

**Material and methods:** 40 patients (27 female) and 40 healthy, age, sex and IQ matched controls were included. The MS clinical manifestations were evaluated according to EDSS by a qualified neurologist. Beck depression inventory II was used for depression. We used Wisconsin Card Sorting Task (WCST) and Time Perception Task (TPT) for DLPFC and Iowa Gambling Task (IGT), Delayed Discounting Task (DDT) and Balloon Analogue Risk Task (BART) for assessment of VMPFC functions.

**Results:** MS patients had more perseveration errors (15.49 VS 8.77) ( $P=0.007$ ) in WCST. In TPT patients tend to over-estimate and over-reproduce time intervals. MS patients have more delay in selection of risky choices cards on IGT, (3.39 seconds vs 2.48 seconds). In DDT patients have lower discounting amounts over delays. In Bart patients have lower levels of risky behavior tendency.

**Conclusion:** Decision making is being processed logically in dorso-lateral and emotionally in ventromedial parts of prefrontal cortex. According to our study, MS patients follow a "conservative strategy" in their decision makings both logically and emotionally. This may be explained by "multiple disconnection syndrome" seen in MS particularly in frontal lobes or because of the specific effects of disease-stigma burden on patients' behavior. Slowing of information processing speed as a primary causative factor must be mentioned.

## P277

Evoked far-field potentials originating from the brainstem – new diagnostic possibilities for Alzheimer's disease?

A.J. Fallgatter, F. Metzger, A.C. Ehlis, M.J. Herrmann, J. Langer, T. Polak. *Department of Psychiatry and Psychotherapy, University of Wuerzburg, Wuerzburg, Germany*

**Background and aims:** Recently, the vagus nuclei in the brainstem have come into the focus of interest in psychiatric and neurological research mainly for two reasons: Firstly, their function is altered early in the course of Alzheimer's disease (AD; Parvizi et al., 2001). Secondly, in a small pilot study the electrical stimulation of the left vagus nerve in the neck by means of an implanted stimulator has shown to improve cognitive impairments in patients with AD (Sjogren et al., 2002).

**Methods:** Based on these findings a method for the non-invasive measurement of far-field potentials from the vagus nuclei evoked by means of an electrical stimulation via a peripheral branch of the nerve in the outer ear is a potentially interesting diagnostic procedure.

**Results:** Vagus Sensory Evoked Potentials (VSEP) can be elicited in a reliable manner in younger and elderly healthy subjects. VSEP-latencies have been found to increase with age in healthy subjects. In a first clinical application, VSEP-latencies in patients with mild to moderate AD were found to be prolonged as compared to age-matched healthy participants.

**Conclusions:** This new, none-invasive measure is very easy to apply and may be a disease marker for AD, possibly also in preclinical stages. Further studies are necessary which systematically investigate changes in VSEP measures in patients with neurodegenerative disorders in order to elucidate their diagnostic specificity and validity.

## P278

Cognitive effects of a prolonged-release formulation of galantamine (PRC) in patients with Alzheimer's disease (AD) - an open-label phase-IIIb-study

M. Gerwe<sup>1</sup>, B. Ibach<sup>1</sup>, J. Czekalla<sup>1</sup>, H.J. Moeller<sup>2</sup>. <sup>1</sup> *Medical & Scientific Affairs, Janssen-Cilag, Neuss, Germany* <sup>2</sup> *Department of Psychiatry, Ludwig-Maximilian-University, Munich, Germany*

**Background:** Randomized controlled clinical trials demonstrated efficacy of galantamine-PRC in the treatment of AD-patients. Objectives of this clinical trial were to further study the overall effect of galantamine-PRC on cognition and function in patients with AD.

**Methods:** Open-label, multi-center clinical trial (GAL-DEM-3002). Patients with mild to moderate AD (NINCDS-ADRDA criteria) received 16-24 mg/day galantamine-PRC for 6 months. Primary objectives were to examine the effects on cognitive function using ADAS-cog and DemTect. Response-rate at endpoint was defined as percentage of patients with change in ADAS-cog of 0 or less. Statistical analyses based on intent-to-treat population (LOCF, t-test, Wilcoxon-test for dependent samples).

