significantly less deterioration in their functionality. The Severe Impairment Battery showed significant differences favoring memantine − donepezil group.

Conclusion: Treatment with memantine was well tolerated and reduced agitation / aggression, irritability, and appetite eating disturbances.

P0022

The role of proportion of cerebrospinal fluid total Tau-protein and phosphorylated Tau-protein levels in differential diagnosis of CJD

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Background and Aims: Diagnosis of Creutzfeld-Jacob disease (CJD) is based on typical clinical features and can be supported by detection of 14-3-3 protein in the cerebrospinal fluid (CSF).

Present study suggests the importance of investigating the ratio between CSF total tau-protein and CSF phosphorylated tau-protein in differentiating CJD from other dementias.

Methods: Thirty-one patients with Alzheimer disease (AD) of Frontotemporal dementia (FTD) and four patients with definitive diagnosis of Creutzfeldt-Jacob disease were included into the study. All study subjects underwent MRI scan of the brain and extended neuropsychiatric examination at baseline to classify the patients as having AD or FTD. Results were compared with an age-matched cognitively normal control group. Tau-protein was analyzed using a commercially available ELISA and 14-3-3 protein was assessed by Western blotting. Three markers were put into comparison: total tau-protein (cutoff value of 355 pg/ml), phosphorylated tau-protein (cutoff value of 55 pg/ml), and beta amyloid (cutoff value of 458 pg/ml). The receiver operating characteristic (ROC) curve has been designed to achieve the best possible sensitivity and specificity for each marker.

Results: High ratio between CSF total tau-protein and CSF phosphorylated tau-protein has been found in all patients diagnosed by CJD, even in those with negative 14-3-3 protein blots results. Contrary, marker s analysis in patients with AD revealed the highest ratio between CSF beta amyloid and CSF phosphorylated tau-protein levels.

Conclusions: CSF tau-protein and phosphorylated tau-protein are valuable diagnostic biomarkers for CJD, especially in patients with negative 14-3-3 protein findings.

P0023

The new standard computerized reading span test and the early detection of dementia

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Background and Aims: The new standard computerized reading span test (RST), which is a complex verbal working memory test, was tested.

Methods: Sixty native Dutch speakers, divided over four different groups (average age of 20, 26, 51, 75), entered the study.

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