**Results:** 133 patients (48% with mild, 52% with moderate AD; mean age±SD 75.4±7.8 years; 68% women) were enrolled, 71% of patients completed the study. 53% of the patients received 24mg/day galantamine-PRC. After 6 months mean total scores changed significantly, both in ADAS-cog, from 23.3±9.3 (baseline) to 20.4±9.7 ( $p<0.0001$ ) and DemTect from 7.3±2.9 to 9.2±4.3 ( $p<0.0001$ ). The response-rate was 64.2%. CGI demonstrated an improvement or stabilization for 83% of patients. 64% of the patients had at least one AE. Most frequent AEs (>5%) were nausea, vomiting and headache. 28 patients discontinued due to AEs. 15 patients experienced a serious AE with 3 SAEs thereof considered as possibly related to study medication (syncope, hypotension, agitation). 2 deaths (sudden death, renal failure) were rated as unrelated to galantamine-PRC.

**Conclusions:** This clinical trial supports the evidence from placebo-controlled trials that galantamine-PRC is tolerated and effective in the treatment of AD-patients in a clinical setting.

## P279

Cognitive function in patients with Alzheimer's dementia and concomitant cerebrovascular disease treated with galantamine - a one year open-label phase-IIIb-study

B. Ibach<sup>1</sup>, M. Gerwe<sup>1</sup>, S. Schwalen<sup>2</sup>, M. Riepe<sup>3</sup>. <sup>1</sup> *Medical and Scientific Affairs, Janssen-Cilag GmbH, Neuss, Germany* <sup>2</sup> *Medical and Scientific Affairs, Janssen-Cilag EMEA, Neuss, Germany* <sup>3</sup> *Department of Psychiatry, Campus Benjamin Franklin, University of Berlin, Berlin, Germany*

**Background:** Galantamine has been demonstrated to be effective and generally safe in patients with Alzheimer's disease and cerebrovascular pathology (AD+CVD) in placebo-controlled trials. The aim of this open-label clinical trial (GAL-GER-5) was to observe cognitive function during long-term treatment with galantamine in patients with AD+CVD.

**Methods:** Open-label, multi-center clinical trial (phase IIIb). Patients with mild to moderate AD+CVD (meeting NINDS-AIREN criteria) received galantamine (4-12 mg bid) for 12 months. Cognitive function was examined using the AKT ("Alters-Konzentrations-Test") and DemTect. Statistics were based on intent-to-treat population (LOCF, t-test and Wilcoxon-test for dependent samples).

**Results:** 84 patients (43% with mild, 56% with moderate AD+CVD; mean age±SD 75.5±6.8 years; 58% women) were enrolled. 80% of the patients completed the study. Modal daily galantamine dose was 16mg for 44%, and 24mg for 51% of the patients. After 12 months mean total score in AKT showed a stabilization from 49.0±6.7 (baseline) to 49.2±6.9 ( $p=0.7807$ ) and DemTect increased significantly from 7.8±2.0 to 9.4±3.9 ( $p<0.0001$ ). CGI demonstrated an improvement or stabilization for 71% of patients. 56% of the patients had at least one adverse event (AE). Most frequent AEs

with an incidence >5% were nausea and vomiting. 8 patients discontinued due to AEs. 21 patients experienced a SAE with 4 SAEs considered as possibly related to study medication (heart failure, syncope, aggravated dementia, urinary retention).

**Conclusions:** This open-label study supports evidence from placebo-controlled trials of the efficacy and safety of galantamine in patients with AD+CVD and suggests similar cognitive effects and safety through 12 months.

## P280

Safety and efficacy of inhibitors of cholinesterase during the treatment of DAT-long-term follow

D. Ignjatovic<sup>1</sup>, M. Ignjatovic<sup>1</sup>, M. Kniskova<sup>1</sup>, R. Hruby<sup>2</sup>, T. Baska<sup>3</sup>. <sup>1</sup>Non-State Department of Psychiatry, Psychomed Svatosavsky, Spol.S R.O., Banska Bystrica, Slovakia <sup>2</sup>Department of Psychiatry, Central Military Hospital, Ruzomberok, Slovakia <sup>3</sup>Institute of Epidemiology, Jessenius Medical Faculty, Martin, Slovakia

**Background and aims:** DAT is chronic, degenerative disease, which decrease quality of patients' life. DAT is one of the most frequent type of dementia (Pidman, Kolibáš).

The most important signs of DAT are: cognitive deficit, behavioral and psychological symptoms of dementia (depression, apatia, incontinencia...) (Spar, Rue, 2003).

We have 34 patients with DAT in our retrospective study, the age: 76,6 years (65-92y).

The goal of our study was follow the efficacy and safety of donepezil, rivastigmine and galantamine during titration phase and continuing phase.

**Methods:** The efficacy of the treatment with inhibitors of cholinesterase we assessed with MMSE and Clock test on first day, 3rd, 6th and 12th months and NPI (Neuropsychiatric Inventory test) during titration and continuing phases.

The safety of the treatment we assessed with the test of side effects, the most frequent were agitation, depression, aggression and incontinencia.

Statistically we used CHÍ test ( $p=0,05$ ) and ANOVA test.

**Results:** The efficacy and safety of all inhibitors of cholinesterase were comparable, there were no significant differences and they have very good efficacy during one year treatment.

There were no frequent gastrointestinal side effects during the treatment with rivastigmine during titration and continuing phase and the result were comparable with donepezil and galantamine without significant differences. There were no important cardiovascular side effects during the long-term treatment with inhibitors of cholinesterase.

**Conclusion:** The efficacy and safety of all inhibitors of cholinesterase were comparable during titration and long-term treatment and without significant differences.

## P281

Clinical and expert assessment of emotional state and cognitive functions of patients with cerebrovascular diseases

S.A. Igumnov. *Research Institute for Medical and Social Evaluation and Rehabilitation, Minsk, Belarus*

**Backgrounds and aims:** We conducted a complex clinical and psychological examination of 50 patients with cerebrovascular pathology.

**Methods:** All the patients were divided into four expert-rehabilitation groups (ERG) in accordance with the main indices which characterize psychological state (the state of cognitive functions, visual and motor coordination) and the degree of the expression of neurological deficiency. The aims and tasks were worked out for each ERG, as well as an individual plan of rehabilitation.

**Results:** The patients of the first ERG (15 persons) differed from the major group in general in the level of asthenia, persons of second ERG (10 persons) – in the level of anxiety ( $P \leq 0,05$ ), people of the third ERG (15 persons) – in the level of anxiety and depression (reliably higher). The most significant differences with the major group were characteristic of the patients of the fourth ERG (10 persons). They showed a reliably lower level of the state of cognitive functions, visual and motor coordination, locus of control. Lower indices of cognitive functioning were kept in the fourth ERG in the dynamics during the whole course of earlier stationary rehabilitation, which points to the urgent necessity of the continuation of the whole course of correction and rehabilitation work, including psychosocial rehabilitation, on the following outpatient stage.

**Conclusions:** The division into the ERG allowed us to join the cases of diseases with similar symptoms and approximately identical technology of psychosocial and rehabilitation measures, their cost and supposed efficiency.

## P282

Cognitive dysfunctions and depressive symptoms in graves-basedow disease

K. Jablkowska<sup>1</sup>, K. Nowakowska<sup>1</sup>, A. Borkowska<sup>1,2</sup>. <sup>1</sup>Medical Psychology Unit, Medical University in Lodz, Lodz, Poland <sup>2</sup>Clinical Neuropsychology Unit, Nicolaus Copernicus University Torun, Collegium Medicum Bydgoszcz, Poland

Cognitive dysfunction and depressive symptoms seem to play significant role in clinical picture of hyperthyroidism.

The aim of this study was to assess cognitive functions connected with prefrontal cortex in relation to intensity of depressive symptoms in patients with Graves-Basedow disease.

The studied group consisted of 45 patients (37 female, 8 male) aged 18-55 (mean 42,2) with Graves-Basedow disease. The control group consisted of 30 healthy persons matched with age, gender and education for experimental group. The Neuropsychological assessment included the Wisconsin Card Sorting Test (WCST) and N-back test (1-back) for different aspects of working memory and executive functions estimation. The intensity of depressive symptoms were assessed by Beck Depression Inventory.

Investigated patients show significant impairments on performance on all parameters of WCST compared to healthy persons. Also the results of N-back test show severe disturbances on visuospatial working memory on 1-back task.

The results show significant disturbances on frontal function (particularly working memory and executive functions) in patients with Graves-Basedow disease in relation to healthy subjects. In 1/3 patients with Graves-Basedow disease the intensity of depressive symptoms was observed. The higher intensity of depressive symptoms were correlated with greater cognitive deficits in the neuropsychological tests. These results suggest that depressive symptoms may increase cognitive deficits, especially connected with prefrontal cortex in the group of Graves-Basedow disease patients.